THE MANAGEMENT OF DYSLIPIDEMIA IN A PRIVATE HEALTH CARE SETTING: A MANAGED PHARMACEUTICAL CARE APPROACH

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"Happiness lies for those who cry, those who hurt, those who have searched, and those who tried, for only they can appreciate the importance of people who have touched their lives."

This dissertation is dedicated to my family especially my mother and grandmother whose love and support are unutterable and whose faith in me is everlasting

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[1] The heavens declare the glory of God; the skies proclaim the work of his hands. [2] Day after day they pour forth speech; night after night they display knowledge. [3] There is no speech or language where their voice is not heard. [4] Their voice goes out into all the earth, their words to the ends of the world.

In the heavens he has pitched a tent for the sun, [5] which is like a bridegroom coming forth from his pavilion, like a champion rejoicing to run his course. [6] It rises at one end of the heavens and makes its circuit to the other; nothing is hidden from its heat.

[7] The law of the LORD is perfect, reviving the soul. The statutes of the LORD are trustworthy, making wise the simple. [8] The precepts of the LORD are right, giving joy to the heart. The commands of the LORD are radiant, giving light to the eyes. [9] The fear of the LORD is pure, enduring forever. The ordinances of the LORD are sure and altogether righteous.[10]They are more precious than gold, than much pure gold; they are sweeter than honey, than honey from the comb. [11] By them is your servant warned; in keeping them there is great reward.

[12] Who can discern his errors? Forgive my hidden faults. [13] Keep your servant also from willful sins; may they not rule over me. Then will I be blameless, innocent of great transgression. [14] May the words of my mouth and the meditation of my heart be pleasing in your sight, O Lord, my Rock and my Redeemer.

ABSTRACT

Title: The management of dyslipidemia in a private health care setting: a managed pharmaceutical care approach.

Keywords: Dyslipidemia, managed pharmaceutical care, drug utilization review, pharmaco-economics, prevalence and medicine treatment cost, medicine reference price system, prescribed daily dose and defined daily dose.

The global anti-dyslipidemic market grew by 19% from 2000 to 2001, achieving sales of over $21 billion (Smith, 2004: 2). This market is currently well served by a number of effective and well-tolerated treatments. Lipid-lowering drugs are considered as the first choice drugs in control of dyslipidemias and they are well tolerated by most patients. As with many drug therapies, there should be a balance between the benefits of cholesterol lowering agents, increased medication cost and the overall risk of adverse drug reactions. According to Ballesteros (2001: 514), hypolipidemic drugs are consumed on a large scale and most consumers are elderly. This warrants a study of expenditure incurred because of inadequate prescribing of these agents.

The general objective of this study was to determine the utilisation and cost of hypolipidemic drugs in the private health care environment in South Africa. A quantitative retrospective drug utilisation review was performed using a medicine claims database. Data for twenty-four consecutive months (May 1, 2001 to April 30, 2003) were used to determine and compare the utilisation patterns and cost of drugs associated with the management of dyslipidemia a year before (1st May 2001 to 30 April 2002) and a year after (1st May 2002 to 30 April 2003) the implementation of a medicine reference price system (MPL). Data analysis was done by calculating the average value, the standard deviation, effect size, and cost-prevalence indices.

The results of this study revealed that hypolipidemic drugs constituted 2.70% (n = 21820911) and 2.78% (n =27277825) of the total number of all medicine items for the first and the second study years respectively. On the other hand, the total cost of all hypolipidemic drugs accounted for 6.33% (n= R3 097 604 602) and 6.23 % (n= R 4 053 280 295) of the total cost of all medicine items claimed during the first and the second study years respectively. The prevalence of generic hypolipidemic drugs accounted for 0.89% (n=589036) and 4.88% (n=759675) of the total number of hypolipidemic drugs claimed during the first and second study year respectively. Innovator drugs, on the other hand, constituted 99.11% (n=589036) and 95.11% (n=759675) of

the total number of hypolipidemic drugs claimed during the first and second study years respectively. It was found that R23 694.5 and R603 277.36 could have been saved for generic bezafibrate and generic simvastatin respectively if they had been sold at MPL prices. The total cost of generic hypolipidemic drugs accounted for 0.60% and 2.94%. The total cost of innovator hypolipidemic drugs accounted for 99.40% and 97.06% of the total cost of hypolipidemic drugs claimed during the first (n=R 196 076 050) and second (n=R 252 919 285) study year respectively. With respect to the prescribed daily dose, it was found that most prescriptions for individual hypolipidemic drugs did not conform to the defined daily dose. It was, however, found that most prescriptions whose prescribed daily dose was for one tablet once daily and whose strength was similar to the defined daily dose conformed to the defined daily dose.

The conclusion is that there was an insignificant difference in both the prevalence and cost of hypolipidemic drugs a year before and after the implementation of MPL. It was further concluded that increased utilisation of generic hypolipidemic medicine items a year after the implementation of the MPL, could have been brought about by the introduction of generic simvastatin into the market as opposed to the implementation of the MPL. Recommendations for further studies will be formulated.

OPSOMMING

Titel: Die bestuur van dislipidemie in 'n private gesondheidssorg opset: 'n bestuurde farmaseutiese benadering.

Sleutelwoorde: Dislipidemie, bestuurde farmaseutiese sorg, medisinale gebruiksoorsig, farmako-ekonomie, voorkomssyfer en medisinale behandelingskoste, medisinale verwysingsprysstelsel, voorgeskrewe daaglikse dosis en gedefinieerde daaglikse dosis.

Die globale anti-dislipidemie mark het tussen 2000 en 2001 met 19% gegroei om verkope van meer as $21 biljoen te bereik. Hierdie mark word tans goed bedien deur 'n aantal effektiewe en goed-verdraagsame behandelings. Lipied-verlagende medisyne word geag as die eerste keuse vir die beheer van dislipidemies en hierdie behandelings is in die meeste gevalle goed verdraagsaam. Soos met baie medisinale behandelings, moet daar 'n balans wees tussen die voordele van cholesterol-verlagende agente, stygende medikasiekoste en die oorkoepelende risiko van nadelige medisinale reaksies. Volgens Ballesteros (2001: 514), word hipolipidemie medikasie op groot skaal gebruik en meeste van die gebruikers is bejaardes. Dit oorloof 'n studie van die uitgawes wat aangegaan word as 'n gevolg van die ontoereikende voorskryf van hierdie medikasie.

Die algemene doel van hierdie studie was om die gebruik en koste van hipolipidemie medikasie in die private gesondheidssorg-sektor in die Republiek van Suid-Afrika te bepaal. 'n Kwantitatiewe, terugskouende medisyne gebruikoorsig is uitgevoer deur 'n ondersoek op die medikasie-eise databasis. Bykans vier-en-twintig agtereenvolgende maande (1 Mei, 2001 tot 30 April, 2003) se data is benut om die gebruikspatrone en koste van medikasie wat gebruik word in die beheer van Dislipidemie te bepaal vir een jaar voor (1ste Mei 2001 tot 30 April 2002) en een jaar na (1ste Mei 2002 tot 30 April 2003) die implementering van 'n medisinale verwysingsprysstelsel (MPL). Die statistiese analise stelsel is gebruik om die data te analiseer. Data analise is gedoen deur die gemiddelde waarde, die standaard afwyking, effekgrootte en kostevoorkeur-indekste te bereken.

Die resultate van hierdie studie het te voorskyn gebring dat hipolipidemie medikasie 2.70% (n = 21820911) en 2.78% (n =27277825) uitmaak van die totale hoeveelheid van alle medikasie items vir die eerste en die tweede studiejare onderskeidelik. Aan die ander kant, die totale koste van alle hipolipidemie medikasie maak 6.33% (n= R3 097 604 602) en 6.23 % (n= R 4 053 280 295)

uit van die totale koste van alle medikasie items ge-eis gedurende die eerste en die tweede studiejare onderskeidelik. Die voorkoms van generiese hipolipidemie medikasie maak 0.89% (n=589036) en 4.88% (n=759675) uit van die totale hoeveelheid hipolipidemie medikasies wat ge-eis is gedurende die eerste en tweede studiejare onderskeidelik. Ontwerpersmedikasie maak ongeveer 99.11% (n=589036) en 95.11% (n=759675) uit van die totale hoeveelheid hipolipidemie medikasie wat ge-eis is gedurende die eerste en tweede studiejare onderskeidelik. Die bevinding is dat R23 694.5 en R603 277.36 gespaar kon word vir generiese bezafibraat en generiese simvastatin onderskeidelik indien hulle verkoop is teen MPL pryse. Die totale koste van generiese hipolipidemie medikasie beslaan 0.60% en 2.94%, die totale koste van ontwerpers-hipolipidemie medikasie maak 99.40% en 97.06% uit van die totale koste van hipolipidemiese medikasie wat ge-eis is gedurende die eerste (n=R 196 076 050) en tweede (n=R 252 919 285) studiejare onderskeidelik. Met betrekking tot die voorgeskrewe daaglikse dosis is bevind dat meeste voorskrifte vir individuele hipolipidemiese medikasie nie voldoen aan die gedefinieerde daaglikse dosis nie. Dit is egter bevind dat meeste voorskrifte wat 'n dosis van een tablet daagliks voorskryf, waar die sterkte voldoen aan die gedefinieerde daaglikse dosis, wel daaraan gekonformeer het.

Die gevolgtrekking is dat daar 'n onbeduidende verskil in beide die voorkoms en koste van hipolipidemiese medikasie is in die jare voor en na die implementasie van die MPL. Verder is bevind dat toenemende gebruik van generiese hipolipidemiese medisyne die jaar na die implementasie van die MPL, toegeskryf kan word aan die bekendstelling van generiese simvastatin aan die mark teenoor die implementasie van die MPL. Voorstelle vir verdere studie is geformuleer.

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CHAPTER 1: INTRODUCTION

This dissertation focuses on the management of dyslipidemia in the private health care sector in South Africa. In this chapter the problem statement, research objectives and research methodology will be discussed. The discussion on the division of chapters will mark the end of the chapter.

1.1 PROBLEM STATEMENT

The past decade has seen an increase in media coverage and public awareness of medical issues and as a result, dyslipidemia and its treatment have received generous publicity (Thornton & Holt, 2000: 407). The increase in the usage of lipid lowering drugs creates more questions than answers. Bhatnagar (1998:206) believed that if any strategy for the management of dyslipidemia that includes the criteria for the selection of drugs were to succeed, then there would be a comprehensive understanding of the spectrum of disorders of lipid metabolism and the underlying principle and goals of lipid lowering.

Cardiovascular diseases are a leading cause of death and are responsible for one third of all global fatality (World Health Organization, 2002: 1). According to Jafari *et al.* (2001: 1403) coronary artery disease is the leading cause of disability and death in the United States. On an annual basis in the United States, atherosclerosis causes an overwhelming 700,000 deaths. This disease leaves families disrupted, corporations crippled and millions disabled. The majority of the estimated 32 million heart attacks and strokes that occur annually are caused by one or more cardiovascular risk factors such as hypertension, diabetes, smoking, increased concentration of the lipids in blood and physical inactivity (World Health Organization, 2002: 1). Taking proper action against these risk factors can prevent the majority of these cardiovascular disease events (Baron, 2002: 1252).

Dyslipidemia is common in westernised and industrialised communities (Steyn *et al.*, 2000: 720). Data for the burden of diseases that have been collected by medical schemes, show that dyslipidemia is the third most prevalent of all the chronic conditions in South Africa (Council for medical schemes, 2002/3: 48). It affects eight out of ten westernised South Africans (Anon, 2002: 1). Though background setting is often a substitute for socio-economic differences between groups of people in South Africa, it is imperative to identify groups that have different

biological as well as environmentally determined risk profiles in order to ensure that groups with high risk factors for chronic diseases due to lifestyles are identified and therefore specifically targeted for appropriate interventions (Steyn *et al.*, 2000: 720).

Coronary heart disease is most prevalent in the Indians and White South Africans, whilst in coloured groups there is a lower incidence. In blacks it is still relatively uncommon but risk factors for possible emergence of cardiovascular diseases are already apparent. These include obesity, tobacco, smoking, hypertension, diabetes mellitus and hyperlipidemia (Berger & Marais, 2002: 166).

For health care, the classical expression *"it was the best of times, it was the worst of times"* has never appeared more suitable. The health care system has never been blessed with such a wide collection of pharmaceuticals, treatment strategies and resources that improve the health care of our patients. Simultaneously, providers are faced with an increasing loss of independence and ever increasing financial pressures. The health care of all patients can be optimised if there is a balance between the growing opportunities with current and future restrictions (Bennett *et al.*, 2002: 1).

There is a growing fear about the expenditure for pharmaceutical products in the United States. In 2001, national health care expenditures exceeded $1.4 trillion, accounting for 14% of the country's gross domestic products. In that same year, retail prescription drugs accounted for 10% of the total national health care spending. This figure is expected to reach 2.8 trillion by 2011 and that will contribute exactly 17% of the gross domestic products, up from its year 2000 level of 13.2 per cent (Heffler *et al.*, 2002: 207).

Cost continued growing into the first term of office of the democratic government of South Africa (Doherty & McLeod, 2002: 42). In 1998/1999 R70.2 billion was dedicated to health care in South Africa. This represented 8.8% of Gross Domestic Product (GDP)*. This proportion is unusually higher compared to international standards. Venezuela, the country that is closest to South Africa in terms of development got the GDP of 7.5 %. The value of health care resources grew on average at 7 % per annum. This shows that South Africa is devoting increasing amounts to health care (Doherty *et al.*, 2002: 14).

* Refer to glossary

As with many drug therapies, there should be a balance between the benefits of cholesterol lowering agents, increased medication cost and the overall risk of adverse drug reactions (Irons *et al.*, 2002: 1618). According to a study that was performed by Johannesson *et al.* (1997: 332), the analysis of the cost effectiveness of simvastatin treatment to lower cholesterol level was assessed in relation to age, sex and level of cholesterol before treatment of patients with coronary heart disease. It was found in that study that the cost of each year of life gained ranged from 3,800 dollars for 70-year-old men with 309mg of cholesterol per decilitre to 27,400 dollars for 35-year-old women with 213mg of cholesterol per decilitre. The analysis was limited to direct cost.

Drug treatment agents that are available for dyslipidemia in South African MIMS™ are fibrates, e.g. bezafibrates, fenofibrate, gemfibrozil; HMG-CoA reductase inhibitors, e.g. fluvastatin, atorvastatin, pravastatin and simvastatin; acipimox; probucol®; cholestyramine; Lipostabil® (Snyman, 2002: 151-160).

According to Lopez (2002: 1178) statins are highly effective for improving cardiovascular positive outcomes in high-risk patients, but they are frequently under prescribed. Statins (inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A reductase) are highly effective LDL-cholesterol–lowering agents that reduce the incidence of initial and recurrent cardiovascular events (Resenson, 2002: 2). Lopez (2002:1174) emphasised this by stating: *"Despite the proven benefit of statin therapy, most of the eligible patients are either untreated or inadequately treated with these agents"*.

According to Ballesteros *et al.* (2001: 514) hypolipidemic drugs are consumed on a large scale. This warrants a study of expenditure incurred because of inadequate prescription of these agents. In addition to that there is an increase in the number of elderly consumers of these drugs. Ballesteros *et al.* (2001: 516) investigated the economic cost generated in one year in primary care because of inadequate (unnecessary) prescriptions of hypolipidemic agents.

It was found that the cost of inadequate prescription for hypolipidemic drugs reached 1166480.60 US dollars (1997 values) for quality level one (patients whose age, risk factors, total cholesterol level and low-density lipoprotein cholesterol level were known before pharmacological intervention) and 37893.37 US dollars for level two (patients whose low-density lipoprotein levels and diet were unknown before pharmacological intervention). It was also found that 12.3% of the health professionals ordered all their prescriptions inadequately. Of

the total inadequate prescriptions expenditure, 20.4% represented treatment initiated by family physicians and 35.3% by specialists. Statins made up 78.2% of the total cost; the inadequate expenditure for this therapeutic group reached 88797 US dollars. Of the prescriptions for fibrates, 88% were inadequate (Ballesteros *et al.*, 2001:513).

Truter and Kotze (1996: 1397-1404) conducted a study whose objective was to estimate average prescribed daily doses for selected hypolipidemic agents available in South Africa, comparing estimated prescribed daily doses with defined daily doses. It was found in that study that the average prescribed daily doses for three most prescribed lipid lowering drugs were 414.4 mg for bezafibrate, 12.5 mg for pravastatin, and 12.6 mg for simvastatin. The prescribed daily doses were on average lower than the established daily doses.

The above-mentioned discussion indicates that there might be hidden problems associated with the diagnosis, drug treatment, management and the medicine treatment cost of dyslipidemia. Therefore it has become imperative that research should be conducted on the management of dyslipidemia in the private health care sector in South Africa with specific reference to drug treatment.

The following research questions can be formulated on the basis of the preceding discussion:

- What does dyslipidemia and the management thereof entail?
- What do managed care; drug utilisation review, pharmaco-epidemiology, pharmaco-economics and pharmaceutical care entail?
- What are the prevalence and the medicine treatment cost of dyslipidemia in the private health care sector in South Africa?
- What could the application of managed pharmaceutical care principles in the management of dyslipidemia be?
- Which recommendations may be formulated regarding the management of dyslipidemia in the private health care sector in South Africa?

1.2 RESEARCH OBJECTIVES

This research includes general and specific objectives:

1.2.1 General research objective

The general research objective of the study was to analyse and review the medicine management of dyslipidemia in the private health care sector in South Africa by determining the prevalence and medicine treatment cost of dyslipidemia

1.2.2 Specific research objectives

1.2.2.1 Phase 1: Literature review

The specific research objectives of the literature study were:

- to describe the epidemiology of dyslipidemia;
- to differentiate between the different lipoproteins and types of dyslipidemia;
- to determine the pathophysiology of dyslipidemia;
- to define and differentiate between the different types of dyslipidemia;
- to identify possible risk factors for dyslipidemia;
- to describe the diagnosis and test procedures for diagnosis of dyslipidemia;
- to describe the signs and symptoms, candidates for screening as well as the complications of dyslipidemia;
- to describe the treatment protocols and the drugs that are used in the management of dyslipidemia;
- to determine the relationship between dyslipidemia and other diseases such as hypertension, cardiovascular heart disease and diabetes;
- to describe and define the concept of managed pharmaceutical care;
- to investigate the application of managed pharmaceutical care principles in the management of dyslipidemia;
- to investigate the application of pharmaco-economic principles in the management of dyslipidemia;
- to investigate the application of pharmaco-epidemiological principles in the management of dyslipidemia; and
- to investigate the application of drug utilisation principles in the management of dyslipidemia.

1.2.2.2 Phase 2: Empirical investigation

The specific research objectives of the empirical investigation were

- to investigate the differences in the utilisation patterns of drugs in general before and after implementation of the Medscheme® price list;
- to investigate the differences in the utilisation patterns of hypolipidemic drugs before and after implementation of the Medscheme® price list;
- to determine the effect of the Medscheme® price list on the cost of hypolipidemic drugs;
- to determine and compare the difference in prevalence of innovator medicine items vs. generic medicine items that has been claimed before and after implementation of the Medscheme® price list for drugs in general and and hypolipidemic drugs specifically;
- to determine the difference in cost between the innovator and the generic drugs for both the general data and hypolipidemic drugs;
- to determine the cost savings that could have been incurred if hypolipidemic drugs were sold at MPL prices;
- to determine the cost savings that could have been incurred if generic products were prescribed on behalf of innovator products (provided that the patent time on the original drug is over);
- to compare the prescribed daily dose with the defined daily dose of individual hypolipidemic drugs; and
- to formulate recommendations with regard to the medicine management of dyslipidemia.

1.3 RESEARCH METHODOLOGY

The research project consisted of the following phases.

1.3.1 Phase one: Literature review

The literature review was divided into two chapters. The first literature chapter deals with the management of dyslipidemia including drug and non-drug therapy as well as the effect of other contributing factors on the disease. The second chapter describes the application of managed pharmaceutical care, pharmaco-economics, and pharmaco-epidemiological principles in the management of dyslipidemia.

1.3.2 Phase two: Empirical investigation

The empirical study consisted of the following steps:

- Research design
- Composition of the study population
- Selection of research instrument
- Analysis of data
- Reliability and validity
- Discussions based on the findings of the empirical investigation
- Conclusion and recommendations based on the results of the empirical investigation

Data for this study were extracted from Medscheme™ database from May 2001 to May 2003. The steps of the empirical investigation will be fully outlined in chapter 4.

1.4 DIVISION OF CHAPTERS

The chapters will be presented as follows:

Chapter 1: Introduction

Chapter 2: Dyslipidemia

Chapter 3: Managed pharmaceutical care

Chapter 4: Research methodology

Chapter 5: Results and discussion

Chapter 6: Conclusion and recommendations

1.5 CHAPTER SUMMARY

In this chapter the problem statement, research questions and objectives, research methodology, research design and division of chapters were discussed.

The management of dyslipidemia will be discussed in chapter 2.

CHAPTER 2: DYSLIPIDEMIA

This chapter provides the further elucidation of the concept of dyslipidemia. The definition, risk factors, pathophysiology, epidemiology, diagnosis and management of dyslipidemia will be outlined.

2.1 INTRODUCTION

For patients with known coronary artery disease, cholesterol lowering leads to reduction in morbidity and total mortality in men, women, middle-aged patients and in older patients (Stein, 2002: 50c). However, if we wait for susceptible individuals to develop symptoms before deciding to treat, the earliest symptom is often sudden death. The degree of risk above which benefit is seen, includes only a smaller minority of the population (Bhatnagar, 1998: 206).

2.2 EPIDEMIOLOGY OF DYSLIPIDEMIA

Total cholesterol and low-density lipoprotein cholesterol increase throughout life in both men and women. Based on the National Health and Nutrition Examination Survey (NHAES) in America, 40% of all adults aged 20 to 74 years require fasting lipoprotein analysis and 29% (52 million Americans) are candidates for diet therapy. If the assumption is made that dietary intervention would reduce low-density lipoproteins by 10%, then about 7% (approximately 12.7 millions) Americans might be candidates for lipid lowering drugs (Talbert, 1999: 350).

In South Africa, despite the severe consequences of a raised blood cholesterol

- over 4.8 million South African adults suffer from raised cholesterol levels,
- only 58% of urban South Africans have ever heard of cholesterol,
- only 14% of urban South Africans have had their cholesterol tested, and
- less than 4 % know what their cholesterol level is (Anon., 2002: 1).

2.3 MAIN LIPOPROTEINS

There are two main types of lipids in blood namely cholesterol and triglycerides (Baron, 2002: 1251). Triglycerides can also be attached to cholesterol molecules forming phospholipids (Siguel, 2000: 2). Both cholesterol and triglycerides join with different types of proteins in the

blood to form lipoproteins (AAFP, 1998: 1). The lipoproteins contain proteins known as apolipoprotein (Baron, 2002: 1251).

Lipoproteins are classifies as very low-density lipoproteins "VLDL", low-density lipoproteins "LDL", high-density lipoproteins "HDL" and intermediate density lipoproteins "IDL", depending on the density of the proteins (Siguel, 2000: 2). The density is determined by the amount of triglycerides (making them less dense) and apoproteins (making them more dense). The less dense particles are called chylomicrons (Baron, 2002: 1251). Table 2.1 gives a summarised description of main lipids. A short discussion of these lipids will follow.

Table 2.1 Main lipids (Anaizi, 1997: 3)

Cholesterol ▪ A steroid alcohol synthesized in the liver with variable amount of cholesterol obtained from diet ▪ Average total cholesterol in the body = 150g of which 90% is part of the cell membrane structure. ▪ Necessary for synthesis of steroid hormones.
Triglycerides ▪ Exist as saturated, unsaturated and monounsaturated fat.
Very low-density lipoprotein cholesterol (VLDL) (density <1) ▪ Produced in the liver, rich in triglycerides (>65%) and cholesterol (20%) ▪ Serves to transport endogenous lipids (particularly triglycerides) to extrahepatic sites ▪ Hydrolysed to intermediate density lipoprotein or low-density lipoprotein cholesterol
Low-density lipoprotein cholesterol (LDL) (density ~ 1) ▪ Product of very low-density lipoprotein cholesterol catabolism ▪ Contains > 60% cholesterol and accounts for > 60% of total plasma cholesterol ▪ Taken up by hepatic and extra hepatic tissues ▪ Has a high atherogenic potential.
Intermediate density lipoprotein cholesterol (IDL) (density~1.05) ▪ Derived from both VLDL and HDL ▪ IDL particles are either taken up by the liver or they may be reduced to more triglycerides
High-density lipoproteins (density~ 1.15) ▪ Produced by extrahepatic tissues and serve as a vehicle for the transfer of cholesterol from the tissues to the liver ▪ Take up the cholesterol liberated in the course of normal cell membrane turnover

2.3.1 Chylomicrons

Chylomicrons, the largest of the lipoproteins (Malloy & Kane, 1998: 564), are formed in the small intestinal mucosa principally from dietary triglycerides, cholesterol, and fat-soluble vitamins (Scheig, 1995: 304). They rise as a creamy layer when non-fasting serum is allowed to stand (Baron, 2002: 1251). Chylomicrons have a high triglycerides and low cholesterol content (Anaizi, 1997: 4). An enzyme, lipoprotein lipase found in capillaries of muscles and adipose tissues, hydrolyses triglycerides in the chylomicrons (Scheig, 1995: 304), through a pathway shared with very low-density lipoprotein cholesterol (Malloy & Kane, 1998: 564).

2.3.2 Very low-density lipoproteins (VLDL)

Very low-density lipoproteins manufactured in the liver (Scheig, 1995: 305) from its own stores of fat and carbohydrate (Baron, 2002: 1251), provide a means for exports of triglycerides to peripheral tissues (Malloy & Kane, 1998: 564). VLDLs are hydrolysed by lipoprotein lipase mainly in the muscle capillaries releasing free fatty acid, which is later taken up by the muscle cells (Anaizi, 1997: 4). The resulting depletion of triglycerides produces remnants known as intermediate density lipoprotein (Malloy & Kane, 1998: 564). They then become low-density lipoprotein particles (Baron, 2002: 1251). Thus the two main functions of very low-density lipoproteins are to deliver energy and to serve as precursors of low-density lipoproteins (Scheig, 1995: 305).

2.3.3 Low-density lipoproteins (LDL)

Low-density lipoproteins are transporters of cholesterol (Scheig, 1995: 305), which is needed by all animals for membrane synthesis (Malloy & Kane, 1998: 564). They are sometimes referred to as "bad" cholesterol because they can cause plaque build-up and blockage of the arteries (Schneider, 2002: 1). When the low-density lipoprotein cholesterol (LDL-C) level is elevated, it builds up in the walls of the arteries and forms atherosclerosis (Anaizi, 1997: 4). The plaque will with time cause the arteries to harden and narrow thereby impeding blood flow to the tissues and the heart muscle (Schneider, 2002: 1). (LDL-C) is used as a guide in the management of dyslipidemia because it is the most atherogenic. Its value can be calculated using the following equation (Friedwald *et al.*, 1972: 499).

LDL = TC – HDL – 0.2 TGs

LDL ~ Low-density lipoprotein cholesterol
HDL ~ High-density lipoprotein cholesterol
TC ~ Total cholesterol
TG's ~ Triglycerides
0.2 ~ Constant

2.3.4 High-density lipoproteins

High-density lipoprotein particles are synthesised in the liver and intestine and facilitate the transport of apoproteins (Baron, 2002: 1251). They appear to be responsible for reverse cholesterol transport (Scheig, 1995: 305), either by transferring cholesterol into other lipoprotein or directly into the liver (Baron, 2002: 1251). High-density lipoprotein also acquires cholesterol from peripheral tissues (Malloy & Kane, 1998: 564). According to Schneider (2002: 1), high-density lipoprotein cholesterol is referred to as "good cholesterol", because it brings cholesterol from cells in the periphery to the liver, where cholesterol is either excreted in bile or converted to bile salts, which are later excreted in bile (Scheig, 1995: 305).

2.4 LIPID METABOLISM

Lipid metabolism entails amalgamation of fat in the gut and its build-up into chylomicrons. Triglycerides are removed from chylomicrons by lipoprotein lipase as they pass through adipose or muscle tissue. Some of the surface of the chylomicrons is incorporated into the high-density lipoprotein (Anon., 2003: 1). Part of the lipid metabolism is defined in paragraph 2.3 under individual lipoproteins. Abnormal lipid metabolism is explained under pathophysiology of dyslipidemia. (See paragraph 2.5).

2.5 PATHOPHYSIOLOGY OF DYSLIPIDEMIA

Cholesterol and other lipoproteins were fully discussed in paragraph 2.3. Low-density lipoprotein accounts for 60% to 70% of total serum cholesterol (Anaizi, 1997: 3). Upon its oxidation, it becomes toxic and contributes to the development of atherosclerosis, but when it is in excess, low-density lipoprotein causes cholesterol to be deposited outside the cell, thereby causing the formation of atherogenic plaques in the vascular endothelium (Thornton & Holt, 2000: 413).

The uptake of low-density lipoproteins is through particular receptors whose numbers are influenced by genetic and regulatory factors. The production of those particular receptors is increased when intracellular cholesterol concentration is low. When there is an inherited deficiency in those particular receptors, patients tend to suffer from familial primary hypercholesterolaemia (type IIa) (Anaizi, 1997:4).

Intermediate density lipoproteins are formed by the depletion of triglycerides (Malloy & Kane, 1998: 564). Their abnormal metabolism, which results from abnormal apolipoprotein E, creates a condition known as type III hyperlipidemia or dysbetalipoproteinemia (Anaizi, 1997:4).

High-density lipoprotein particles are rich in cholesterol and are involved in the process of reverse cholesterol transport (Thornton & Holt, 2000: 410). An increased level of high-density lipoprotein cholesterol is termed a negative risk factor because it is claimed to protect against atherosclerosis by reversing cholesterol transport (Anaizi, 1997:4). Negative risk factors are defined according to Thornton and Holt (2000: 413) as risk factors that decrease the risk of developing coronary heart disease.

2.6 DEFINITION AND CLASSIFICATIONS OF DYSLIPIDEMIA

The following paragraph will define and classify dyslipidemia

2.6.1 Definition of dyslipidemia

Ahmed *et al.* (1998: 1) defined dyslipidemia as "*disorders of lipoprotein metabolism, including lipoprotein overproduction or deficiency*". These disorders may be manifested by increased level of serum total cholesterol, low-density lipoprotein cholesterol and triglyceride concentrations, and a decrease in the high-density lipoprotein concentration (Malloy & Kane, 1998: 563; Ahmed *et al.*, 1998: 1) and are more likely caused by genetic defects (Siguel, 2000: 6). Berger and Marais (2000: 164) defined dyslipidemia as "*a clinically significant modification in the circulating lipids and lipoprotein predisposing to coronary heart disease and related disorders.*"

2.6.2 Classification of dyslipidemia

Berger and Marais (2000: 168) classified dyslipidemia as either primary or secondary in terms of causation, though in many disorders the aetiology is significantly mixed. Genetic dyslipidemia is

classified conveniently in terms of hypercholesterolaemia, hypertriglyceridaemia, familial combined hyperlipidemia or a mixed picture, in which cholesterol and triglyceride levels are more or less equally increased (Ahmed *et al.*, 1998: 2; Berger & Marais, 2000: 168). Pure hypertriglyceridaemia is considered a less atherogenic form of dyslipidemia but when it is severe it can result in acute pancreatitis and other clinically adverse outcomes (Berger & Marais, 2000: 168).

2.6.2.1 Primary dyslipidemia

In primary dyslipidemia, an autosomal dominant gene is inherited (Berger & Marais, 2000: 168) and homozygous familial hypercholesterolaemia can lead to coronary disease in childhood; and is characterised by very high levels of cholesterol in serum (Malloy & Kane, 1998: 568). Thus, one may expect half the children in an affected family with familial dyslipidemia and similar dyslipidemias to present with hyperlipidemia (Berger & Marais, 2000: 168). The various patterns of abnormal lipoprotein distribution are elucidated in table 2.2 (Anaizi, 1997: 5; Bhatnager, 1998: 208; Malloy & Kane, 1998: 567)

Table 2.2 Classes of primary dyslipidemia (Anaizi, 1997: 5; Bhatnager, 1998: 208; Malloy & Kane, 1999: 567)

Class	Cause	Abnormal
I Familial hyperchylomicronemia	Lack of Lipoprotein lipase	↑Chylomicrons; ↑Triglycerides (TG); Pancreatitis
IIa Familial hypercholesterolaemia (can be homozygous or heterozygous)	LDL receptor defect	↑LDL; ↑Total cholesterol (TC)
IIb Familial combined hyperlipidemia	High apolipoprotein B synthesis + defective Apolipoprotein E; premature coronary artery disease.	↑VLDL; ↑LDL; ↑TC
III Familial dysbetalipoproteinemia	Abnormal IDL metabolism; increased chylomicron remnants and VLDL remnants	↑IDL; ↑TC; ↑TG's
IV Familial hypertriglyceridaemia (can be severe or moderate)	Abnormal VLDL metabolism	↑↑TG's; ↑TC; ↑VLDL; risk of pancreatitis
V Familial mixed Hypertriglyceridaemia	Abnormal VLDL and Chylomicrons	↑↑TG's +↑TC. ↑VLDL⇔LDL

(↑ Overproduction of; TG, triglycerides; VLDL, very low-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol).

Some important examples of primary dyslipidemia are discussed below:

2.6.2.1.1 Familial hypertriglyceridaemia

Familial hypertriglyceridaemia can either be severe, usually mixed lipemia, which results from impaired removal of triglyceride-rich lipoproteins or moderate (endogenous lipemia), which is worsened by factors that increase the rate of very low-density lipoprotein secretion from the liver (Malloy & Kane, 1998: 567). It often presents in childhood only and has variable patterns of inheritance (Berger & Marais, 2000: 169). It further presents with tuberous xanthomata, which is associated with high intermediate density lipoprotein (Anon., 2003: 1). Depending on the severity of the lipemia, eruptive xanthoma, lipemia retinalis, epigastric pain and overt pancreatitis are variably present (Malloy & Kane, 1998: 568).

2.6.2.1.2 Familial hypercholesterolaemia

In familial hypercholesterolaemia, the genetic abnormality is in the low-density lipoprotein receptor, which results in increased plasma low-density lipoprotein concentration (Berger & Marais, 2000: 168). These levels of low-density lipoprotein tend to increase throughout childhood and the diagnosis can often be made on the basis of increased umbilical cord blood cholesterol (Malloy & Kane, 1998: 567). In South Africa, it is prevalent mostly in Afrikaners (about 1% of population) as well as in other groups including Asians, Jews and Lebanese. It is also known to occur in the coloured and in Black populations (Berger & Marais, 2000: 168).

The patients can either be heterozygous or homozygous (Malloy & Kane, 1998: 568). The homozygotes usually die before the age of twenty and the heterozygotes have up to 20-fold increased risk of premature heart disease (Anon., 2003: 1). Familial hypercholesterolaemia can cause severe hypercholesterolaemia, tendon xanthoma (Berger & Marais, 2000: 168) and early tuberous xanthomatosis (Malloy & Kane, 1998: 568). Familial hypercholesterolaemia produces a trimodal distribution of plasma cholesterol levels across a family (Anon., 2003:1). In adults, the plasma cholesterol is usually >7.5 mmol/l (LDLC > 5) and often > 9 mmol/l before dietary modification (Berger & Marais, 2000: 168).

2.6.2.1.3 Familial combined hyperlipidemia

Familial combined hyperlipidemia is characterised by a two-fold increase in very low-density lipoprotein secretion (Malloy & Kane, 1998: 568). It may cause an autosomal leading birthright of hypercholesterolaemia, which may manifest in affected family members (Berger & Marais, 2000:170). In those family members, individuals may have elevated levels of very low-density lipoprotein, low-density lipoprotein or both and the pattern may change with time (Malloy & Kane, 1998: 568). This disorder does not lead to tendon xanthomas and the gene defects are not known (Berger & Marais 2000:170).

2.6.2.1.4 Familial hyperchylomicronemia

In familial hyperchylomicronemia the lipoprotein lipase deficiency and lipoprotein lipase cofactor deficiency are usually associated with severe lipidemia (Malloy & Kane, 1998: 568). This disorder causes recurrent abdominal pain and pancreatitis (Anon., 2003: 1) and may not be diagnosed until an attack of acute pancreatitis occurs (Malloy & Kane, 1998: 568). It may occur in poorly controlled diabetes, as insulin is required for action of lipoprotein lipase cofactor (Anon, 2003:1).

2.6.2.1.5 Familial dysbetalipoproteinemia

In familial dysbetalipoproteinemia, there is an accumulation of remnants of chylomicrons and very low-density lipoprotein cholesterol. The level of serum cholesterol is as high as that of triglycerides because the remnants are rich in cholesterol esters. Patients often develop xanthomas, some tend to be obese and some have impaired glucose tolerance (Malloy & Kane, 1998: 568)

2.6.2.2 Secondary dyslipidemia

According to Berger and Marais (2000:170) secondary dyslipidemia is characterised by normal or only minor gene defects. The environment, underlying incidental disease and several factors including drugs may create secondary dyslipidemia (Berger & Marais 2000:170). Table 2.3 summarises some causes of secondary dyslipidemia. These factors are important to correct the principal conditions in order to prevent the need to treat the apparent lipid disease. Alcohol use and diabetes are commonly associated with high triglyceride levels that decrease with improvement in glycaemic control or reduction of alcohol (Baron, 2002: 1254).

Medications, which can cause high concentration of lipids in the blood, include amongst others contraceptives, steroids and anti-hypertensive (AAFP, 1998: 2). Thiazide diuretics, cephalosporins, and glucocorticoids can alter lipid metabolism, and can hence also cause lipid disorders (Anaizi, 1997: 5). Severe hypertriglyceridaemia develops when patients are given small doses of oestrogen such as those found in oral contraceptives. If oestrogen therapy is needed in dyslipidemic patients, then the drug must be given transdermally in order to avoid the first pass metabolism by the liver (Malloy & Kane, 1998: 567).

Table 2.3. Some causes of secondary dyslipidemia (Bhatnager, 1998: 209; Baron, 2002: 1254; Anaizi, 97: 6; Malloy & Kane, 1998: 564)

	Increase in serum cholesterol	Increase in serum triglycerides	Mixed hyperlipidemia
Diseases	Nephrotic syndrome Obstructive liver disease Hypothyroidism Cushing's syndrome Acute intermittent porphyria Von Giercke's disease Anorexia nervosa Resolving lipemia	Uncontrolled diabetes mellitus Chronic renal failure Peritoneal dialysis Septicaemia Hepatic disease (cirrhosis) Acromegaly Partial lipodystrophy Systemic lupus erythematosus Gaucher's disease Tay Sach's disease Severe necrosis Uremia	Type II diabetes mellitus Ethanol excess Renal transplantation Haemodialysis Monoclonal gammopathies
Drugs	Thiazide diuretics[1] ↑LDL Cyclosporine Dioxins Excess of corticosteroid	β-Adrenoreceptor blockers[1, 2] ↓HDL Anabolic steroids ↓HDL Oral contraceptives Oestrogens Isoretinin	Glucocorticoids ↑VLDL, ↑LDL Phenytoin

↑ ~ Overproduction of
↓ ~ Decreased production of
[1]Short term effects only
[2] Beta-blockers with intrinsic sympathomimetic activity, such as pindolol and acebutolol, do not affect lipid levels.
HDL ~ High-density lipoprotein
VLDL ~ Very-low density lipoprotein
LDL ~ Low-density lipoprotein

2.7 RISK FACTORS FOR HIGH CHOLESTEROL

Risk factors for high cholesterol can be divided into controllable and uncontrollable categories.

2.7.1 Controllable risk factors

Controllable risk factors are factors that when taken in cognisance, reduce the incidence of severity of the disease (Siguel, 2000: 3). These factors include disease conditions such as diabetes mellitus and hepatic diseases (Schneider, 2002: 2). According to Siguel (2000: 3) these kinds of risk factors are associated primarily with bad diet, lack of exercise and overweight. Smoking is also considered to be a risk factor. However, the history of smoking is not considered a risk factor therefore patients are advised to quit smoking (Thornton & Holt, 2000: 412 - 413).

2.7.2 Uncontrollable risk factors

Schneider (2002: 2) defined uncontrollable risk factors, as genetically inherited disorders, which can cause very high cholesterol levels in blood. In addition to genetically inherited diseases, age and gender are also regarded as uncontrollable risk factors. Individuals with genetically inherited diseases still have an increased risk of dying from premature death even if they have controlled their diets (Siguel, 2000: 3).

2.8 RISK ASSESSMENT FOR CORONARY ARTERY DISEASE

The main objective of treating patients with dyslipidemia is to reduce the risk of coronary artery disease, peripheral vascular disease or acute pancreatitis (Bhatnagar, 1998: 213). Once the low-density lipoprotein cholesterol levels are obtained, the next step is to assess the patient's risk of coronary artery disease (Irons *et al.*, 2002: 1616). The major positive and negative risk factors are explained in paragraph 2.5. Patients with dyslipidemia need to be treated for life, and any decision to use a lipid lowering medication must be taken with due considerations (Bhatnagar, 1998: 213).

Patients with clinical evident atherosclerosis are categorised as being at high risk for a cardiovascular event (Fodor *et al.*, 2000: 1442). Those with diabetes who are over the age of 30 years are also classified as being at very high risk for coronary artery disease (Irons *et al.*, 2002: 1616). The short-term risk of individual patients without clinical evidence of cardiovascular

diseases or diabetes is calculated using the Framingham risk model table 2.8 (Fodor *et al.,* 2000: 1442). It should be noted that each patient with dyslipidemia should be assessed individually, and as with many approaches to any disease, there is no replacement for a good record and a careful medical assessment (Bhatnagar, 1998: 213). Risks assessment can be categorised according to cholesterol concentration as indicated in table 2.4.

Table 2.4 Broad categories of risk according to total cholesterol concentration (Berger & Marais, 2000: 166)

Category	**Description**
Cholesterol level<5.0mmol/l	This level of cholesterol is considered to contribute insignificant risk in a healthy individual. These patients do not require further specific diagnostic investigation or individualised attention, but follow up is recommended in 5 years. Further assessment is required, in the presence of obvious additional risk factors.
Cholesterol level 5.0-7.5 mmol/l	This category carries a high and increasing risk for which, in the absence of additional risk factors, beginning of lipid modifying drug therapy is generally not a good point. More strong non-pharmacological involvement and more repeated follow up are necessary, careful medical and laboratory assessment for additional risk factors and for the possible cause of the hyperlipidemia should be carried out. A major percentage of patients in this group have other risk factors, which raise the overall probability of future coronary heart diseases (CHD) sufficiently to value the use of suitable lipid altering drugs. Some will have a principal clinical disorders inclining toward hyperlipidemia, this is referred to as 'secondary dyslipidemia' it is discussed in detail in paragraph 2.6.2.2. Treatment of the fundamental illness may alleviate the harshness of the lipid abnormality.
Cholesterol level >7.5 mmol/l	The use of drug therapy should be considered in all patients in whom lifestyle modification did not achieve the desired lipid profile. A certain proportion of the people in this category, will have the following conditions, which further increase the need for effective treatment: ▪ familial hyperlipidemia; ▪ overt CHD; or ▪ other additional clinical risk factors such as diabetes mellitus and hepatic diseases.

2.9 RISK FACTORS FOR CORONARY HEART DISAESE

The following paragraph will conceptualise risk factors for coronary heart disease:

2.9.1 Coronary heart disease risks based on cholesterol levels

There is a direct relationship between low-density lipoprotein and cardiovascular morbidity and mortality (Anaizi, 1997: 1). The risk of atherosclerotic heart disease is greater when the low-density lipoprotein cholesterol level is higher (Baron, 2002: 1251).

The target low-density lipoprotein cholesterol can now be individualised for the patients:

- One or no risk factor: < 160 mg/dl or 4.1 mmol/l.
- More than one risk factor: < 130 mg/dl or 3.4 mmol/l.
- If there is the presence of diabetes or other clinical forms of atherosclerosis: <100mg/dl or <2.5 mmol/l (Griffith, 2001:1; Schneider, 2002: 1).

Low high-density lipoprotein cholesterol is also a major risk factor for coronary heart disease (Irons *et al.,* 2002: 1616) that is < 40mg/dl or 0.9mmol/l. If high-density lipoprotein is over 60 mg/dl, one risk factor is removed from the total count (Griffith, 2001:1) (refer to paragraph 2.3.4)

Table 2.5 Classification of blood lipids (Griffith, 2001:1; Irons *et al.,* 2002: 1616; Fodor *et al.,* 2000: 1444; Thornton & Holt, 2000: 412)

Serum lipid concentration	(Mg/dl)	Mmol/l	Classification level
LDL cholesterol	<100 100-129 130-159 160-189 >= 190	<2.5 <3.4 3.4-4.1 >4.1	Optimal Near optimal/above optimal Borderline high High Very high
Total cholesterol	<200 200-239 >= 240	<5.2 5.2-6.2 >6.2	Desirable Borderline high High
HDL cholesterol	<40 >= 60	<0.9 >1.5	Low High
Triglycerides	200 200-400 400-1000	<2.3 2.3-4.5 4.5-11.3	Normal Borderline high High Very high

2.9.2 Coronary heart disease risks based on risk factors other than low-density lipoprotein cholesterol level

Major positive risk factors other than low-density lipoprotein levels are the age of the patients (≥ 45 years for men and ≥55 years for women) (Irons *et al.,* 2002: 1616), cigarette smoking, hypertension (blood pressure greater than 140/90 mmHg), and a family history of premature heart diseases (Griffith, 2001:1) and in women risk increases with menopause (Berger & Marais, 2000: 168).

Patients with diabetes are also considered to be in the highest risk category for coronary events (Irons *et al.,* 2002: 1616) in both sexes, especially in women (Berger & Marais, 2000: 168). High HDL cholesterol levels are known as a negative risk factor for coronary artery disease (Ahmed *et al.*, 1998: 3). Thornton and Holt (2000: 413) describe negative risk factors as risk factors that decrease the risk of developing coronary heart disease.

Table 2.6 Risk factors other than low-density lipoprotein cholesterol level (Bhatnager, 1998: 215; Ahmed *et al.,* 1998: 3; Anaizi, 1997: 1; Berger & Marais, 2000: 168; Thornton & Holt, 2000: 413; Cranberry & Patchin, 2003: 595).

POSITIVE RISK FACTORS		
Lifestyle/ behavioural factors	Other modifiable risk factors/ clinical/ biochemical	Non-modifiable risk factors/ genetic/ biological
Atherogenic diet Cigarette smoking Lack of physical exercise Drug abuse (alcohol and anabolic steroids)	Hypertension Diabetes mellitus Glucose intolerance Obesity Thrombogenic factors Low HDL cholesterol Hypertriglyceridaemia	Male ≥ 45 years Female ≥ 55 years or postmenopausal women without oestrogen replacement therapy Family history of premature CHD or peripheral vascular disease. Personal history of CHD or peripheral vascular disease
*NEGATIVE RISK FACTOR		
High HDL cholesterol level (≥ 1.6 mmol/l).		
HDL= high density lipoprotein * Subtract one positive risk factor if negative risk factor is present		

2.9.3 Risk categories and therapeutic goals

The patient's risk for coronary heart diseases is explained in paragraph 2.8. The risk categories based on a number of risk factors are presented in Table 2.6. For patients with zero or one risk factor, no risk assessment is needed for determining appropriate therapy (Irons *et al.,* 2002: 1616). However for patients with two or more major risk factors, a further estimation of the 10-year coronary heart disease risk calculation using a Framingham model (Table 2.8) is recommended (Fodor *et al.,* 2000: 1443). The overall goal of primary prevention is to reduce the occurrence of cardiovascular events in patients without a history of coronary heart disease (Irons *et al.,* 2002: 1617). The goal of secondary prevention is to prevent the recurrences of clinical events and to increase survival of patients with coronary artery disease (Hawkins & Jackson, 2001: 181).

Once the coronary heart risk has been determined, definite treatment objectives are derived as in Table 2.7. For the patient with zero or one risk factor, the desired low-density lipoprotein cholesterol goal is 5.0 mmol/l (Irons *et al.,* 2002: 1617).

Table 2.7 Target lipid values by level of risk (Irons *et al.,* 2002: 1617; Fodor *et al.,* 2000: 1444)

Risk category	Level of risk	LDL cholesterol goal mmol/l	Non-HDL cholesterol goal (mmol/l)	Triglycerides levels, goal mmol/l
10-yr risk of CHD >30%	Very high*	< 2.5	< 4	< 2.0
CHD or CHD risk equivalents (10-year risk, >20%)	High*	< 3.0	< 5	< 2.0
Two or more risk factors (10-year risk, ≤20%	Moderate$^{\alpha}$	< 4.0	< 6	< 2.0
Zero or one risk factor	Low$^{\beta}$	< 5.0	< 7	< 3.0

* Start medication and lifestyle changes if values are above these targeted values

α Start medication if target values are not achieved after 3 months of lifestyle modification

β Start medication if target values are not achieved after 6 months of lifestyle modification

LDL ≈ Low-density lipoprotein

HDL ≈ High-density lipoprotein

CHD ≈ Coronary heart disease

Non-HDL cholesterol ≈ total cholesterol minus HDL cholesterol

Table 2.7 and Table 2.8 can be used to estimate the person's 10-year risk of asymptomatic coronary artery disease and lipid target levels (Fodor *et al.,* 2000: 1443). The estimation for risk points is based on age, total cholesterol, systolic blood pressure, high-density lipoprotein cholesterol and smoking status (Irons *et al.,* 2002: 1617). In order to obtain the absolute risk for coronary artery disease, the points for each risk category must be added and it should correspond with the patient's gender. For blood pressure, the highest score must be used (Berger & Marais, 2000: 169).

Table 2.8 Framingham model for calculating 10-year risk of coronary artery disease

Model for calculating the 10-year risk of CAD in a patient without diabetes mellitus or clinically evident cardiovascular disease, using Framingham data (Fodor *et al,* 2000: 1443; Irons *et al.,* 2002: 1263-1264; Berger & Marais, 2000: 169)

Step1: DETERMINE RISK POINTS		
	Risk points	
Risk factor	Men	Women
Age, yr		
30-34	-1	-9
35-39	0	-4
40-44	1	0
45-49	2	3
50-54	3	6
55-59	4	7
60-64	5	8
65-69	6	8
70-74	7	8
[1]Total cholesterol level, mmol/l		
<4.14	-3	-2
4.15-5.17	0	0
5.18-6.21	1	1
6.22-7.24	2	2
≥ 7.25	3	3
[2]HDL-C level, mmol/l		
<0.90	2	5
0.91-1.16	1	2
1.17-1.29	0	1
1.30-1.55	0	0
≥ 1.56	-2	3
[3]Systolic blood pressure, mm Hg		
<120	0	-3
120-129	0	0
130-139	1	1
140-159	2	2
≥ 160	3	3
[4]Smoker		
No	0	0
Yes	2	2
Record the points		
Age		
TC	_	_
HDL-C	_	_
BP	_	_
Smoker	_	_
Add total risk point		

Step 2: CALCULATE RISK		
Total	10-year risk, %	
risk point	Men	Women
1	3	2
2	4	3
3	5	3
4	7	4
5	8	4
6	10	5
7	13	6
8	16	7
9	20	8
10	25	10
11	31	11
12	37	13
13	45	15
14	≥ 53	18
15		20
16		24
17		>27

Step3: Compare risk with that of an overage person of the same age		
Age, yr	Average risk	Low risk
Men		
30-34	3	2
35-39	5	3
40-44	7	4
45-49	11	4
50-54	14	6
55-59	16	7
60-64	21	9
65-69	25	11
70-74	30	14
Women		
30-34	<1	<1
35-39	<1	<1
40-44	2	2
45-49	5	3
50-54	8	5
55-59	12	7
60-64	12	8
65-69	13	8

[1]total cholesterol should be the average of at least two measurements.

[2]high-density lipoprotein values should be the average of at least two measurements.

[3]smoker is defined as any cigarette smoking in the past month

[4]the average of several blood pressure measurements is recommended

For example, a 55-year old man who has a total cholesterol level of 5.43 mmol/l, high density lipoprotein cholesterol level of 1.23 mmol/l, and a systolic pressure of 148 mmHg and who smokes would have the total risk score of 9 (Step 1). His 10-year risk for coronary artery disease would therefore be 20% (Step 2); according to step 3, the average risk for an average person of his age in the Framingham study population would be 16% (Fodor *et al.*, 2000: 1443).

This Framingham scoring system improves the therapeutic management of patients at high risk for cardiovascular events (Irons *et al.*, 2002: 1617) but it does not apply to people with extreme or unusual risk factors such as severe hypercholesterolaemia or those with very low levels of high-density lipoprotein cholesterol (Fodor *et al.*, 2000: 1443).

2.10 DIAGNOSIS OF DYSLIPIDEMIA

Blood cholesterol measurement should be conducted in people over 20 years of age with a lipogram (AAFP, 1998: 2). Berger and Marais (2000: 166) recommended that blood cholesterol measurement should be performed at least once in the life of each adult, whereas Ahmed *et al.* (1998: 3) recommended that total cholesterol and high-density lipoprotein cholesterol levels should be measured every five years in patients without coronary heart disease and other atherosclerotic diseases. According to Berger and Marais (2000: 166), measurement of low-density lipoprotein level is highly recommended for those at high risk for dyslipidemia.

Patients with cardiovascular disease have a high prevalence of lipid abnormalities as such; a complete lipid profile (total cholesterol, high-density lipoprotein cholesterol and triglycerides levels) should be obtained as a screening test after an all night deprivation of food. Measurement should be repeated at least once for those with suspected elevated low-density lipoprotein cholesterol (Baron, 2002: 1255). Patients with hypercholesterolaemia of greater than 5 mmol/l on screening, and physical signs of a lipid disorder must have a full serum lipoprotein profile or plasma lipoprotein profile performed on them (Berger & Marais, 2000: 166).

Strategies that have been proposed for initial measurement of cholesterol include measuring total cholesterol alone, measuring total cholesterol or measuring low-density lipoprotein cholesterol and high-density lipoprotein cholesterol (Berger & Marais, 2000: 166).

According to Baron (2002: 1556), the above-mentioned approaches are acceptable but the treatment decisions are based on the low-density lipoprotein cholesterol and high-density lipoprotein cholesterol levels. Though being the least expensive of all measurement, total cholesterol measurement is only adequate for low-risk individuals. Re-evaluation with a fasting low-density lipoprotein and high-density lipoprotein cholesterol measurement should be done on patients with cholesterol levels of greater than 5.2 mmol/l.

Although the diagnosis based on low-density lipoprotein cholesterol is designed for men and women, observational studies suggest that low high-density lipoprotein cholesterol levels less than 0.9 mmol/l is a more important risk factor for coronary heart disease (Thornton & Holt, 2000: 413; Bhatnager, 1998: 213) in women than a high low-density lipoprotein. It is suggested that cholesterol is not a risk factor for coronary heart disease in patients over 75 years of age and it is preferable for clinicians to stop screening for such patients (Baron, 2002: 1257).

2.11 TEST PROCEDURES FOR DIAGNOSIS

The essential component of the diagnostic procedure for patients in cholesterol categories 2 and 3 (see table 2.4) and for patients with total cholesterol levels of < 5 mmol/l but established coronary heart disease is the determination of the lipoprotein profile (Berger & Marais, 2000: 170). According to Berger and Marais (2000: 170), a specimen for a lipoprotein profile requires 12 hours overnight fast in adults and older children. The blood sample should be taken between 08h00 and 10h00. The patient should be sitting and undue venestasis should be avoided.

Blood should be collected in tubes without anticoagulant and allowed to clot or into tubes containing heparin or ethylene diamine tetra acetic acid (EDTA) and mixed carefully by inversion. The tubes should be filled to the top to avoid dilution errors if EDTA is used. Plasma or serum should ideally be separated from the cells within two hours of sampling and definitely within six hours (Berger & Marais, 2000: 170).

Care should be taken to avoid pre-analytical errors (such as recent or current illness, non fasting state, delayed processing). When assessing the results, normal biological variation of 5 to 10%

for total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, apolipoprotein B and 25% for triglycerides must also be considered (Berger & Marais, 2000: 170). When considered necessary, the decision must be to initiate treatment with lipid modifying drugs on at least two or three fasting low-density lipoprotein measurements (Ahmed *et al.,* 1998: 2) obtained 1 week or more using the single laboratory to minimise variability (Berger & Marais, 2000: 170).

The low-density lipoprotein cholesterol level can be measured directly or can be calculated as follows: LDL = total cholesterol – HDL/ (triglycerides/5) (Friedwald *et al.,* 1972: 500). This formula cannot be used when triglyceride levels are greater than 4.5 mmol/l (Ahmed *et al.,* 1998: 2). If discrepancies of more than 10% occur between these two samples, a third sample is advisable (Berger & Marais, 2000: 170).

After myocardial infarction, the acute-phase reaction is observed within a day and marks a lower cholesterol measurement for at least 6 weeks. This is important in the diagnosis of dyslipidemia after myocardial infarction. For reasons beyond the investigator's control, severe hypertriglyceridaemia may be underestimated and many renders cholesterol estimates less accurate (Berger & Marais, 2000: 170). Laboratory tests for exclusion of secondary dyslipidemia should include thyroid, renal and liver function tests as well as random or fasting glucose, serum albumin, protein electrophoresis and a urinary screen for protein, glucose, bilurubin and urobilinogen (Griffith, 2001: 2).

2.12 CANDIDATES FOR SCREENING

Any person considered to be at high risk for coronary heart disease should be screened (Berger & Marais, 2000: 166). The following categories of people should be routinely screened to obtain a fasting lipoprotein profile (total cholesterol, high-density lipoprotein cholesterol, triglycerides and calculated low-density lipoprotein cholesterol level):

- Men over the age of forty.
- Women over the age of fifty.
- Adults with two or more risk factors for coronary artery disease.
- Patients with clinical evidence of coronary artery disease, peripheral vascular disease or carotid atherosclerosis.
- Patients with diabetes mellitus.

- Patients with xanthoma or other stigma of dyslipidemia and patients with a family history of dyslipidemia or coronary artery disease (Fodor *et al.*, 2000: 1442; Baron, 2002: 1255-1257).

2.13 SIGNS AND SYMPTOMS

An increased cholesterol level in blood generally manifests as a silent condition that rarely causes its own symptoms (Bhatnagar, 1998: 213; Baron, 2002: 1254; AAFP, 1998: 2; Schneider, 2002: 2), as such most people find it hard to detect their high cholesterol as a problem (Schneider, 2002: 2). As a result, the majority of the people detect their lipid abnormalities through laboratory tests (Baron, 2002: 1254). Patients may often complain of symptoms related to complications of dyslipidemia (described below under heading complications) (Bhatnagar, 1998: 213).

Extremely high levels of chylomicrons and very low-density lipoproteins result in the formation of eruptive xanthomas (red-yellow papules) especially on the buttocks (Baron, 2002: 1255). In some patients, the first symptom of dyslipidemia is usually a heart attack or stroke (Schneider, 2002: 2). High low-density lipoprotein concentration and extremely high triglyceride levels result in tendinous xanthoma and lipemia retinalis (Baron, 2002: 1255). Diseases that are related to dyslipidemia such as non-insulin dependent diabetes mellitus, gout and hypertension should not be confused with the symptoms of dyslipidemia (Bhatnagar, 1998: 213).

Signs associated with disorders of lipoprotein metabolism are summarised according to the affected area as below (Bhatnagar, 1998:207).

Eyes

- Corneal arcus
- Corneal opacities

Skin

- Xanthelasmata
- Tendon xanthomata
- Eruptive xanthomata
- Tubero-eruptive xanthomata
- Planar xanthomata
- Palmar xanthomata

Systemic

- Aortic stenosis
- Ataxia
- Lipemia retinalis
- Peripheral neuropathy
- Hepatosplenomegaly

2.14 COMPLICATIONS OF DYSLIPIDEMIA

The complications for dyslipidemia include angina pectoris, intermittent claudiation, transient ischaemic attacks (TIA) or abdominal pain (Bhatnagar, 1998: 213). Dyslipidemia manifests to atherosclerosis (Schneider, 2002:2), coronary artery disease, peripheral vascular disease or acute pancreatitis and as a result, some patients will already have a long-standing history of established arterial disease or a history of abdominal operation in case of recurrent pancreatitis (Bhatnagar, 1998: 213).

Atherosclerosis is defined by Anaizi (1997: 40) as a disease process in which cholesterol and other fatty material are deposited within the walls of medium and large diameter arteries. The arteries get fatter and harder; over time the extra cholesterol precipitates and forms crystals. Narrow arteries and fats reduce blood flow to the heart and this is referred to as coronary artery disease (Schneider, 2002:2). Due to lack of blood, there will be lack of oxygen. The tissues deprived of oxygen will have ischaemia and when the brain experiences less oxygen supply stroke will result. Similar problems can occur in the organs (Siguel, 2000: 4). Patients with dyslipidemia need to be treated for life and decision to use lipid lowering drugs must be taken with due consideration (Bhatnager, 1998: 213).

2.15 ALGORITHM FOR THE MANAGEMENT OF DYSLIPIDEMIA

Any person considered being at high risk for coronary heart disease should be screened for elevated lipids (Berger & Marais, 2000: 166). The only exceptions are patients in whom lipid lowering is not indicated (Baron, 2002: 1255). Because of the high prevalence of lipid abnormalities in patients with cardiovascular diseases, a complete lipoprotein profile should be obtained. Patients with elevated low-density lipoprotein should have at least one repeat measurement. This algorithm has been explained in figure 2.1.

The goal of therapy should be to reduce low-density lipoprotein cholesterol to below 2.5 mmol/l and this reduces the risk of fatal coronary heart disease and fatal myocardial infarctions. If LDL remains high after dietary therapy, then drug therapy should be commenced. Treatment for high low-density lipoprotein cholesterol is discussed in detail in paragraph 2.16.

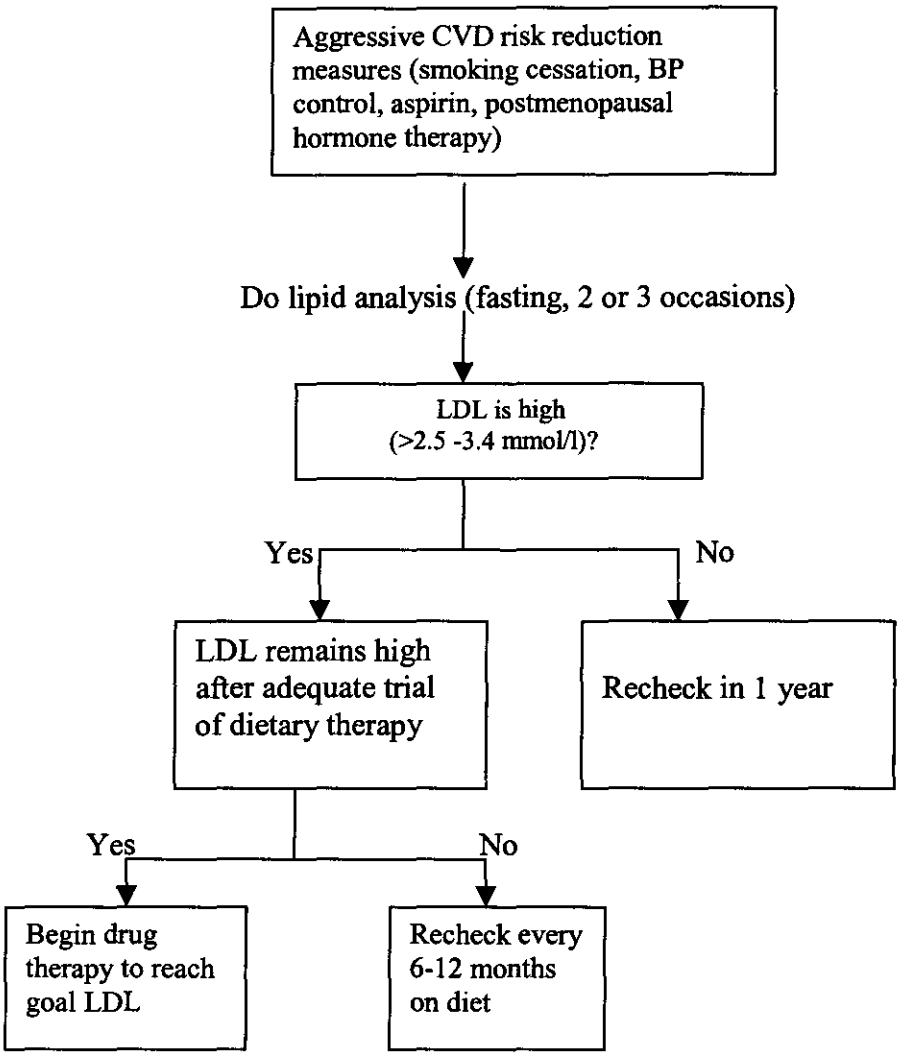


Figure 2.1 Algorithm for screening and management of patients with cardiovascular disease (Baron, 2002: 1255; Thornton & Holt, 2000: 414)

Individuals without cardiovascular disease can then be stratified according to risk factors as elucidated in figure 2.2. The first step is the reduction of cardiovascular disease risk. If the serum cholesterol level is high, then cholesterol levels must be measured in non-fasting state. Screening must be performed as outlined below until the decision to start drug therapy is reached.

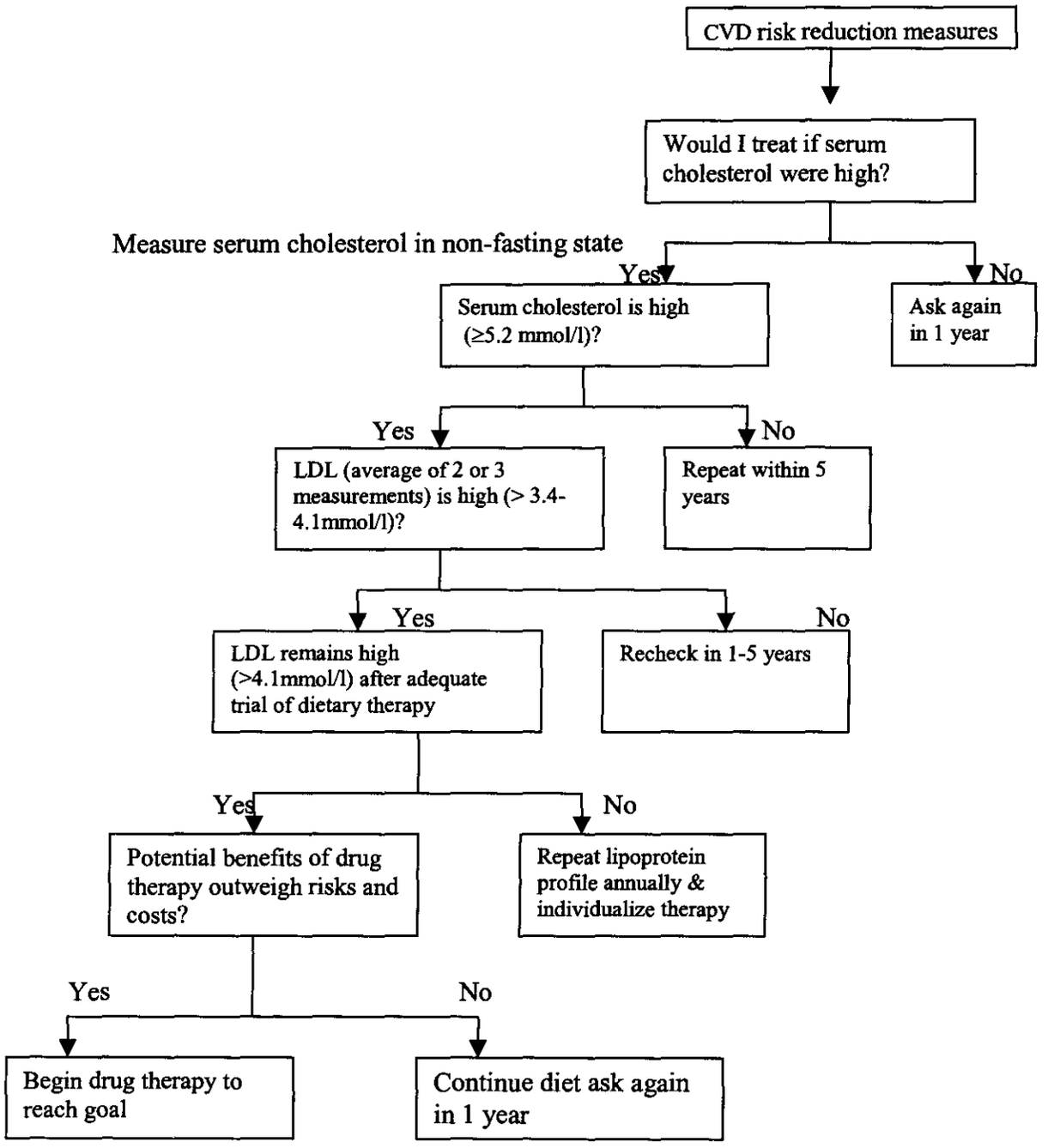


Figure 2.2 Algorithm for screening and the management of patients free of cardiovascular disease (Baron, 2002: 1256; Thornton & Holt, 2000: 414).

2.16 TREATMENT OF DYSLIPIDEMIA

Treatment of dyslipidemia will be explained in the following paragraph

2.16.1 Introduction

Cholesterol does not kill but ignorance does kill (Anon., 2002: 1). Lipids and the family of lipoproteins play a major role in the formation and progression of atherosclerosis and atherosclerosis has no cure (Bakker-Arkema *et al.,* 1997: 18). However, lipid-lowering therapy has shown to decrease both mortality and morbidity in patients with coronary artery disease (Lucas, 2002: 2101).

2.16.2 Goals of therapy

The main purpose of treating people with dyslipidemia is to reduce the risk of coronary artery disease, peripheral vascular disease and acute pancreatitis (Bhatnagar, 1998: 213). The reduction of the lipoprotein level is also aimed at reducing the incidence of atherosclerosis (Anaizi, 2002: 4).

The other objective is to help people to quit smoking, controlling their blood pressure and hence reducing their risk of coronary artery disease (Baron, 2002: 1257) and improving treatment outcomes (Irons *et al.*, 2002: 1615).

2.16.3 Different types of treatment of dyslipidemia

The two key fundamentals in the management of dyslipidemia are (Berger & Marais, 2000: 171)

- lifestyle modification, which is advantageous in all patients; and
- the use of appropriate lipid modifying drugs particularly in patients at high risk for cardiovascular disease.

2.16.4 Non pharmacological therapy

2.16.4.1 Lifestyle modification

Lifestyle modification, including dietary modification, is an important factor in reducing low-density lipoprotein levels (Anaizi, 1997: 6). The main targets of lifestyle modification are a healthy diet, regular aerobic exercise, loss of weight and quitting smoking (Berger & Marais, 2000: 171). A sufficient trial of lifestyle modification usually lasts up to 3 to 6 months (Anaizi, 2000: 6). At initiation of therapeutic lifestyle changes, the patient is instructed to reduce

saturated fat and dietary cholesterol (Griffith, 2001: 2) and participate in regular aerobic exercises (Berger & Marais, 2000: 171).

2.16.4.2 Diet therapy

Once the decision is taken to initiate treatment of dyslipidemia, dietary measures are always initiated first and may obviate the need for drug therapy (Malloy & Kane, 1998: 569). The effect of diet therapy may vary amongst individuals, as some have a reduction in low-density lipoprotein cholesterol of up to 25 to 30 % (Baron, 2002: 1257). Exceptions are in patients with familial hypercholesterolaemia or familial combined hyperlipidemia, because in those patients, drug therapy and dietary measures must be initiated simultaneously because of the severity of the conditions (Malloy & Kane, 1998: 569).

Patients should receive encouragement and reinforcement at every visit at the clinic to help them reach their low-density lipoprotein levels, because complying with dietary guidelines is difficult (Thornton & Holt, 2000: 414). Patients should be instructed on increasing fruit, vegetable and fibre intake (Berger & Marais, 2000: 171). Foods that are high in calories (processed foods, snacks, red meat) should be avoided or restricted (Thornton & Holt, 2000: 415).

If lifestyle modification fails to achieve its objectives, plant stanols and sterols can be added to the diet to increase fibre intake (Irons *et al.*, 2002: 1617) and the patient can be referred to the qualified dietician (Berger & Marais, 2000: 171). Several nutritional approaches to diet therapy are listed in table 2.9.

2.16.4.3 Physical activity and weight reduction

Increased physical activity and weight reduction are pivotal keys to the successful management of dyslipidemia (Irons *et al.*, 2002: 1617). The minimum effective target is 30 minutes of brisk walking, 3 times a week. Using stairs rather than lifts, gardening and housework can further advance the exercises. The physical activity should increase heart rate to about 75% of the age-related maximum heart rate (220 beats per minutes minus age in years) to reduce the risk of coronary heart disease (Berger & Marais, 2000: 171).

2.16.4.4 Cessation of tobacco use

The single most important therapeutic action in the management of dyslipidemia is cessation of smoking (Berger & Marais, 2000: 171). Quitting smoking reduces the effect of cardiovascular risk factor (high cholesterol level) and it may increase the high–density lipoprotein level (Baron,

2002: 1257). Patients who are unable to quit on their own should be provided with information on smoking cessation, nicotine replacement therapy, and drug therapy where indicated (Fodor *et al.,* 2000: 1445). Smoking cessation is important as the risk alleviates with cessation and after two years the additional risk becomes zero (Berger & Marais, 2000: 171).

Table 2.9 Macronutrient compositions of three lipid-modifying diets (Baron, 2002: 1258; Thornton & Holt, 2000: 415).

	Recommended Intake		
Nutrient	Step 1 diet	Step 2 diet	Mediterranean diet*
Total fat[#]	<30% of calories	<30% of calories	<40% of calories
Saturated fat[#]	<10% of calories	<7% of calories	<10% of calories
Polyunsaturated fat[#]	<10% of calories	<10% of calories	<10% of calories
Monounsaturated fat[#]	<10% of calories	<10% of calories	<20% of calories
Carbohydrate[#]	50-60% of calories	50-60% of calories	40-50% of calories
Protein[#]	10-20% of calories	10-20% of calories	10-20% of calories
Cholesterol	<300mg/d	<200mg/d	<300mg/d
Total calories	For desirable weight	To maintain optimal weight	For desirable weight

* Diet that maintains total fat as approximately 35 to 40 % of total calories but saturated fat is replaced with monounsaturated fat such as that found in olives, peanuts, avocados, and their oils.
[#] Percentages of total daily calories
Step 1 diet, reduction of total fat to 30%, saturated fat to 10% and dietary cholesterol should be limited to 300mg/d
Step 2 diet, saturated fat should be reduced to 7 % of calories and dietary cholesterol to 200mg/d

2.16.5 Pharmacological therapy

Pharmacological intrusion may be initiated in patients with severe coronary heart disease due to severe dyslipidemia that is not likely to be corrected by diet and other lifestyle modification (Anaizi, 1997: 6). The decision to use such therapy must be based on the specific metabolic defects and their potential for causing atherosclerosis or pancreatitis (Malloy & Kane, 1998: 570). The introduction of lipid modifying drugs must be approached with care placing special emphasis on the expense, possibility of side effects and the necessity for lifetime compliance (Berger & Marais, 2000: 172). The major drugs used for the treatment of dyslipidemia are summarised in table 2.12 (Anaizi, 1997: 6).

Drug treatment should be avoided in women who are likely to become pregnant or who are lactating and it is generally not indicated before the age of eighteen (Malloy & Kane, 1998: 570). The use of medications must balance cost against clinical efficacy and the risk of coronary artery disease (Berger & Marais, 2000: 172).

2.16.5.1 Niacin (nicotinic acid)

2.16.5.1.1 Mechanism of action

Niacin was the first lipid-lowering agent (Baron, 2002: 1258), dating back to the 1950's, and it is most commonly used in a rapid release formulation (Stein, 2002: 52c). Although niacin (Cosaldon retard®) is from the vitamin B family its lipid lowering action is unrelated to its role as vitamin (Bhatnagar, 1998: 219). It has an advantage of being tolerated and inexpensive when compared to other lipid modifying drugs (Berger & Marais, 2000: 174).

2.16.5.1.2 Therapeutic uses and dosages

The lipid lowering effect is used when nicotinic acid is used in pharmacological doses (Bhatnagar, 1998: 219) such as 1.5 to 3.5 grams daily for hypercholesterolaemia (Malloy & Kane, 1998: 570). It is the only lipid-regulating agent that decreases lipoprotein (a) levels (Xydakis & Ballantyne, 2002: 5). It is also useful in reducing triglyceride levels and increasing high-density lipoprotein cholesterol (Berger & Marais, 2000: 174), producing increases of 10% to 15% at doses of 750mg to 1500mg and increases of 20% to 30% at higher doses (Stein, 2002: 52c) as well as decreasing the production of very low-density lipoprotein cholesterol levels (Bhatnagar, 1998: 219).

2.16.5.1.3 Drug related problems

The major drawbacks with nicotinic acid are patient's compliance (Stein, 2002: 52c) and side effects, which include prostaglandin-mediated flushing, pruritis, gastro-intestinal discomfort, hyperuricemia, gout and elevated liver function tests (Ahmed *et al.*, 1998: 12). Prostaglandin mediated effects can be reduced by either taking 0.3 g of aspirin about half an hour beforehand or ibuprofen taken once daily (Malloy & Kane, 1998: 571). Starting nicotinic acid therapy with a very small dose, e.g. 50 to 100 mg with the evening meal may also decrease flushing (Baron, 2002: 1259).

Niacin should always be taken with food (Berger & Marais, 2000: 176). Nicotinic acid therapy worsens glycaemic control, exacerbate gout and can occasionally lead to hepatitis, and it should

be avoided in diabetics (Bhatnagar, 1998: 219; Hansten, 1976: 267). Niacin derivative, acipimox (Olbetam®), has similar but weaker action, unlike niacin, it may be anti-diabetogenic (Berger & Marais, 2000: 176).

Adverse drug interactions may be seen in patients taking nicotinic acid concomitantly with drugs such as alcohol, nicotine, aspirin (Stockley, 1999: 820) and sulfinpyrazone (Tatro, 2002: 1151).

2.16.5.2 Bile acid-binding resins (cholestyramine, Questran®, Colestipol)

2.16.5.2.1 Mechanism of action

Bile acid sequestrants are ion exchange resins that exert their effect by interrupting the enterohepatic circulation of bile acids (Bhatnagar, 1998: 213) through the conversion of cholesterol to bile acid (Malloy & Kane, 1998: 572).

2.16.5.2.2 Therapeutic uses and dosages

These gut-acting, non-absorbable agents have been used for the reduction of low-density lipoprotein cholesterol for more than three decades (Stein, 2002: 52c). Colestipol and cholestyramine can only be used in the management of hyperlipoproteinemia involving elevated levels of low-density lipoprotein (Malloy & Kane, 1998: 572). Treatment with this agent has no significant effect on total mortality but it reduces the event of coronary heart diseases in middle-aged men by about 20% (Baron, 2002: 1260).

The dose of cholestyramine is 12 to 36 grams of resins per day in divided doses with meals, mixed in water or more palatable juice. Doses of colestipol are 20% higher (Baron, 2002: 1260). The maximum daily dose is 16 grams and the total dose of 30 to 32 grams per day may be needed for maximum effects (Malloy & Kane, 1998: 572). The pre-packaged doses are more expensive than the bulk forms (Baron, 2002: 1260).

2.16.5.2.3 Drug related problems

Bile acid binding resins are effective lipid lowering agents, but their bulk, adverse drug reactions and interactions with other drugs result in their declined use (Bhatnagar, 1998: 214) and compliance may be a problem (Ahmed *et al.*, 1998: 11).

The chief contra-indication to the usage of these drugs is their high incidence of gastro-intestinal side effects such as gastric discomfort, bloating, constipation and nausea (Berger & Marais,

2000: 176). Resins may impair absorption of drugs with neutral or cationic charge as well as anions (Malloy & Kane, 1998: 573). Patients with the need for concomitant medications may experience adverse drug interactions (Bhatnagar, 1998: 215). Drugs involved include digitalis glycosides, thiazide, warfarin, tetracycline, vancomycin, thyroxin, iron salts, pravastatin, fluvastatin, folic acid, phenylbutazone, aspirin and ascorbic acid (Malloy & Kane, 1998: 573).

2.16.5.2.4 Minimisations of drug related problems

Drug interactions may be minimised if additional medications are given 1 hour before or four hours after administration of the resin to ensure adequate absorption (Bhatnagar, 1998: 215). Reducing the dose, increasing dietary fibre, taking bile acids sequestrants with meals and letting the resin to stand in liquid for 10 minutes before taking it can minimise side effects (Ahmed *et al.*, 1998: 11). Constipation can be ameliorated by concomitant administration of a bulk laxative and stool softener (e.g. psyllium) (Berger & Marais, 2000: 174).

2.16.5.3 Fibric acid derivatives (gemfibrozil (Lopid®), fenofibrate (Lipsin®), bezafibrate (Bezalip & Rolab-Bezafibrate®), clofibrate (Lipaten®).

2.16.5.3.1 Mechanism of action

The introduction of the fibric acid derivatives was a major advance in the treatment of dyslipidemia when nicotinic acid was the only drug available (Bhatnagar, 1998: 216). They primarily lower triglyceride levels and elevate high-density lipoprotein cholesterol concentrations (Berger & Marais, 2000: 174). They further decrease low-density lipoprotein cholesterol levels by 10 to 20% and triglyceride levels by about 40% and raise high-density lipoprotein cholesterol levels by about 15 to 20% (Baron, 2002: 1260).

2.16.5.3.2 Therapeutic uses and dosages

Fibric acid derivatives are generally used in the treatment of hypertriglyceridaemia in which there is an excess of very low-density lipoproteins and in dysbetalipoproteinemia (Malloy & Kane, 1998: 573). The usual dose of gemfibrozil is 600 mg once or twice daily (Baron, 2002: 1260). Fenofibrate is given in doses of 100 mg three times a day whereas bezafibrate is given in doses of 200 mg three times a day (Malloy & Kane, 1998: 573).

2.16.5.3.3 Drug related problems

The use of fenofibrate is accompanied with a low incidence of side effects (Najib, 2002: 2). Side effects include anorexia, alopecia, decreased glumerular filtration rate, muscle pain and stiffness,

increased transaminase levels (Berger & Marais, 2000; 174), cholelithiasis, hepatitis, myostosis of which the incidence of the two latter conditions may be higher in patients taking other lipid lowering drugs concomitantly (Baron, 2002: 1260). The dose of the drugs should be reduced when given to elderly patients or in patients with renal or hepatic diseases (Berger & Marais, 2000: 174).

The potentially life threatening effects can be seen when fibrates are given concomitantly with anticoagulants (e.g. warfarin) (Hansten & Horn, 2002: 59). Bleeding and death due to hemorrhage have occurred and this combination should be avoided (Tatro, 2002: 97). Other agents that may cause adverse drug reaction when given concomitantly with fibrates include cyclosporin, atorvastatin, pravastatin, simvastatin and hypoglycemic agents (Hansten & Horn, 2002: 59; Tatro, 2002: 97; Stockley, 2001: 519).

2.16.5.4 HMG-CoA reductase inhibitors (Statins)
(simvastatin (Zocor®), fluvastatin (Lescol®), pravastatin (Prava®), atorvastatin (Lipitor®)

2.16.5.4.1 Mechanism of action

HMG-CoA reductase inhibitors are structural analogs of (3-hydroxy-3-methylglutaryl-coenzyme A) HMG-CoA (Malloy & Kane, 1998: 573). They act by inhibiting the rate-limiting enzyme (HMG-CoA reductase), the enzyme responsible for converting HMG-CoA to mevalonate, for cholesterol synthesis (Cranberry & Patchin, 2003: 594). They reduce myocardial infarctions and total mortality in secondary prevention (Baron, 2002: 1260). Inhibition of HMG-CoA reductase produces a substantial decrease in plasma cholesterol levels, although part of the effect is due to an increase in the synthesis of low-density lipoprotein cholesterol receptors (Bhatnagar, 1998: 215).

2.16.5.4.2 Therapeutic uses and dosages

Statins are drugs of choice in patients with pure hypercholesterolaemia and in those with mixed hyperlipidemia in whom cholesterol lowering is a necessity (Berger & Marais, 2000: 172). They are by far the most powerful, best tolerated and complied with agents of the low-density lipoprotein cholesterol reducers (Stein, 2002: 51c). Atorvastatin being an exception, statins are better taken at night when most of cholesterol synthesis takes place (Berger & Marais, 2000: 172). They are useful alone or in combination with other drugs in treating disorders involving elevated plasma levels (Malloy & Kane, 1998: 573).

Statins effectively reduce cholesterol concentration by 20 to 55% (Cranberry & Patchin, 2003: 595). With the large number of available statins (Bhatnager, 1998: 216), the degree of lipid lowering response is dependent on drug selection, treatment dose and individual patient's response toward the drug (Cranberry & Patchin, 2003: 595).

Apart from their use in cholesterol reduction, experimental and clinical evidence, conducted and stated by (Laws *et al.,* 2004: 6) reported that statins improve endothelial dysfunction, are anti-inflammatory, anti-proliferative, anti-thrombogenic and anti-proteolytic. These effects are known to inhibit atherogenesis and improve plaque stability. In the future, statin use may include patients at risk of ischemic reperfusion injury, neointimal hyperplasia and aneurismal disease (Laws *et al.,* 2004: 6)

Statins vary in potency, which is the capacity to lower plasma cholesterol levels depending on the mass of the drug (refer to Table 2.11) (Berger & Marais, 2000: 172). Statins reduce the production of very low-density lipoprotein cholesterol levels and hence decrease the concentration of apolipoprotein B containing lipoproteins (Xydakis & Ballantyne, 2002: 4). Atorvastatin is the most effective statin in its ability to reduce low-density lipoprotein cholesterol levels, achieving decrements of 42% to 55% at its highest dose of 80mg table 2.11 (Stein, 2002: 51c).

Atorvastatin may be the preferred drug treatment in patients requiring greater than 30% reduction in low-density lipoprotein cholesterol or in patients with both elevated low-density lipoprotein cholesterol and triglycerides concentrations (Yee & Fong, 1998: 1030). Pravastatin and fluvastatin are limited to about 34% low-density lipoprotein cholesterol concentration reduction at their highest doses, lovastatin and simvastatin achieving 6% and (20% to 50%) respectively at their highest doses (Stein, 2002: 51c).

Doses are as follows: lovastatin, 10 to 80 mg/d; pravastatin, 10 to 40 mg/d, simvastatin, 5 to 40 mg/d; fluvastatin, 20 to 40 mg/d; and atorvastatin, 10 to 80 mg/d (Baron, 2002: 1260). These agents are given once a day in the evening at the high end of the dose ranges, twice a day dosing may be used (Malloy & Kane, 1998: 574).

2.16.5.4.3 Pharmacoeconomics of statins

Statins are well tolerated, cost effective and have been used to reduce coronary events as well as the need for revascularisation procedures (Ahmed *et al.*, 1998: 11). When the cost associated

with dyslipidemia intervention is assessed in consideration with the patient's risk, it is found that when the patient's risks increase, treatment with statins becomes more cost effective (Cranberry & Patchin, 2003: 595). Analysis of the cost effectiveness of simvastatin treatment to lower cholesterol showed that simvastatin therapy in patients with coronary heart disease was cost effective among both men and women at the ages and cholesterol levels studies (Johannesson, 1997: 332).

2.16.5.4.4 Drug related problems

Current doses of all statins are safe, although significant elevation of hepatic transaminase has been observed with a small number of patients on statins. These resulted in having to stop the drug or reducing the dose (Stein, 2002: 51c). Patients complain more frequently of indigestion but infrequently of tiredness and muscle aches (Bhatnagar, 1998: 216).

High doses of simvastatin have been associated with rhabdomyolysis (Scrabal *et al.*, 2003: 581). Rare case reports of rhabdomyolysis have been associated with the use of atorvastatin (Malhotra & Goa, 2001: 1837) and no reported cases with the use of pravastatin (Brink, 2003: 48). Manufacturers recommend that patients on statins should have liver and muscle enzyme monitoring.

Agents such as erythromycin and cyclosporine reduce metabolism of statins (Baron, 1999: 1260). Azoles antifungals (Diflucan®, Sporanox® and Nizoral®) increase serum concentration of simvastatin and these drugs must be used only if benefit outweighs the risk (Hansten & Horn, 2002: 59). If concurrent administration of these agents cannot be avoided, then the dose of HMG-CoA inhibitors must be reduced (Tatro, 2002: 656). Other agents that interact with HMG-CoA inhibitors include fenofibrate, gemfibrozil, verapamil, diltiazem, grape fruit juice, saquinavir, ritonavir, cholestryramine, oat bran, warfarin and phenytoin (Stockley, 1999: 834-5; Tatro, 2002: 656-666; Hansten & Horn, 2002: 59-63).

2.16.5.5 Other drugs

The cholesterol absorption inhibitor, ezetimibe, though not yet available in South Africa, is another class of potential low-density cholesterol lowering agents (Stein, 2002: 56c). Probucol (Lurselle®) is a lipid-lowering drug (Bhatnagar, 1998: 219) with an unknown mechanism of action. It reduces low-density lipoprotein levels by 10 to 15% with potentially important adverse

effects of lowering high-density lipoprotein levels by 10%. Probucol is reserved for patients with clear genetic disorders who have failed other therapies (Malloy & Kane, 2002: 1260).

Table 2.10 Dosages and average responses to lipid lowering drugs registered in South Africa according to classes (Berger & Marais, 2000: 174; Baron, 2002: 1259; Ahmed *et al.*, 1998: 10; Fodor *et al.*, 2000: 1445)

Group	*Substance*	*Trade name*	*Dose range (per day)*	*Change in LDLC (%)*	*Change in TG (%)*	*Change in HDLC (%)*
Statins (once daily)	Atorvastatin	Lipitor®	10-80mg	-35 to-55	-5 to -25	+4 to +12
	Fluvastatin	Lescol®	20-80mg	-20 to-35		
	Pravastatin	Prava®	10-40mg	-20 to-30		
	Simvastatin	Zocor®	10-80mg	-20 to-50		
Resin (Divided doses)	Cholestyramine	Questran®	4 -16g	-15 to-25	25 to 100	5
*Niacin (Divided doses)	Niacin/ nicotinic acid	Cosaldon retard®	0.4 - 3g	-15 to-25	-20 to-30	+20 to +35
	Acipimox	Olbetam®	500-750 mg		-15 to-25	
#Fibrates (Divided doses)	Bezafibrate	Bezalip®	400 mg	-15	-30	Varies
	Fenofibrate	Lipsin®	0.3 -0.6g	-20	-35	+5 to +30
	Gemfibrozil	Lopid®	1.2g	-12	-45	

* Use with caution in patients with diabetes

\# Use in caution in patients with renal insufficiency

The changes in low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides and dosages of each drug have been discussed under individual drugs in paragraph 2.16.

Table 2.11 Comparative efficacy of available statins (Stein, 2002: 53c)

Atorvastatin Dose (mg)	Simvastatin Dose (mg)	Lovastatin Dose (mg)	Pravastatin Dose (mg)	Fluvastatin Dose (mg)	TC %↓	LDL %↓
–	10	20	20	40	22	27
10	20	40	40	80*	27	34
20	40	60		160#	32	41
40	80				37	48
80					42	55

LDL = low-density lipoprotein cholesterol; TC; total cholesterol.

*** 80 mg XL formulation**

#2 x 80 mg XL is not yet approved in South Africa.

The effectiveness of statins in reducing low-density lipoprotein cholesterol concentration is highly predictable and this makes comparisons of statins easy and reliable (Stein, 2002: 51c). Atorvastatin 10 to 40 mg/day is associated with significant greater reductions in low-density lipoprotein cholesterol than simvastatin 10 to 40 mg/day, lovastatin 20 to 40 mg/day, fluvastatin 20 to 40 mg/day, pravastatin10 to 40 mg/day (Lopez, 2002: 1175). It appears that there is a possibility that all these statins would achieve greater reduction in low-density lipoprotein cholesterol levels if doses were doubled, the limiting factor preventing doubling of doses is an increase in hepatic toxicity and/or muscle toxicity which is observed with increased doses of these drugs (Stein, 2002: 51c).

Table 2.12 Summary of the major drugs used for the treatment of dyslipidemia (Anaizi, 1997: 6)

Lipid-lowering drugs			
Drugs	Mechanism Of Action	Effects On Lipid Profile	Major Side Effects (disadvantages)
Bile Sequestrants Cholestyramine (e.g. 4 g twice daily with meals) and Colestipol (4 or 5 g bid)	⇒⇑Bile excretion ⇒⇑ # of LDLRs ⇒⇑LDL clearance.	⇓ LDL (20%) ⇑TG's (10%) ⇑HDL (4%)	Gastrointestinal problems (bloating, constipation, abdominal pain) ⇓drug absorption ⇓absorption of ADEK vitamins ⇑TG
Niacin (Nicotinic Acid; vitamin B3) (dose titrated over a 10-week period up to 2 g twice or three times a day).	⇒⇓ VLDL production ⇓VLDL ⇓LDL ⇓VLDL =⇓ TG level	⇓TG (35%) ⇓ LDL (25%) ⇓TC (20%) ⇑HDL (20%)	Flushing of face and neck; pruritis; stomach upset. Insulin resistance Hyperuricemia May ⇒hepatotoxicity. (Contraindicated in patients with diabetes mellitus)
Fibric Acid derivative. Gemfibrozil (600 twice daily)	⇒⇑Catabolism of VLDL and IDL ⇒⇓hepatic FFA extraction and ⇓VLDL production	⇓TG (45%) ⇓LDL (10%) ⇑HDL (10%)	Headache and fatigue; Gastrointestinal upset; hepatotoxicity; glucose intolerance; gallstones; myositis May⇒ ⇑ LDL; ⇒⇑free warfarin
HMG-CoA Reductase Inhibitors (atorvastatin-, fluvastatin-, lovastatin-, pravastatin-, simvastatin-) All are fungal derivatives except atorvastatin and fluvastatin Lovastatin and simvastatin are prodrugs	⇒⇓ Conversion of HMG-CoA to mevalonate ⇒ ⇓ hepatic cholesterol production ⇒ ⇓ intracellular [cholesterol] ⇒⇑synthesis of LDLRs ⇒ ⇑ hepatic LDL uptake and catabolism.	All statins significantly ⇓ LDL and TC Effect depends on the dose and the statin used; Atorvastatin⇒ greatest reductions. ⇒ ⇑HDL (8%) It is the only statin that lowers TG's (20%)	Generally well tolerated. Gastrointestinal problems (nausea; bloating, constipation or diarrhea; abdominal pain); headache; rash. May ⇒ myopathy Rarely⇒ hepatotoxicity Monitor Liver values and creatinephosphokinase regularly **Drug interactions**: tacrolimus, Ca-channel blockers, erythromycin, azole antifungals, niacin, gemfibrozil and warfarin. The combination of a statin + tacrolimus) + a Calcium-channel blockers

			may ⇒ rhabdomyolysis

⇓ ≈ Decreased
⇑ ≈ Increased
⇒ ≈ may result in
bid ≈ twice a day
tid ≈ Three times a day
ADEK vitamins ≈ Fat soluble vitamins (Vitamins A, D, E & K)
TG ≈ triglycerides
HDL ≈ high-density lipoprotein
LDL ≈ low-density lipoprotein
LDLR ≈ low density lipoprotein receptors
[] ≈ Concentration
HMG-CoA ≈ 3-hydroxy-3-methylglutaryl-coenzyme A
FFA≈ Free fatty acids

The use of lipid-lowering drugs is associated with the development of side effects and that poses a more frequent cause of referral to the specialist. The most common side effect is indigestion, which can be combated before initiating therapy by starting treatment alongside antacid. Other side effects are diarrhoea, nausea, skin rash, fatigue, worsening of eczema and generalized aches and pains. When such side effects are encountered treatment with lipid lowering drugs should be stopped for 2 to 3 weeks until the condition is completely settled (Bhatnagar, 1998:221).

2.16.5.6 Combination therapy

Single therapy with statins, fibrates, niacin or other drugs has shown to provide benefit in patients with combined dyslipidemia; the benefit can be added by combining different agents (Xydakis & Ballantyne, 2002: 5). Patients whose dyslipidemia is not controlled by dietary modification or a single lipid-lowering drug may respond to combination therapy (Berger & Marais, 2000: 176).

Combined therapy of a statin plus any above-mentioned lipid modifying drug can assist the patients in achieving their lipid goals (Stein, 2002: 53c). Combination of lipid modifying drugs may be more cost effective than high doses of single medications (Baron, 2002: 1261). For severe dyslipidemia, combinations of a statin and a bile acid sequestrant are often required (Berger & Marais, 2000: 176). Combination therapy with a statin plus niacin, in either an intermediate or sustained release form, also yields an additional 10% to 12% decrease in low-density lipoprotein cholesterol levels (Stein, 2002: 53c).

2.16.5.7 Hormone replacement therapy

Coronary heart disease typically occurs 10 years later in women than in men. In addition, the development of coronary heart disease is delayed in women on oestrogen therapy after menopause (Thornton & Holt, 2000: 420). A retrospective study that was conducted over the last decade has established that hormone replacement therapy has shown favourable results in modifying blood lipids in postmenopausal women (Crespo *et al.*, 2002: 1675). Hormone replacement therapy may be combined with other cholesterol lowering drugs to achieve an even more favourable reduction of lipid profile (Davidson *et al.,* 1997: 1186).

2.16.5.8 Other therapeutic modalities

According to Frost *et al.* (1996: 2381), garlic is thought to lower cholesterol level by decreasing the hepatocytes cholesterol synthesis. Fish oil preparations are also used in lowering serum triglycerides in patients with hypertriglyceridaemia (Bhatnager, 1998: 219). The beneficial effect of fish oil results from the reduction in the production of very low-density lipoprotein and plasma homocysteine levels. Fish oil is available in capsules containing 600 mg of Ω-3 fatty acid and the starting dosage is three capsules twice a day with meals (Hoeg *et al.,* 1984: 555).

Plasma exchange in combination with niacin reduces plasma cholesterol levels by about 50% in homozygous familial hypercholesterolaemia over 5 years (Talbert, 1999: 367).

According to Journoud and Jones (2004: 1), fermented yeast rice lowers cholesterol levels moderately compared to other statin drugs, but has the added advantage of causing fewer adverse effects.

An important consideration is to give all the patients, whose risk for coronary heart disease is considered high for pharmacological therapy, aspirin prophylaxis at a dose of 81 to 325 mg/d unless there are contraindications such as haemorrhage, aspirin sensitivity or active peptic ulcer (Baron, 2002: 1258).

2.16.5.8.1 Gene therapy

Gene therapy is the more innovative form of therapy that involves the transfer of genetic material into patients for therapeutic purposes (Baylor College of Medicine, 2002: 1). It can therefore be

regarded as a technique for correcting defensive genes responsible for disease development (Department of Energy, 2003: 1)

It is ideal for use in patients with genetic disorder such as familial hypercholesterolaemia (Gotto, 1996: 31). Genetic disorders results when genes are altered such that they are unable to perform their normal functions (Department of Energy, 2003: 1). It should not be used in dyslipidemic patients whose coronary heart disease is exogenous (Gotto, 1996: 31).

2.15.5.8.2 Surgical modalities

Partial ileal bypass that eliminates the reabsorption of bile acids at the distal portion of the ileum has shown improvement in treatment of severe cases of dyslipidemia (Buchwald *et al.,* 1990: 946). Ileal bypass removes the site of bile acid reabsorption, depleting the bile acid pool and increasing the catabolism of cholesterol. (Talbert, 1999: 367). Liver transplantation, though not first line treatment, has also shown effectiveness in treating severe hypercholesterolaemia (Ahmed *et al.,* 1998: 14).

2.17 CHAPTER SUMMARY

This chapter focused on the management of dyslipidemia. The definition, risk factors, classification and diagnosis of dyslipidemia were discussed. Both the non-pharmacological and pharmacological management of dyslipidemia were fully elucidated. Chapter 3 will describe the concept of managed pharmaceutical care.

CHAPTER 3: HEALTH CARE CONCEPTS

3.1 INTRODUCTION

In the following chapter the focus will be on managed care, pharmaceutical care, drug utilisation review, pharmaco-epidemiology and pharmaco-economics. An introduction to managed care will be conceptualised in paragraph 3.1. A definition of pharmaceutical care, an outline of the forces driving pharmaceutical care, the impact of morbidity and mortality on pharmaceutical care and the concept of pharmaceutical care will be discussed in paragraph 3.2.

In paragraph 3.3 an outline the concept of drug utilisation review, the classification as well as the objectives of drug utilisation review will be presented. The concept of pharmaco-epidemiology will be outlined in paragraph 3.4. Paragraph 3.5 will include a definition of pharmaco-economics and the applications thereof as well as different pharmaco-economic methodologies. The relationship between health care concepts marks the adjournments to the chapter.

3.2 RELATIONSHIP BETWEEN HEALTH CARE CONCEPTS

To create a holistic approach of health care behaviour, stakeholders or decision makers involved in health care and their relationship to each other must be identified and recognised (Bennett *et al.*, 2002: 3). The stakeholders are not individuals but groups with common goals and objectives (Bennett *et al.*, 2002: 3). The different participants in health care are - the patient, health care professionals, insurance companies and the health care industry and they have different approaches and have developed different methods, systems and concepts (Van Mil *et al.*, 1999: 203). Each of these groups views therapeutic alternatives from the group's own perspective and assesses the choices accordingly (Bennett *et al.*, 2002: 3). In addition to that, these stakeholders' activities are interrelated and cannot be viewed in isolation. For instance, a change in patient's prescription can necessitate serious and costly treatment by physicians in a hospital (Draugalis & Coons, 1995: 91).

According to Bennet *et al.* (2002: 3) significant stakeholders must have an interest in health care behaviour, such as public or personal health, product sale, workforce maintenance or profit. The different levels of stakeholders' involvement in health care are displayed in figure 3.1.

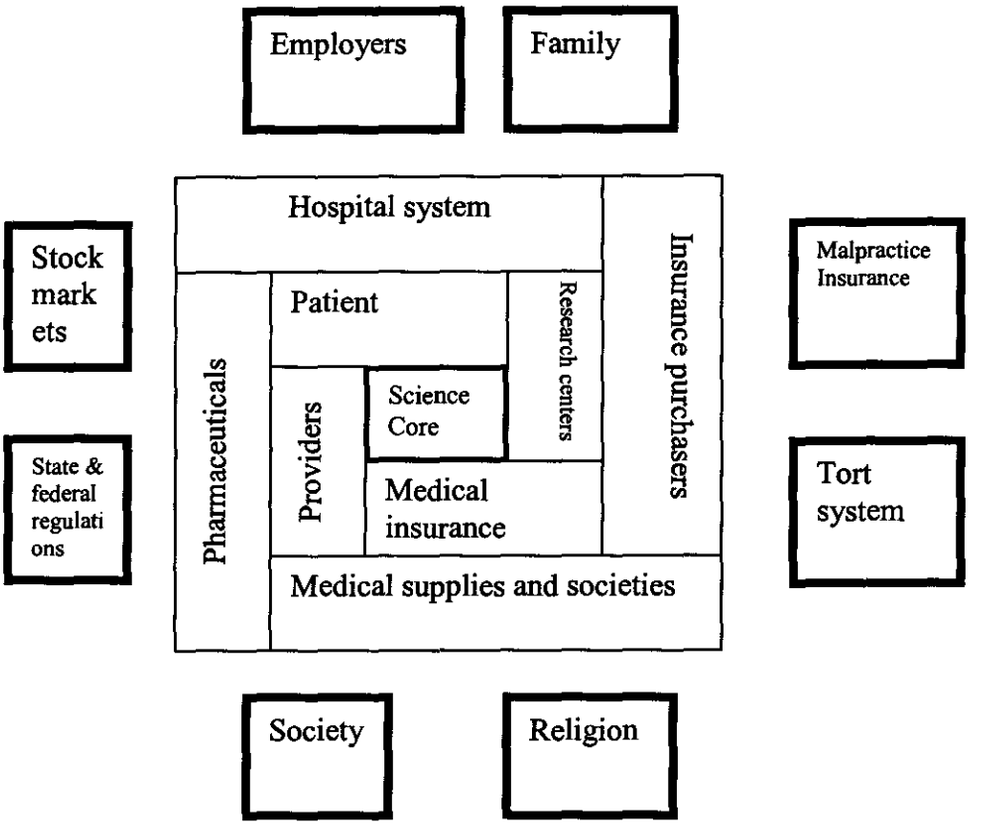


Figure 3.1: Different stakeholders in the health care system (Bennett *et al.*, 2002: 4)

According to the above diagramme, the science core puts in a nutshell all the knowledge developed by evidence-based studies and it represents the science of medicines. Although the science core is placed at the centre of the health care system, it is important to remember that the patient is the customer and his interaction with the science core constitutes the foundation of the health care system (Bennett *et al.*, 2002: 3).

The outer perimeter represents secondary stakeholders, which for the purpose of this paper are divided into hospital systems, pharmaceuticals, medical societies, medical supplies and insurance purchasers (Bennett *et al.*, 2002: 4). There is a major difference between the different forms of care within the secondary stakeholders in a sense that the driver and the subject of the process differ. Managed care, disease management and pharmaceutical care are concepts that are initiated by different groups with specific interest within the secondary stakeholders (Van Mil *et al.*, 1999: 203).

The tertiary stakeholders consist of society, religions, employers, government and federal regulations. It should be borne in mind that higher order (tertiary) stakeholders provide less

direct impact on final therapeutic decisions. It should further be noted in order to improve a patient's quality of life; all the stakeholders must work together (Bennett *et al.*, 2002: 4)

The above paragraph gave a description of the overall relationship of stakeholders in the health care system. The following schematic diagramme shows a clearer vision of the position of pharmaceutical care as a health care concept and its relationship with other health care concepts within the health care system (Serfontein, 2002: 22). Other health care concepts will be outlined below the diagramme. The idea of the figure below is to show how the different health care concepts work together in enhancing patient care.

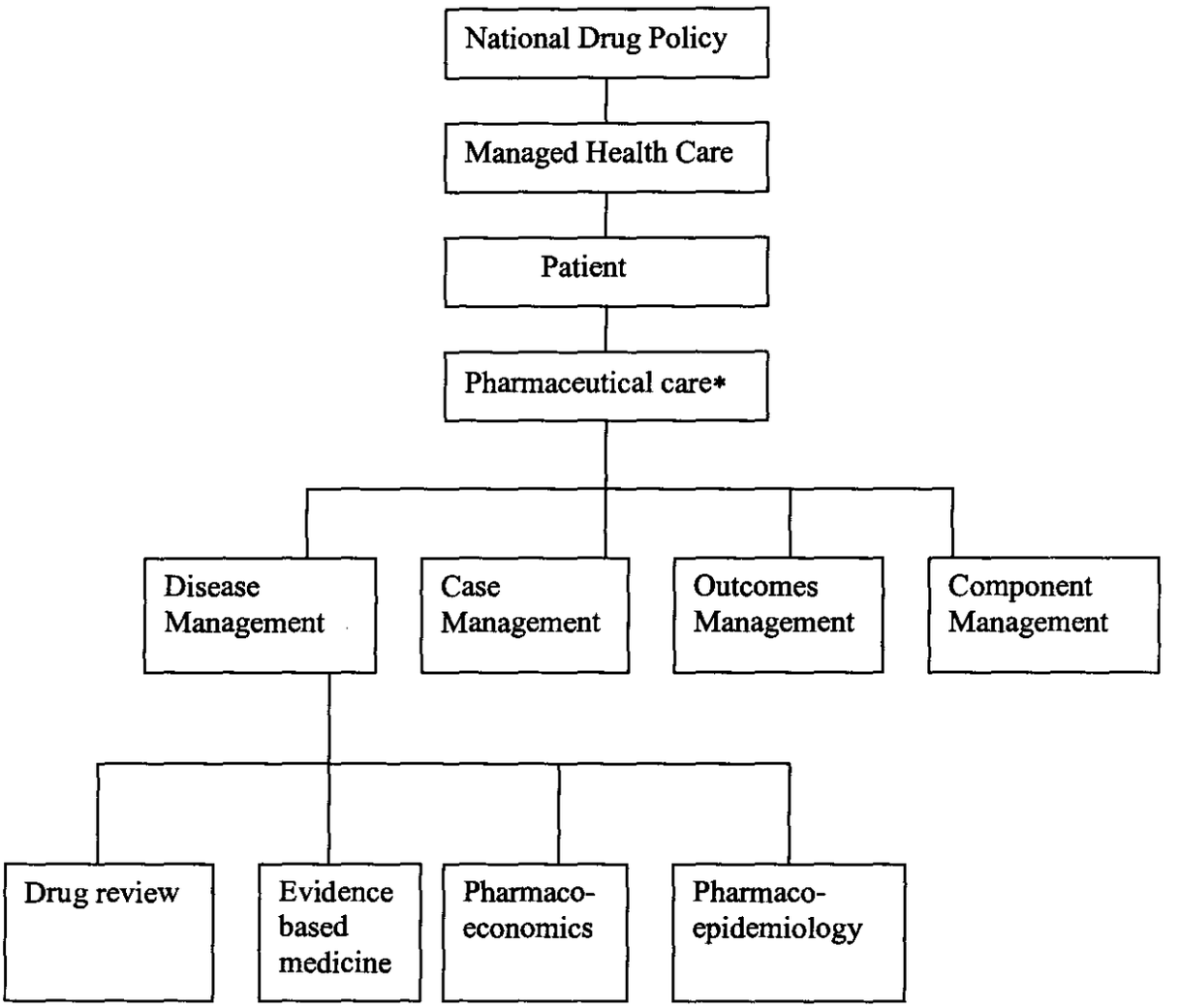


Figure 3.2: Relationship between different health care concepts (Serfontein, 2000: 22).

Managed health care will be described in paragraph 3.3. Refer to paragraphs 3.4 and 3.5 for the descriptions of the terms pharmaceutical care and managed pharmaceutical care respectively.

Reference could be made to paragraphs 3.6, 6.7 and 3.8 for descriptions of drug utilisation review, pharmaco-epidemiology and pharmaco-economics.

Disease management is an understandable, intertwined approach to care and reimbursement based on the disease's natural course, with treatment designed to address an illness with maximum effectiveness and efficiency (Zitter, 1997: 4). It provides a variety of education to change patient behaviour and it co-ordinates physician, hospital and home care (Siefker *et al.*, 1998: 158). The goal of disease management is to decrease health care costs and utilisation over the life of the patient regardless of the short term impact or whether drug benefit costs increase as a result of more aggressive management (Olson, 2002: 253).

Case management is defined according to Al- Assaf (1998: 3) as "*the process by which an individual patient's care is managed by a plan to assure appropriate, cost-effective treatment in a timely approach*". Case management is an element of the utilization management process and it controls the costs of health insurances (Siefker *et al.*, 1998: 4). It is therefore a process which assesses, plans, implements, coordinates, monitors, and evaluates options and services to meet an individual's health care needs through communication and available resources (Powell, 2000: 5).

Component management is a traditional approach to managing health care cost. In component management, the individual health care transaction (the doctor's consultation or procedures) is viewed as a relevant unit of service and cost. The duration of treatment, various transactions, and component categories are analysed to establish norms for unit of cost. The unit of cost of each component is then driven as low as possible through aggressive contracting, utilisation management, case management and other cost controlling techniques. Component management provided one of the very first tools of addressing the increased growth of health care costs (Tremonti, 1998; 1)

Evidence-based medicine (EBM) is defined according to Sackett *et al.* (1996 71) as the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence-based medicine means integrating individual clinical expertise* with the best available external clinical evidence from systematic research. EBM has been progressively establishing itself as a tool for rationalising the use of resources, which lead to lower costs and an improvement in ethical standards (WHO, 2000: 5).

Evidence-based medicine was not accepted initially by all clinicians, but however, over the last decade or more, has largely been accepted as being critical to the development of appropriate medical practice (Murray & Frenk, 2001: 2). Murray and Frenk, (2001: 3) believed that EBM will produce better evidence over time, and has the potential to improve the lives of ordinary people through the development of better policies. As a result, increased prominence is being given to the use of best current evidence in clinical practice, health services and programme management and decision-making (Rodrigues, 2000: 1344).

3.3 MANAGED HEALTH CARE

Managed care will be conceptualised in the following paragraph.

3.3.1 Introduction

In the arena of healthcare, the word "*managed care*" has been used more often during the last decade (Tate *et al.*, 2001: 261) due to factors such as increased cost of annual health care expenditure, which is causing changes in the health care system. The emergence of managed health care organisations (MCO)*, health maintenance organisations (HMO), preferred provider organisations (PPO) and integrated service networks have forced every component of the health care delivery system to re-focus, re-examine, re-evaluate roles, functions and attributes of practice responsibilities (Fincham, 1997: 1).

Managed care dominates the pharmaceutical markets and is initiated by the health care insurers and payers (Mason, 2000: 855). One fifth of the insured population in the United States of America receive care from the health maintenance organisations, and that limits their choices of providers or services in a way (Power, 1996: 201).

3.3.2 Definition of managed care

The word "managed care" lacks a commonly accepted definition (Bootman *et al.*, 1999: 244). However, Al-Assaf (1998: 4) described it as "*a process used to deliver cost-effective care without limiting quality or access. It is achieved by controlled access to providers, comprehensive regulatory controls, emphasis on preventative care, risk sharing, quality and*

* Refer to glossary for individual clinical expertise
* Refer to glossary for the description of MCO, HMO and PPO

behavior modification of both the participants and the providers". It is used to characterise health care plans that incorporate mechanisms designed to review and control cost, quality and use of health care services and to generally limit enrollees' choice of providers to a specified network of health providers. Generally, managed care involves the delivery of health care benefits to a defined population on a prepaid basis (Bootman *et al.*, 1999: 244).

3.3.3 Objectives of managed care

Managed care is the primary force driving the development and expansion of health care strategies which are designed to control the use of medical recourses and to assess the value of pharmaceutical products and services to the consumers (Szeinbach *et al.*, 1998: 1).

The principle of a managed care organisation is to provide quality health care services within a mandate to control costs. Managed care organisations put emphasis on a broader and more integrated view of the cost of patient care and use an outcome based perspective to assess the total cost of treatment rather than to simply assess the pharmacy related expenses (Draugalis, 1995: 89-90).

Pharmacy benefit management companies have been structured to reduce drug costs and be profitable, and not necessarily to evaluate long-term patient outcome, either clinical or humanistic. This means that in some instances patients are given sub-optimal drug therapy and this in return enhances the occurrence of drug-related problems (Fincham, 1997: 3). Therefore pharmacy benefit managers face considerable challenges when making decisions about drug coverage in a managed care organisation (Jon Clouse, 2002: S5111). With that in mind, pharmacy benefits have been carved out in most third parties or managed health care plans (Fincham, 1997: 4).

3.3.4 A South African perspective of managed health care

A new set of activities governing managed health care in South Africa started being used as from the 1st of January 2003 (Council for medical schemes, 2003: 1). According to the Council for medical schemes (2003: 19) managed health care within the South African perspective refers to a diverse range of health care organisational strategies that are aimed at containing cost, improving access and assuring the quality of care provided to the beneficiaries of the medical schemes.

Managed health care was defined in the Regulations published in terms of the Medical Scheme Act (131/1998) as "clinical *and financial risk assessment and management of health care, with a view to facilitating appropriateness and cost effectiveness of relevant health services within the constraints of what is affordable, through the use of rules-based and clinical management based programmes".*

According to the Council of Medical Schemes (2003: 3) the advantages of managed health care include (but are not limited to) the following:

- To promote the use of the most cost-effective health care delivery mechanisms, thereby achieving cost reduction.
- To align the financial incentives of providers and financiers to reduce unreasonable incentives for unnecessary care.
- To strongly establish mechanisms to maintain or improve the quality of health care.
- To encourage the development of standardised treatment protocols.
- To support the members in gaining access to the most suitable treatment interventions.
- To promote an integrated and holistic approach to managing the health care needs of patients.

Application of managed health care to prescribed minimum benefits (PBMs).
Prescribed minimum benefit means the scope of level of benefits that are available to beneficiaries as prescribed by the Medical Schemes Act (131/1998). Any benefit that is offered by the medical scheme must pay in full, without payment sharing or the use of deductibles, the diagnosis, treatment and care costs of the prescribed minimum benefit conditions. However, the co-payment or deductibles may be forced on members who have received their health care from persons other than their designated service providers. (Regulations for Medical Schemes Act (131/1998). Designated health provider is defined according to the Regulations publicised for the Medical Scheme Act (131/1998) as *"a health care provider or group of providers selected by the medical schemes as the preferred provider or providers to provide to its members diagnosis treatment and care in respect of one or more of the prescribed minimum benefit conditions".*

The PBM has been introduced into the South African health care system to avoid incidence where individuals are put at serious financial risk due to unfunded usage of medical services. The list of the PBM consists of disease conditions, which all medical schemes are obliged to cover. In addition to that, the PBM has got the chronic disease list (CDL) that consists of 25

chronic disease conditions, which all the medical schemes are also obligated to pay for. Hyperlipidemia is one of the conditions listed on the CDL (Regulations for the Medical Schemes Act (131/1998).

3.3.5 Conclusion.

Greater opportunities exist within managed care organisations for cutting costs through risk reduction in patients with dyslipidemia, hypertension or recent myocardial infarction (Shalowitz & Heaton, 1996: 72s). Avoiding both under-utilisation and over-utilisation of health care services can enhance the cost effectiveness of primary and secondary prevention of diseases (Al-Assaf, 1998: 18). Elimination of variability in prescribing practices could help with capitalisation on the efficacy of certain agents in preventing morbidity and adverse cardiovascular events in patients with coronary artery diseases (Shalowitz & Heaton, 1996: 72s).

3.4 PHARMACEUTICAL CARE.

The following paragraph will conceptualise pharmaceutical care.

3.4.1 Introduction

Pharmaceutical care means different things to different people, and there are several definitions internationally. Some people think it means any professional activities over and above dispensing. Some think it is a medication review; some, giving prescribing advice to doctors. Still others think it is counselling patients about their medicines. One person's pharmaceutical care is another person's medicine management. Therefore defining pharmaceutical care becomes difficult (Mason, 2000: 854).

The difference in definition is the result of international cultural differences in pharmacy practice, linguistic difficulties, the national and social environment in which health care is provided and the different interpretations of the word "*managed care*" and "*disease management*". All these concepts contribute to the continuous development of the concept of pharmaceutical care internationally (Van Mil *et al.,* 1999: 202).

3.4.2 Why Pharmaceutical Care?

Mortality and morbidity due to drug consumption was estimated to cost 76.6 billion dollars in the ambulatory setting in the United States (Bootman, 1995: 2). Placing special emphasis on dyslipidemia, there is evidence that dyslipidemia is both inappropriately treated and under treated in South Africa (Berger & Marais, 2000: 166). Coronary heart disease continues to be the leading cause of mortality. It is associated with one third of all global deaths annually with an estimated economic burden of more than 100 billion dollars annually (World Health Organization, 2002: 1).

The need for pharmaceutical care varies between patients and clinical situations. The provision of pharmaceutical care can effectively address significant problems within the national's health care system (Lubbe, 2000: 431). The above-mentioned discussion shows that there is a problem associated with the medication use process and pharmacists are showing a positive response to help resolve these problems. The forces of change have provoked the pharmacy profession to alter its societal mission and function (Knowlton & Penna, 1996: xiii). Pharmaceutical care creates a relationship between pharmacists and patients. It improves the professional image of the pharmacist and the acceptance of pharmacists by patients (Lubbe, 2000: 431).

3.4.3 Definition of pharmaceutical care

Looking at literature, pharmaceutical care is a way of dealing with patients and their medications. It is structured as a way in which people should receive and use their medications according to instructions. Depending on the time and the country of origin, different definitions of pharmaceutical care are being used (Van Mil *et al.*, 1999: 202). Some of these definitions will be outlined below. In addition, language difference signifies that the term pharmaceutical care cannot be adequately translated (Mason, 2000: 1).

Pharmaceutical care is a form of professional care and therefore the patient's role as well as the health care provider's role in the delivering of such care is important. Although there are many different separated activities in a pharmacy that are in support of pharmaceutical actions, pharmaceutical care is aimed at interacting with individual patients and it forms part and parcel of those activities (refer to Figure 3.2 (Van Mil *et al.*, 1999: 205).

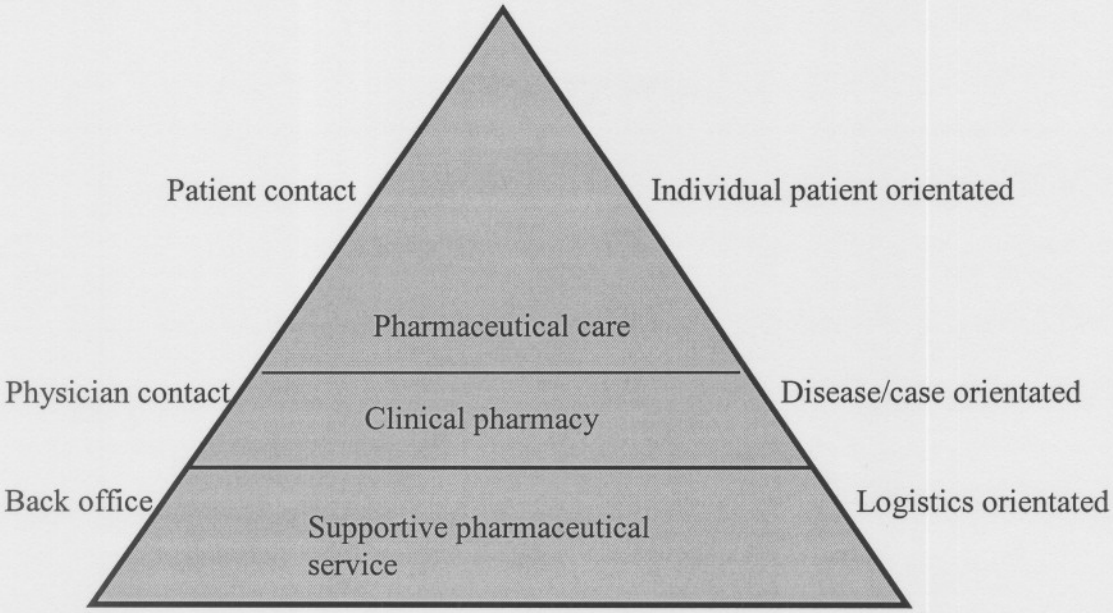


Figure 3.2: Pharmacy activities (Van Mil *et al.*, 1999: 205).

3.4.3.1 The initial definition of pharmaceutical care.

The term pharmaceutical care was used for a number of times for activities that were needed for compounding and dispensing of medicine (Van Mil *et al.*, 1999: 205). Mikael *et al.* (1975: 567) described pharmaceutical care as the care that a given patient requires and receives which assures safe and rational drug usage. In 1980 a new comprehensive definition of pharmaceutical care was stated by Brodie *et al.* (1980: 267) as the determination of drug needs for a given individual and the provision not only of the drug required but also of the necessary services to assure optimal safe and effective therapy. This is what the clinical pharmacists generated as the definition of pharmaceutical care in the United States of America (Van Mil *et al.*, 1999: 205).

3.4.3.2 The definition by Hepler and Strand (1990:539).

Hepler and Strand (1990: 539) defined pharmaceutical care as the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life. The above-mentioned outcomes are the cure of a disease, elimination or reduction of the patient's symptomatology, arresting or slowing of the disease process, or preventing a disease or symptomatology.

Pharmaceutical care is a process where there is cooperation between other health care professionals and the patients in order to implement, design and monitor a therapeutic plan that produces the desired therapeutic outcome for the patient (Plumridge & Wojnar-Horton, 1998: 175). This involves the ability to identify, resolve and prevent potential and actual drug-related problems (Hepler & Strand, 1990: 539). Pharmaceutical care as an important element of health care should be intertwined with other elements such as managed care and disease management (Van Mil *et al.*, 1999: 203). There is a mutual beneficial exchange between pharmacists and patients in which patients grant authority to the provider who gives competence and commitment to the patient (Hepler & Strand, 1990: 539).

3.4.4 Mission of pharmaceutical care

According to Fedder (1996: 110) the mission of pharmacy is described as to serve the society as the profession responsible for the appropriate use of medications, devices and services to achieve therapeutic outcomes. This is in line with the definition of pharmaceutical care by Hepler and Strand (1990: 539). In order to achieve this, patients must be educated on directions for drug use and be advised on any expected manifestation of drug effects.

3.4.5 The impact of drug-related morbidity and mortality on pharmaceutical care

According to Strand *et al.* (1990: 1093), a drug therapy problem is any undesirable event experienced by the patient that is suspected to involve drug therapy and may interfere with the desired therapeutic outcome. It is well known that pharmaceuticals are dangerous substances, but most of their danger and risk are found in their use and not in their chemical composition. It is also claimed that the problems arising from drug usages are the results of the drug itself (Cipolle *et al.*, 1998: 37) but in some cases problems arise from patient non-compliance with a medication regimen (Fincham, 1997: 5).

Fincham (1997: 5) has used different categories to classify forms of noncompliance and these are presented in Table 3.1. Variation exists between definitions of compliance and noncompliance. Compliance is not a patient behaviour; therefore the definition of compliance must be varied to reflect patient behaviour. Patients who are taking multiple therapies may fall in one or more categories of compliance at the same time (Fincham, 1997: 6). Patients who are at high risk of experiencing such drug therapy problems are elderly patients because of their reduced renal

function; they are more defenceless to drugs that are eliminated via the renal function (Cipolle *et al.*, 1998: 102).

Drug-related morbidity is often preceded by drug-related problems. Strand *et al.* (1990: 1095) identified eight categories of drug related problems in addition to those caused by patient non-compliance. These categories were:

Untreated indications. The patient does not receive the drug for his diagnosed indication.
Improper drug selection. The patient is taking the wrong drug in spite of his drug indication.
Sub-therapeutic doses. The patient is getting the right medication but is being given insufficient dosage.
Failure to receive drugs. The patient is not receiving drugs for his condition because of either psychological or economic reasons.
Over dosage. The patient is treated with an excess of the correct drug for his medical condition.
Adverse drug reactions. The patient develops a medical problem as a result of adverse drug reactions.
Drug interactions. The patient develops a disease state as a result of drug-drug, or drug-food interactions.
Drug use without indication. The patient is taking drugs for no valid indication. The patient tends to abuse medications.

Pharmaceutical care has as its focus, a mandate to resolve drug-related problems by establishing a philosophy of practice (pharmaceutical care) and an organisational structure to support this philosophy (pharmaceutical care system) (Plumridge & Wojnar-Horton, 1998: 177).

Table 3.1. Types of noncompliance (Fincham, 1997: 5).

Types of noncompliance	**Description**
Initial non-compliance	The patient receives a written prescription, transfers it to a pharmacy; or has a prescription phoned to a pharmacy, but does not wait or return to pick up the filled prescription. Patients who do not present written prescriptions for filling could be included in this group.
Varying compliance	The patient takes the prescribed or dispensed prescription at a level less than the prescriber or dispenser intended
Compliance	The process of complying with a prescribed regimen precisely as the prescriber and dispenser intended. Compliance may also be referred to therapeutic endpoint, such as normal tension for hypertensive patients.
Hyper compliance	The situation in which a patient takes a prescribed and dispensed medication at a level over or above the recommended and intended dosing interval

In a study conducted by Johnson and Bootman (1995: 1949-1956) it was found that $76.6 billion was annually used for the management of drug-related mortality and morbidity in the ambulatory setting in the United States. The largest proportion of this total cost ($47.4 billion) was associated with hospitalisation due to misuse of drug therapy. The cost associated with the practice of pharmaceutical care was estimated to be $45.6 billion; therefore pharmaceutical care is a suitable strategy in preventing and controlling drug-related morbidity and mortality.

3.4.6 Pharmaceutical care system

Pharmaceutical care system is the system that ensures that pharmacists take responsibility for monitoring the unwanted drug effects and take initiatives in resolving drug-related problems before they manifest to become drug-related morbidities (Segal, 1996: 195). The pharmaceutical care system recognies that the safe and effective drug therapy requires three steps: preparing therapeutic plans for the patients, which include identification of patient specific therapeutic objectives, dispensing a prescription and educating the patient at the same time and monitoring of drug therapy in a system of care that includes patients, pharmacists, physicians and the overall

health care professions (Hepler & Strand, 1990: 539). The pharmaceutical care system identifies that more things still need to be done to ensure best patients outcomes (Segal, 1996: 195).

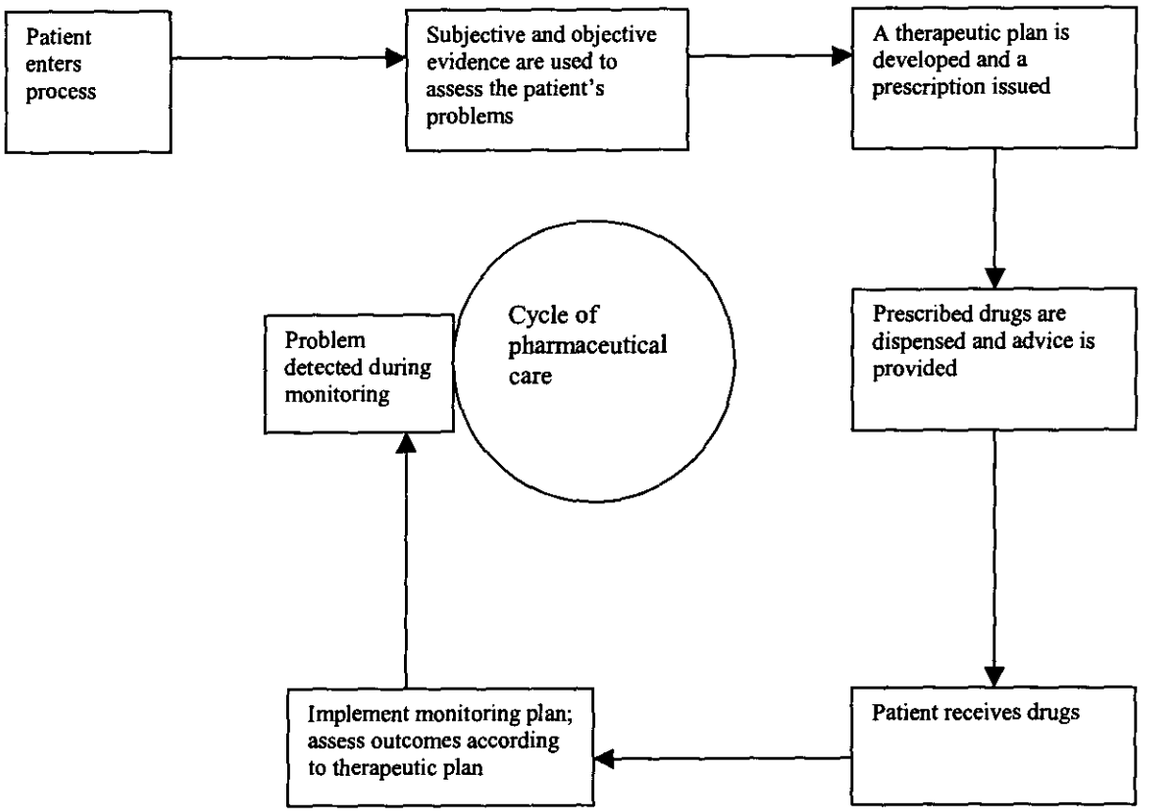


Figure 3.4 Schematic representation of the pharmaceutical care system (Plumridge & Wojnar-Horton, 1998: 177).

3.4.7 Pharmaceutical care practice

Different people have defined pharmaceutical care throughout the literature but it appears that the definition by Hepler and Strand (1990: 539) is more appropriate (Nahata, 2000:25s). It has been defined as the philosophy, a health care service, and a practice (Cipolle *et al.*, 1998: 28). Pharmaceutical care practice is defined according to Cipolle *et al. (*1998: 28) as the practice in which the practitioner takes responsibility for the patient's drug-related needs and is held accountable for this commitment. Pharmaceutical care practice is mutual of individual, practitioner-to-practitioner and practitioner-to-patient relationships (Nahata, 2000:25s).

Pharmaceutical care practice should be the pharmacist's major focus but physicians, nurses, and other health care professionals can also provide it, alone or together with the pharmacist (Cipolle *et al.*, 1998: 28). Pharmaceutical care practice model is described as *"the right thing to do"* for

pharmacy, because it examines whether or not pharmaceutical care practice actually changes health-related outcomes such as mortality, definable clinical events, physiological or biological measure (for example, blood lipid levels, blood glucose levels) that are used as substitute for clinical outcomes (Nahata, 2000:25s).

A new model, which is known as "*primary health care promotion practice*", has been defined by Maguire (2001:2). Maguire (2001:2) defined the above as the active and evidence-based promotion of health, patient empowerment and the facilitation of lifestyle changes to ensure the maintenance of good health, prevention of illness and assurance of disease management. This is a model of multidisciplinary practice. It is about empowering and helping patients to make better use of their medicines and adapting to healthy lifestyles (Maguire, 2001:2). Figure 3.5 shows the schematic representation of the pharmaceutical care practice management system as a component of pharmaceutical care (Cipolle *et al.*, 1998: 29).

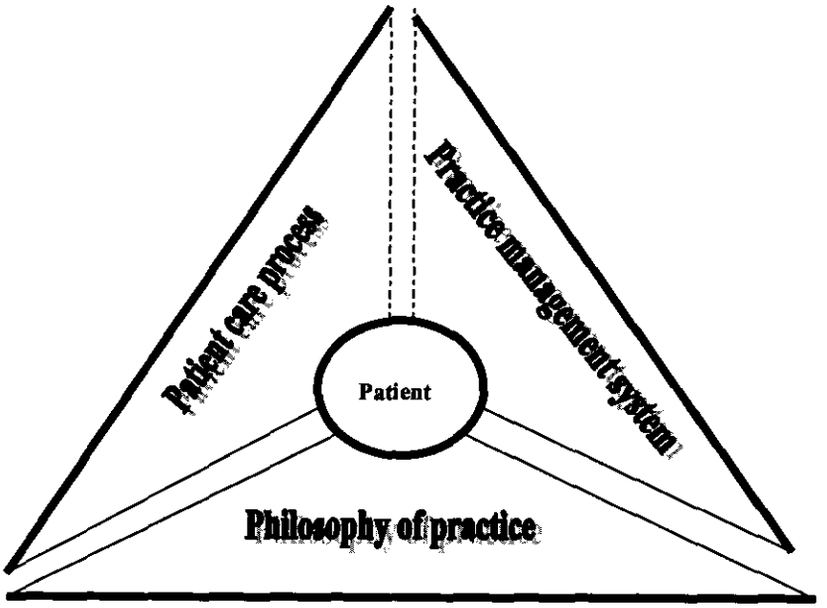


Figure 3.5 Pharmaceutical care practice (Cipolle *et al.*, 1998: 29).

Pharmaceutical care, as a philosophy of practice, consists of norms and expectation of performance that must be accepted by its practitioners. Pharmaceutical care practice is aimed at defining the standard of practice and providing a rationale for those committed to practise it. Based on the above-mentioned discussion, pharmaceutical care practice is defined by its foundation philosophy, dedicated to a patient care process with its responsibilities, and holding all practitioners and interventions through its practice management system (Cipolle *et al.*, 1998: 28).

3.4.8 Patient care process

The patient care process is the rational, organised, comprehensive, problem solving process that allows thorough and consistent provision of quality of care to the patient. It is a care process that is driven by the drug-related needs of the patient. The patient care process is the manner in which the pharmacist fulfils the responsibilities placed by the philosophy of pharmaceutical care practice on a daily basis. Table 3.2 presents the difference between pharmaceutical care process, the philosophy of practice and the practice management system (Cipolle *et al.*, 1998: 121-123).

Table3.2 Characteristics of different practice components (Cipolle *et al.*, 1998: 121 -123)

	PHILOSOPHY OF PRACTICE		PRACTICE MANAGEMENT SYSTEM
	Prescriptive **All practitioners, all patients** **Continuous**		**Predictive** **A group of practitioners. A group of patients** **Future**

As part of the patient care process, the pharmacist plays an important role in cholesterol management (Irons *et al.*, 2002: 1622) because management of dyslipidemia is a critical component of care for patients with existing cardiovascular diseases (Patel & Perez, 2001:12s). The pharmacist contributes to patient care by developing treatment algorithms that target cost effective therapy and extend the benefit of statins to greater percentage of appropriate patients (Lopez, 2002:1177). In addition to the above roles, the pharmacist's role in the management of dyslipidemia includes assessment for drug interactions and suitable drug regimens, provision of education to patient and practitioner, screening for dyslipidemia as well as pharmacological management with lipid lowering drugs (Irons *et al.*, 2002: 1622).

The patient care process allows the practitioner to achieve the objectives of pharmaceutical care (Cipolle *et al.*, 1998: 125). The process involves three major phases:

3.4.8.1. Phase I: Assessment of the patient's drug-related needs

Pharmaceutical care starts with the assessment of the patient's drug-related needs. Drug related-need is described according to Cipolle *et al.* (1998: 77) as "*any concerns, expectations or lack of understanding identified by the patient or practitioners and related to a drug substance*". The primary objective of this step is to ensure that the patient gets the most appropriate, effective, most convenient available therapy and identification of the adverse drug reactions that may arise due to drug therapy (Cipolle *et al.,* 1998: 125).

For patients with dyslipidemia, the practitioner assesses the physical activity as well as diet of the patients (Dambro, 1999: 513). Given the asymptomatic nature of dyslipidemia, the health care team initiates early screening of predisposed or high-risk patients to prevent complications (Irons *et al.,* 2002: 1622). Medications are then indicated if the patient has

- no coronary heart disease and fewer than two risk factors: if low-density lipoprotein level is ≥ 4.8 mmol/l after 6 months of diet and exercise;
- no coronary heart disease but has two or more risk factors: if low-density lipoprotein level is ≥4.1 mmol/l after 6 months of diet and exercise; and
- coronary heart disease: if low-density lipoprotein level is ≥3.4 mmol/l after 6 weeks of diet and exercise (Dambro, 1999: 513).

Refer to table 2.7 and paragraph 2.9.3 for a full discussion of risk categories and therapeutic goals. Medications that are given for patients with dyslipidemia are discussed in detail in chapter 2 under the heading: pharmacological treatment of dyslipidemia.

Once therapy begins, the pharmacists communicate regularly with the patient's physician to provide early intervention (Irons *et al.,* 2002: 1622) and then assess problems that may arise due to the administration of hypolipidemic drugs (Dambro, 1999: 513).

The following are some of the drug-related problems of hypolipidemic drugs in general:

- Cholestyramine – causes complete billiary obstruction and may impede the absorption of fat-soluble vitamins A, D, E, and K.
- Statins – may result in active liver disease and are contraindicated in pregnant patients (Dambro, 1999: 513).

Refer to paragraph 2.16.5 for more detailed information on drug=related problems and drug interactions.

Drug use patterns and patient outcomes are also assessed in order to identify inefficiencies in the clinical management of these patients. Patients are stratified according to low-density lipoprotein cholesterol levels to facilitate the development of a tool that can help the physician make appropriate therapeutic decisions (Patel & Perez, 2001: 14s). This step is completed when the practitioner decides that the patient's drug therapy is appropriate, safe, effective and convenient. If safety is not guaranteed then the practitioner looks into the drug-related problems that are available at the time and the necessary steps that must be taken to prevent such problems in the future (Cipolle *et al.,* 1998: 125).

3.4.8.2 Phase II: Development of the care plan

The care plan represents a joint scheme between the patient and the pharmaceutical care practitioner. The primary objectives of the care plan are to direct the patient's and the practitioner's actions to meet the therapeutic objectives. The care plan contains interventions which will help to resolve drug-related problems due to therapy, accomplish therapeutic goals for medical conditions, and the prevention of new drug-related problems from developing (Cipolle *et al.,* 1998: 125). In this phase, quality improvement proposals are developed in response to findings in phase I and information collected in phase I is now used to develop a multifactorial programme for coronary artery disease (Patel & Perez, 2001: 14s).

According to Cipolle *et al. (*1998: 125), intervention in pharmaceutical care represents the work that the practitioner performs on behalf of the patients and it includes provision of the patient with

- information about particular drug therapies;
- information with regard to non-drug therapy;
- changes in drug regimen;
- instructions for drug administration;
- drugs that the patients requires;
- assistance with regard to drug administration services;
- information from other health care agencies; and
- referrals to other health care practitioners.

In addition to the above, intervention may include: physician education programmes (physicians attend seminars in which results of phase I intervention are presented), treatment algorithms (physicians are provided with specific guidelines to determine the best treatment algorithm for

patients with mild, moderate and severe dyslipidemia), newsletters (they are used to update the physician with the progress of programme and providing feedback on patients' improvements), and academic detailing (this intervention is used to summarise the results of phase I intervention using appropriate and applicable background literature) (Patel & Perez, 2001: 14s-15s).

3.4.8.3 Phase III: Follow up evaluation to determine the patient's actual outcomes.

This is the last step of the patient care process. In this step the patient meets with the practitioner either by telephone or personally in order to record the patient's outcomes. This process ensures continuity of care of the patient (Cipolle *et al.,* 1998: 128). The idea of this step is to

- record actual patient outcomes;
- evaluate progress in meeting therapeutic goals; and
- reassessment for new problems.

For dyslipidemic patients, patient monitoring is performed while the patient is on medication. Cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides and liver enzymes are monitored every 6 weeks until the goal low-density lipoprotein cholesterol level is reached, then every 6 months for patients on statins and niacin. If cholesterol level is less than 200 mg/dl, (5.2 mmol/l) follow up is repeated in 5 years (Dambro, 1999: 513). Evaluations of programme success are based on the comparison of the results from phase I and phase III (Patel & Perez, 2001: 15s). Refer to paragraph 2.15 as well as figure 2.1 and figure 2.2 for the management of dyslipidemia. Refer also to chapter 2 where the management of dyslipidemia is discussed.

The patient care process allows the practitioner to put the philosophy of practice into action for the patient's benefits. Practitioners who provide pharmaceutical care are required to make a comprehensive assessment, individualise a care plan and follow up to evaluate the outcome of care provided (Cipolle *et al.,* 1998: 130).

3.4.9 Pharmaceutical care equation

Achieving the goal of pharmaceutical care requires that patients receive the best drug therapy based on the best available scientific evidence, and utilise a therapy delivery system that certifies error free preparation, appropriate dosage, via the correct route of administration and accurate outcome assessment (Bonal, 2000: 264). According to Walker (1997: 56-59) as referred by

Bonal (2000: 264s) the following equation for pharmaceutical care will be accomplished if best medication reaches the patient for whom it is intended via an appropriate route of administration at the right quantity and right time.

Pharmaceutical care = Pharmacotherapy outcomes + pharmacy service outcomes.

3.4.10 Integrating pharmaceutical care into the health care system

According to Dolinsky and Webb (1996:229) the values and strengths of pharmaceutical care have been understood and well accepted. What still remains to be developed is fitting it into the health care system. Integration of pharmaceutical care is made more complicated by ongoing national debates on both the relative values and roles of specialised medical care and primary health care and their impact as either causes or solutions to the problems that exist in the worldwide health care system.

As health care organisations become more integrated, pharmacists have better access to clinical information needed to perform their responsibilities. The need for a reduction in overall health care expenditure, better access to medical care, and commitment to improved quality and more effective health care all point to the need for pharmaceutical care (Van Mil *et al.*, 1999: 205). This will be better put into practice by the development of a new information system. The system will provide a more effective method of determining patient's outcomes. In this regard, more people will be less affected by financial barriers to health care (Lingle, 1996:65).

3.4.11 Pharmaceutical care and patient outcomes

By virtue of its definition, pharmaceutical care requires an outcomes approach (Maguire, 2001: 1). This shows that pharmaceutical care is aimed at providing the best outcome out of drug therapy (Hepler & Strand, 1990: 539). Kane (1997: 7) describes outcomes as "*the results of several factors which can be classified as risk factors (baseline status, clinical status, and demographic /psychological characteristics) and treatment characteristics (treatment and setting)*". Outcomes measurement as well as outcomes management is about accountability and quality. The process of care determines quality. If the process of care was good enough then the quality is good irrespective of the outcomes that occurred (Rupp, 1996: 134).

Different approaches have been used to classify outcomes. One that is commonly used is the ECHO classification, which stands for economic, clinical and humanistic outcomes (Rupp, 1996: 138). Table 3.3 presents an expanding listing of the elements of outcomes pertinent to the delivery of health care (Fincham, 1997: 2).

Table 3.3. Different types of outcomes pertinent to pharmaceutical care (Fincham, 1997: 2)

Clinical	Therapeutic outcomes
Economic	Cost analyses (Benefit, effectiveness, minimisation, utility)
Humanistic	Quality of life Ethics Patient compliance Adverse drug events

Pharmacists are focusing upon all the above-mentioned outcomes when treating patients in numerous settings of the health care delivery system (Fincham, 1997: 2).

The 5'Ds approach that stands for death, disease, discomfort, disability and dissatisfaction is another classification that helps in the understanding of different outcomes (Rupp, 1996: 138). This classification talks about health from the viewpoint of the provider (Pathak, 1996: 217). It becomes the duty of the health care provider to minimise these five D's and improve patient outcomes (Rupp, 1996: 138).

3.4.12 Reimbursement for pharmaceutical care

Cipolle *et al.* (1998: 267) defined reimbursement for pharmaceutical care as "*the payment for what the pharmacist knows and applies for the benefit of the patient*". The objectives of the reimbursement system for pharmaceutical care are that it will (Cipolle *et al.*, 1998: 284)

- reimburse the practitioner for all the work performed, regardless of whether or not a prescription is involved;
- be based on patient need and not practitioner services, since all other health care practitioners are moving to this method of payment;

- allow for payment in community, hospital, long-term care, or wherever pharmaceutical care is provided;
- be consistent with the practice so that the philosophy of practice and the reimbursement system do not interfere with each other; and
- be consistent with the method used to reimburse other health care practitioners for patient care.

Reimbursement for pharmaceutical care is difficult because patients may not realise that pharmacists can offer more than dispensing services and also may not be accustomed to paying for nondispensing services on the other hand, pharmacists are also not accustomed to requesting payment for nondispensing services (Chen, 2003: 6).

The reimbursement approaches that were considered to meet the above mentioned objectives include: the fee for service, the capitation method and the resource based relative value approach (Cipolle *et al.*, 1998: 284).

Fee for service is a traditional well-established approach that has been used for many years. A practitioner is paid based on the number and type of services provided and documented. A charge is generated each time a service is provided (Cipolle *et al.*, 1998: 284).

The capitation method is a payment method that awards the provider with a fixed amount of reimbursement for a predetermined level of services paid out on a per patient basis for a fixed period of time (Cipolle *et al.*, 1998: 28). Chernew *et al.* (2000: 266-264) conducted a study that compared drug cost growth in a capitated system with that of a managed care systems. It was found that drug cost growth under capitation initially was below growth of other systems but still above targeted rates. The capitation rates rose over time and the amount of risk transferred to physicians declined. Though not in South Africa, cholesterol-lowering drugs were among other drugs that were integrated into the capitation system in 1999 in the above-mentioned study.

The resource based relative value scale system is a very comprehensive system. It has standardised payment levels and policies. It has been broadly applied to include payment for nonphysician practitioner services. The federal government uses this system to pay for a broad range of health care services (Cipolle *et al.*, 1998: 286-287).

3.4.13 Barriers to pharmaceutical care

Although pharmaceutical care as a concept is far-reaching the pharmaceutical world, in daily community pharmacy practice, little has been put into practice so far (Van Mil *et al.*, 2001: 163). Barriers to the provision of pharmaceutical care have been recognised and categorised as follow:

3.4.13.1 Pharmacists' barriers to implementing pharmaceutical care

Past preoccupation of pharmacists with the physical dispensing of drug products and orientation of drug products constitute barriers to the acceptance of pharmaceutical care as a personal philosophy of practice among product orientated practitioners. That is observed particularly in pharmacists who are interested in providing services without taking the patient's outcome into account. Such pharmacists are not likely to be interested in pharmaceutical care (Penna, 1990:545).

Futter and Burton (1998: 2-5) observed the following pharmacist-related barriers in South Africa:

- Pharmacist does not have the time.

Pharmacists complain that it is usually impossible for them to interview each patient because they have more than two hundred scripts per day.

- Pharmacists are busy with other priorities.

Pharmacists reckon that though pharmaceutical care is important, they find it extremely difficult and never implement it. They think that time spent doing records for pharmaceutical care will lead to great irritation of customers. The problems worsen in a pharmacy that has worries of business concerns such as (cash flow, liquidity), because for them losing customers is not an option.

- "The doctor will do the job much easier".

There are a number of tasks, which the pharmacists perceive to be unimportant. The reason for the perception is that they thought doctors should have performed the tasks. Some pharmacists often think that some of the tasks do not really need to be performed.

The pharmacists felt that once they had assessed the patient's needs as well as safety and legality of the prescription and counselled the patient appropriately when supplying the required medicines, they were no longer responsible for how the patient chose to use the given advice. The pharmacists felt that it was impossible for them to be responsible for the patient once they had left the pharmacy.

- "I trust my customers to know what they want".

With regard to requests for medications by the patients, any medication was given with trust. It was assumed that the patients had used the same medication before and it had worked successfully before. The pharmacists felt that they did not have to waste time on things they assumed patients knew.

- "If patients want information they will ask for it".

Pharmacists felt that if patients were experiencing problems they would come to discuss it. Especially problems like the symptoms and side effects of medications that they had been warned of during counselling.

- Lack of assertiveness of pharmacists.

Some pharmacists are shy and they don't want to ask the patients about their medical history. They feel as if they would be digging into other people's private lives. Some are stereotyped.

- Communication difficulties.

Because South Africa is a multicultural country, the majority of patients do not speak English as their first language. Some pharmacists do not monitor patient outcomes to any degree. In most cases, not a single word passes between the patient and the pharmacist. The excuses here again are language barriers (Futter & Burton, 1998:3). In this respect, the recruitment and retention of culturally competent staff are critical. At the very least, the primary languages and cultures of local communities should be reflected in the pharmacy and/or centre staffs (Brown *et al.,* 2003: 76).

- Additional communication is unnecessary.

Pharmacists think that by entering patients' information in the computer during the first patient visit would render further communication with the patients unnecessary.

- Lack of pressure to change from the public.

The pharmacists feel no pressure from the public. "They are happy with their pharmacies, it is a very popular and always busy and the patients seem to have a good relationship with their pharmacists". They do not feel the need to change his setting and implement pharmaceutical care.

- Loss of knowledge through lack of application.

Pharmacists tend to lose their theoretical knowledge and yet their practical knowledge is not satisfying either. They have lost touch with their books. They think that the concept of life long learning does not belong to them. They feel that they are satisfied with how much they know and do not need additional or supplementary studies. Due to their loss of knowledge they cannot pass severely important information to their patients. For instance, if you go with a prescription of warfarin they will not inform you not to take aspirin with it. It is for this lack of knowledge that pharmacists cannot keep up with pharmaceutical care.

- Negative attitude of the pharmacists.

The attitude of the pharmacist directly affects the perceived ease of performing the designated task (Futter & Burton 1998: 4). The success of any concept depends on the people's dedication, determination and belief of the idea. If the pharmacist does not believe in the success of pharmaceutical care then pharmaceutical care will not be practiced and beneficial (Penna, 1990: 547).

- Little interaction with other health care professionals.

Pharmaceutical care must be rendered in cooperation with all those who treat illnesses and prescribe or administer drugs. There are other professionals who are misinformed and will attempt to keep pharmacists in their traditional role. This effort will block the expansion of pharmaceutical care.

- Tasks are too demanding.

Pharmacists feel that providing pharmaceutical care is a very demanding job because patients expect them to be superhuman (to be interested in their complaints, help them quickly and efficiently, dispense the medication, counsel them effectively, update their records and not waste anybody's time).

- Good pharmacy practice guidelines (GPPs) are acceptable in theory but not practically enough.

Some pharmacists feel that the practice criteria proposed in the good pharmacy practice guidelines do not always exhibit an understanding of the practical aspects of retail pharmacy, but were somehow out of touch with reality.

- Reimbursement.

Reimbursement may present a major barrier to the development of pharmaceutical care (Penna, 1990: 546). These are factors following which have contributed to pharmacists' failure to receive payment for pharmaceutical care. These include factors such as:

* *the lack of clear definition of the service for which payment is sought;*
* *the lack of a consensus about the value of the different service;*
* *the lack of pharmacist willingness to provide the service on a consistent basis;*
* *the lack of separation of payment for product and services;*
* *the lack of a documentation system recording the impact of service on patient outcomes;*

3.4.13.2 Pharmacies barriers to implementing pharmaceutical care.

Failure to remove physical barriers inhibiting the practice of pharmaceutical care leads to ineffective provision of pharmaceutical care (Fortner *et al.,* 1999: 2). As a result, physical barriers that impede the implementation of pharmaceutical care have been identified as follows (Futter & Burton 1998: 5-6):

- Computer occupied.

The pharmacists felt that the recording of every over the counter (OTC)) medicine (not on prescription) on the computer is time consuming, and that most of the time the computer is being used for prescription recordings and therefore not available.

- Computer memory may not be large enough to accommodate new software.

The computer software used by many pharmacies does not adequately provide for extensive documentations. With this in mind, pharmacists felt that recording of patient assessment is not feasible because of time constraints and due to the fact that all records are kept on the computer. As a result, new documents will need to be compiled and too much space would be used on hard drives.

- Lack of space.

In most pharmacies, this physical barrier is very difficult to overcome. The pharmacists feel that they have overcrowded the dispensary and they take minimal time to dispense medication.

- Medical aids take up too much time.

Some pharmacists take too much time on the telephone calls for authorisation from the medical aids to ensure that they will get paid for their medications. As a result they do not spend time with their patients.

- Lack of privacy

Most patients prefer a semi-private or private area to receive counselling. In many pharmacies, due to limited space, the addition of a counselling room may not be feasible (Fortner *et al.,* 1999: 2).

- Lack of facilities

The barriers consisted often of lack of time, language, noise and lack of dispensing hatch.

3.4.14 Conclusion

In order for pharmaceutical care to become an effective reality, pharmacists must be willing to accept certain challenges. They must be able to change their paradigm regarding the practice of pharmacy and extend their knowledge base with the focus on individualised care (Fortner *et al.,* 1999: 2).

3.5 MANAGED PHARMACEUTICAL CARE

Managed pharmaceutical care was described in an article of MacKeighan and Larson (1988: 49) as the aspects of managed care that can be undertaken in the pharmacy to improve the patient's quality of care and to control health care resource utilisation that has not been extensively addressed before. According to MacKeigan and Larson, (1988: 49) the following subject areas were identified as aspects of managed pharmaceutical care: clinical services, co-operative arrangements for provision of services, quality assurance and the formulary systems. According to Serfontein, (1998:1) managed pharmaceutical care is aimed at identifying, preventing and resolving medicine related problems in a cost-effective manner.

3.6 DRUG UTILISATION REVIEW (DUR)

Drug utilisation review will be described in the following paragraph.

3.6.1 Introduction

There has been a remarkable increase in the usage of drugs in medical practice. There has, however, been increasing concern that much prescribing may be unnecessary, inappropriate, or irrational (Johnson & Bootman, 1995: 1949). Drug utilisation review has emerged in response to the needs to control both cost and the quality of medication usage (Chriscilles *et al.,* 1996: 172), and it has been adopted as a means for balancing cost-containment and quality in prescription drug programmes (Kreling & Mott, 1993: 414). It is used in conjunction with drug use evaluation in containing costs in both the prescriptions and medical benefit plans (Anon, 2003 (a): 1).

3.6.2 Definition of drug utilisation review

Drug utilisation review has been defined and described in various ways, and there is confusion about what it is or is not. Perhaps confusion is brought about when drug utilization review (drug use review studies) and drug utilisation programmes are viewed as one concept (Stolar, 1978: 76). Drug utilisation studies have been defined by the World Health Organization (WHO) as "the *marketing, distribution, prescription and use of drugs in a society with special emphasis on the resulting medical, social and economic consequences"* (WHO, 1977).

The concept drug utilisation programme is defined according to Stolar (1978: 77) as " *an authorized, structured, ongoing system for improving the quality of drug use within a health care organization by evaluating it using predetermined standards and initiating efforts to correct patterns of drug use which are not consistent with these standards*". The goal of a drug utilisation review programme is not the collection, analysis and reporting of quantitative and qualitative information only, but rather in addition to that information of corrective and educational feedback to the prescriber in order to re-evaluate and improve drug use (Kreling & Mott, 1993: 417).

3.6.3 Why drug utilization review?

The principal aim of drug utilisation research is to facilitate the rational use of drugs in populations (WHO, 2003: 9) and at the same time to reduce needless expenditure and improve the quality of care (Chriscilles *et al.*, 1996: 172).

Drug utilisation studies can be used to ensure that prescriptions are appropriate, medically correct and are aimed at reducing drug-related problems (Anon, 1999: 1). That is achieved through the detection of drug interactions, contraindications, overdoses, over utilisation and under-utilisation (Monane, *et al.*, 1998: 2). It also serves to educate prescribers, dispensers and other health care professionals on the appropriateness of care provided hence enhancing the quality of patient care (Anon, 1999: 1). Savoie and Kazanjian (2001: 95- 100) applied pharmaco-epidemiological principles to study the utilisation of lipid-lowering drugs in men and women. The results indicated that, 74.7% of individuals on statins had no reported history of coronary heart disease. Women without coronary heart disease formed 23.1% of statins recipients and were aged 70 and over.

Drug utilisation review is a major component of most quality assessment processes for drug therapy (Blackburn, 1993: 14). The development of explicit criteria, evaluation of prescribed medicines against the criteria, and implementation of corrective actions characterise this process and it can also be established whether the prescribing patterns have not been appropriately followed (Chriscilles *et al.*, 1996: 172).

The following facts that were observed in America put special emphasis on the need to implement drug utilisation review:

- Eight to ten per cent of hospital admissions are associated with drug interactions.

- Fifteen to twenty per cent of doctor visits are associated with medication problems.
- Drug interactions cause over 125 000 deaths each year (Anon, 2003 (a): 1).

Of total health care expenditure in the United States, inappropriate dispensing and patient non-compliance with their drugs cause $100 billion (Anon, 2003 (a): 1). Drug utilization research does not necessarily provide answers, but it contributes to rational drug use (WHO, 2003: 9).

Below are some of the ways that DUR can help with above-mentioned problems:

- It can be used to estimate the number of patients exposed to specified drugs within a given time period.
- It can describe the extent of drug use at certain moments and/or in certain areas.
- Researchers can estimate to what extent drugs are properly used, overused or underused.
- It can determine the pattern or profile of drug use and the extent to which alternative drugs are being used to treat particular conditions.
- It can be used to compare the observed patterns of drug use for the treatment of a certain disease with current recommendations.
- It can be used in the application of quality indicators to patterns of drug utilisation.

3.6.4 Classification of drug utilisation review.

Drug utilisation can be classified as quantitative and qualitative (Sacristan & Soto, 1994: 300; Stolar, 1978: 76).

3.6.4.1 Qualitative drug utilisation review.

Qualitative drug utilisation review studies are multidisciplinary operations (Stolar, 1978: 76), which include collecting, organising, analysing and reporting information on the rationality of drug usage (Kreling & Mott, 1993: 416; Stolar, 1978: 76). The main aim of qualitative DUR is to determine the suitability of drug consumption (Ferreira, 1999: 1; Sacristan & Soto, 1994: 300). Qualitative DUR requires the establishment of criteria (Ferreira, 1999: 1; Stolar, 1978: 76; Kreling & Mott, 1993: 416; Sacristan & Soto, 1994: 300) (predetermined elements against which aspect of the quality, medical necessity and appropriateness of medical care may be compared) to provide an evaluation of the quality of drug use (Kreling & Mott, 1993: 416).

3.6.4.2 Quantitative drug utilisation review.

Quantitative DUR studies involve collecting, organising and displaying estimates or measurements of drug use. The results of these activities usually take the form of absolute or relative quantitative data describing the use of drug use within specified time frames (Kreling & Mott, 1993: 416). Quantitative data are generally considered suggestive, not conclusive, with respect to quality of drugs (Stolar, 1978: 76).

Quantitative DUR studies have been used to (1) ascertain the quantities of drugs consumed in a specific geographical area; (2) investigate the development of drug utilization over time; (3) compare drug consumption in different geographical areas; (4) identify possible over- and under-utilisation of drugs; (5) estimate the utilization according to variables such as age, sex, social classes; and (6) estimate the prevalence of particular illnesses based on consumption of drugs utilised in their treatment (Baksaas & Lunde, 1981: 5).

3.6.5 Types of DUR studies

DUR may be prospective, retrospective or concurrent (Knapp *et al.,* 1974: 650).

Prospective DUR provides evaluation of drug therapy at the point of sale and has the greatest chance of benefiting the patient before the patient is treated (Knapp *et al.,* 1974: 650). It expects and avoids problems that might occur in a particular patient prior to consumption of the drug (Ferreira, 1999: 1). This type of review is based on professional judgment of pharmacists or on computer assisted alerts (Anis *et al.*, 1996: 3). This review monitors therapeutic appropriateness, over- and under utilisation, appropriate use of generic products and screening for potential adverse drug reactions, interactions and contraindications (Anon, 2003: 1).

Under the prospective drug utilisation system, pharmacy providers who perform pharmaceutical care services have the capabilities of billing their services and responding to prospective drug utilisation review alerts in the same real time of claim submission, though not in South Africa. This system will flicker more pharmacists to take advantage of billing for pharmaceutical care systems (Anon, 2003: 1).

Concurrent DUR on the other hand, involves evaluation of drug therapy and intervention, while the patient is undergoing therapy. Effective review of this type is limited to certain institutionalised patients (Knapp *et al.,* 1974: 650).

Retrospective DUR is a structured ongoing initiative that interprets patterns of drug use in relation to predetermined criteria and attempts to minimise inappropriate prescribing (Soumerai & Lipton, 1995: 1641). Retrospective DUR gathers information and detects problems in a population after they have occurred (Ferreira, 1999: 1; Sacristan & Soto, 1994: 300). It is the form of drug use review presently most frequently practised (Knapp *et al.,* 1974: 650). Most private sector drug benefit programmes implemented retrospective DUR programmes. However, it has not been shown to improve clinical outcomes or reduce the rate of potential prescribing errors (Hennessy *et al.,* 2003: 1494).

3.6.6 The development of criteria in DUR.

Every aspect of DUR requires valuable judgements on issues such as, what data to collect, when to collect the data, who should collect the data, and how to manipulate the data. For drug utilization to be fully comprehended, criteria and norms of carrying out a utilization study should be understood (Knapp *et al.*, 1974: 648).

Knapp *et al.* (1974: 648) defined norms as numerical and statistical measures that represent observed performance in the real world and it may reflect practice as it is. Criteria are defined as *"predetermined elements against which aspects of quality of a medical service may be compared"*. Criteria are established as a means of attaching value to utilisation data. Criteria can be classified as follows (Knapp *et al.* 1974: 648)

3.6.6.1 Absolute criteria.

Absolute criteria are established prior to data collection and function as thresholds or limits. This means that when an element of data is compared to an absolute criterion, it either passes or fails. Relative criteria can be seen as a judgment to the precise boundary (Knapp *et al.*, 1974: 650).

3.6.6.2 Relative or statistical criteria.

According to Knapp *et al.* (1974: 649), relative criteria may be established in relation to the distribution of measurements. It is a judgment as to where to set the region of acceptance and rejection (Knapp *et al.*, 1974: 650).

3.6.6.3 Pragmatic criteria.

Pragmatic criteria are criteria established to judge whether the results are practically or clinically significant (Knapp *et al.*, 1974: 650).

3.6.6.4 Objective or subjective criteria.

This criterion is the cornerstone of scientific method. These sets of criteria are so explicit or specifically defined that any judgment using them can evaluate a given data set identically. Objective measures permit replicable measurements by different judges and by the same judge at different times. This classification system may be used in conjunction with other classifications, in other words, the relative or absolute criteria may be established subjectively or objectively. Subjective or objective criteria judges as to what dimensions and what cut-off points are to be established (Knapp *et al.*, 1974: 649-650).

3.6.6.5 Content based criteria.

Content based criteria focus on factors such as structure, process and outcome. Structural criteria include the demographic and ecological characteristic of the unit of observation (e.g., the set of criteria related to the quality of drug use might involve the prescriber's educational background, speciality training and years of experience etc.) (Knapp *et al.*, 1974: 649). Process criteria refer to the what, the where, the when and the how of care. These represent the instrumental elements of health care. Outcome criteria measure the end results of patient care. Though they are the most difficult to develop, they are important in measuring the effect of the element being evaluated on the total health and the well-being of the patient (Knapp *et al.*, 1974: 650).

3.6.7 Drug utilisation metrics

Drug utilisation metrics such as defined daily dose (DDD), prescribed daily dose (PDD), and unit of presentation of volume will be described in the following sub-paragraphs.

3.6.7.1 Defined daily dose (DDD)

The defined daily dose is the assumed average maintenance dose per day for a drug used for its main indication in adults (Blackburn, 1993: 17; WHO, 2003: 38). The defined daily dose is the unit of measurement (WHO, 2003: 38) therefore the volume of drug sold (reflected in the DDD) usually does not correspond to that of the drugs prescribed because some drugs are often sold without prescription (Sacristan & Soto, 1994: 301). Doses for individual patients and groups of

patients will often differ from the DDD, as they must be based on individual characteristics (e.g. age and weight) and pharmacokinetic considerations (WHO, 2003: 38).

Data from drug utilisation studies are ideally presented as the numbers of DDDs per thousand inhabitants per day (Sacristan & Soto, 1994: 301). Prescription data presented in DDDs per 1000 inhabitants per day provides a rough estimate of the proportion of the study population treated daily with a particular drug or group of drugs (WHO, 2003: 38). This measurement allows comparison between different time periods and between different geographical areas (Sacristan & Soto, 1994: 301; Blackburn, 1993: 17).

When the drug is used for inpatients, DDDs per 100 bed-days may be applied. For drugs that are used for short periods (anti-infectives), the figures are presented as numbers of DDDs per inhabitant per year. The DDDs per inhabitant per year may give an estimate of the average number of days for which each inhabitant is treated annually (WHO, 2003: 38).

3.6.7.2 Prescribed daily dose (PDD)

The prescribed daily dose is defined according to Sacristan and Soto (1993: 301) and the World Health Organization (2003: 39) as "the *average daily dose prescribed as obtained from the representative sample of prescriptions.*" The PDD gives the average daily amount of the drug that is actually prescribed. Pharmaco-epidemiological information (e.g. on gender, age and whether therapy is mono- or combined) is also important in order to interpret a prescribed daily dose (WHO, 2003: 39).

The PDD can vary according to illness treated and national therapeutic traditions. For instance the PDD for Asians and Africans are lower than those of Caucasians. It should be noted that the PDD does not necessarily reflect drug utilisation. This is because some of the prescribed medications are not dispensed, and the patient does not always comply with the prescribed regimen (WHO, 2003: 39).

3.6.7.3 Other units for presentation of volume

Some units such as the number of packages or tablets and number of prescriptions are also used to quantify drug utilisation but then they have certain disadvantages. For instance, numbers of prescriptions do not accurately reflect total use of medications, unless total quantities of drugs

per prescription are also considered. However, prescription counting is valuable in measuring the frequency of prescriptions and in evaluating the clinical use of drugs. Although these units of measurements are useful in making national comparisons, it should however be noted that none of these volume units is usually applicable in cross-national comparisons (WHO, 2003: 39).

3.6.8 Conclusion

The concomitant use of drug utilisation review with pharmaco-economics can result in more cost effective utilisation of medicines and a better utilisation of pharmaco-economic methods, both of which contribute to a more rational use of drugs (Sacristan & Soto, 1994: 299).

3.7 PHARMACO-EPIDEMIOLOGY

3.7.1 Introduction

Epidemiology is the study of the occurrence and transmission of diseases in human population therefore epidemiological studies of drug use make use of the methods and statistical measures to study the occurrence and distribution of drug use and its associated problems (Waning & Montagne, 2001:1&2). Due to growing concern on the frequency and preventability of drug-induced illnesses, pharmaco-epidemiology has emerged (Anon, 2003 (c): 1). Pharmaco-epidemiology is derived from the Greek words (*pharmakon, epi, demos and logos*) meaning the study of poison (drugs) in a population (Chauvin *et al.*, 2002: 455). It sums up two different areas: pharmacology (the study of interactions between drugs and living organisms and epidemiology (defined above) (Ley, 2001: 386).

3.7.2 Definitions.

Pharmaco-epidemiology is defined according to Chauvin *et al.* (2002: 455) as "*the application of epidemiological reasoning, methods and knowledge to the study of the uses and effects (beneficial and adverse) of drugs within a large consumer population*". A more recent and clearer definition of pharmaco-epidemiology was put forward by the World Health Organization (2003: 8) international working group for drug statistics methodology as the study of the use and effects/side-effects of drugs in large numbers of people with the purpose of supporting the rational and cost effective use of drugs in the population thereby improving health outcomes.

3.7.3 The concept of pharmaco-epidemiology.

Initially the basic focus of pharmaco-epidemiology was on the safety of individual drug products (pharmacosurveillance), but now it also includes studies on their beneficial effects (WHO, 2003 : 9). As a result, pharmaco-epidemiology focuses on pharmaceutical care outcomes and the identification of potential and realised drug-related problems. Though it has been used to examine drug epidemics, it can also be used to study illicit drug use. The idea of pharmaco-epidemiology is to measure the source, diffusion, use and effects of drug use in a population and to determine the frequency and distribution of drug use outcomes in that population (Waning & Montagne, 2001:4&5).

3.7.3 Pharmaco-epidemiological research methods.

One of the most challenging areas of research in pharmaco-epidemiology is to understand why individuals respond differently to drug therapy (Maitland-Van der Zee *et al.,* 2000: 121). Because of that, pharmaco-epidemiology has developed three kinds of studies: (1) studies on drug effectiveness on large populations monitored during long-term periods; (2) studies of adverse drug reactions with quantification of risk; and (3) drug utilisation studies to assess the characteristics of drug prescription or consumption according to evidence-based data (Ley, 2001: 386).

The above-mentioned studies are conducted through the use of different designs, i.e. retrospective surveys, cohort surveys and case control studies (Figure3.5) to mention but a few (Chauvin *et al.,* 2002: 456). A brief description of different types of pharmaco-epidemiological study methods follows below (Waning & Montagne, 2001: 5).

- Cross-sectional study: A prevalence survey of health and illness in the population at one point in time.
- Case-control study: A retrospective analysis comparing subjects with the condition (referred to as cases) to those without it (referred to as controls) with respect to possible risk of getting the disease or causative factors for the diseases
- Cohort study: An incidence study that is usually prospective or longitudinal. This incidence study follows a population free of health problems over time, examining subsequent development of problems and factors associated with them.

- Clinical trials: An experimental approach that tests the value of a new treatment or intervention and compares it with the standard treatment or a placebo.

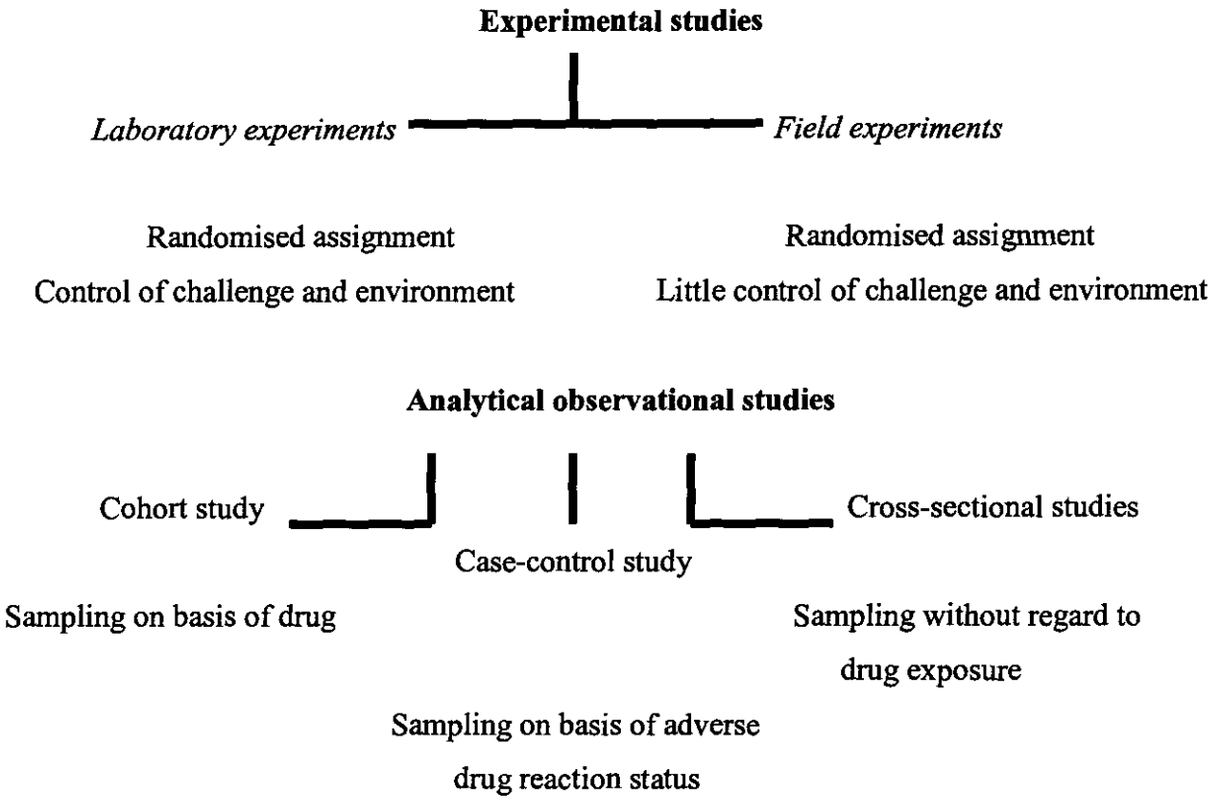


Figure 3.5 Types of epidemiological studies (Chauvin *et al.*, 2002: 456).

3.7.4 Application of pharmaco-epidemiology.

Thus pharmaco-epidemiological studies evolved as an imperative tool to determine the utilisation of drugs amongst people of varied age groups. It can also be used to determine the prescribing practices of hypolipidemic drugs.

In a population-based, case-control study by Meier *et al.* (2000: 3205) whose objective was to determine whether statins, fibrates, or other lipid lowering drugs were associated with reduced bone fracture risk, it was found that current exposure to statins is associated with a decreased risk of fracture in individuals aged 50 years and older.

Eaton *et al.* (2002: 1389) quantified the effect of statins on 1-year mortality, hospitalisations and decline in physical functions among patients with cardiovascular disease aged 65 and older in nursing homes. It was found in that retrospective cohort study that the prevalence of statins was 2.6%. Statin use was varied according to gender, age, comorbid condition, medication use, and

cognitive and physical function. It was concluded that statin therapy improved clinical outcomes, including reduction in 1-year all cause mortality. Statin therapy also decreased death and hospitalisation in older population with cardiovascular diseases.

3.8 PHARMACO-ECONOMICS

In this paragraph, the definition, applications, methods of calculating costs, barriers and basic methodologies of pharmaco-economics will be discussed.

3.8.1 Introduction

In order to get the bigger picture of pharmaco-economics, the word cost should be described. The cost of drug therapy is not the same as the price of a drug product. The cost of a product or service is the monetary value of resources consumed in its production or delivery. Resources usually include labour, equipment and supplies (Larson, 1996: 46). The definitions of different types of cost as described by Larson (1996: 46) are presented below:

- *Direct cost- involves a transfer of money, e.g. money that is exchanged for the use of a resource.*
- *An indirect cost is an unpaid resource commitment. No money was exchanged.*
- *Fixed cost is the cost that is not affected by the volume of output. It does not change with an increase or decrease in output.*
- *Variable cost is cost that varies with output.*
- *Average cost is the resource consumed per unit of output.*
- *Marginal cost is the change in total cost of producing one additional (or one less) unit of output.*
- *Opportunity cost is the amount that a resource could earn in its highest valued alternative use.*

Pharmacological therapy becomes a successful and cost-effective practice when medicines are rationally prescribed and appropriately utilised. However, when these fundamentals are not met, patients will be denied the full benefits of therapy and that will result in an increase in cost of an overburdened health care system (Munroe *et al.*, 1997: 114). The overburdened health care systems have forced health systems to focus on cost containment. This has shifted the emphasis from acute care to ambulatory care and from disease management to disease prevention. As a

consequence, providers are pressured to decrease cost while maintaining or improving quality of health care (Ellis *et al.*, 2000: 1508).

The treatment of coronary heart diseases places a substantial financial burden on health care resources (McMurray, 1999: 2). This is because the cost of coronary heart disease is the sum of three components: (1) the medical resources used to treat the illness, (2) the nonmedical resources associated with it, and (3) lost productivity due to illness (Larson, 1996: 46). As a result, pharmaco-economic analysis of the management and impediment strategies for coronary heart diseases is a valuable tool for comparing the cost-effectiveness of new medical interventions allowing health care decision makers to contain cost by choosing those interventions that are most efficient (McMurray, 1999: 2). This is imperative especially because intervention to lower cholesterol levels with drugs involves large populations of patients and potentially high costs (Johannesson *et al.*, 1997: 332).

3.8.2 Definitions of pharmaco-economics

In 1996 Rajagopalan *et al.* (1996: 1298) defined pharmaco-economic studies as "*studies that are used to identify, measure, and compare the benefit of the interventions and the costs of various health care methods*". Health care methods include drug therapies, surgical procedures and diagnostic tests. Pharmaco-economics have also been defined according to Mauskopf (2001: 2) as "*the measurement and presentation of a comprehensive set of outcomes that describes the consequences of the use of a new drug*".

Differences between clinical trials and pharmaco-economics:

Pharmaco-economics includes exceptional issues that differentiate it from clinical studies, despite the consequences of what is being studied (Rajagopalan *et al.*, 1996: 1298). Unlike clinical trials, pharmaco-economics as a health care intervention can be assessed only if outcomes are measured and considered (Bootman *et al.*, 1999: 7). Table 3.4 shows the differences between pharmaco-economic studies and clinical trials. In pharmaco-economic studies, patients are studied in "real life" situations. They may take simultaneous medications. However, that would be restricted in a controlled clinical trial (Rajagopalan *et al.*, 1996: 1298).

Table 3.4 Differences between pharmaco-economic studies and clinical trials (Rajagopalan *et al.*, 1996: 1298).

[redacted]	[redacted]
An outcome evaluation (no hypothesis is tested)	A trial in which specific hypothesis is tested
Evaluates cost effectiveness	Evaluates efficacy and safety
Predominately observational data collected.	Dictates study procedure
Concentrates on cost and effectiveness data	Concentrates on efficacy and safety
"Real-life" study	A controlled trial

3.8.3 Reasons for studying pharmaco-economics

The major reason for studying pharmaco-economics is to have the ability to estimate and understand the full impact of a new therapy. This impact will be on the individuals' health and safety but also on their utilisation of health care services and the cost of health care, on their quality of life and functional status, on their relatives, friends and society as a whole (Mauskopf, 2001:2-3). A pharmaco-economic study is basically intended to apprise the decision maker (whether it is the patient, the family, the provider, a third party payer, or the policy maker) about the balance between the cost and effects of a new health care practice in comparison with an established method (Rajagopalan *et al.*, 1996: 1298). For all these reasons, it is crucial that all health care decision makers have as much education in pharmaco-economics as possible (Mauskopf, 2001:2-3).

3.8.4 Applications of pharmaco-economics

Economic analysis can be used for a variety of purposes in a managed care setting. One purpose is the use of pharmaco-economic studies to drive treatment protocols thereby influencing how medications are used in a managed care programmes (Draugalis, 1995: 92). Pharmaco-economics is also used in managed care plans to manage drug benefit structures (Bootman *et al.*, 1999: 254). Pharmaco-economic data can also be used as a tool to determine the amount of patient co-payments and can provide a basis for allocation of limited health care resources (Draugalis, 1995: 92).

3.8.5.Pharmaco-economic methodologies

Different methodologies that have been used to conduct pharmaco-economic analysis are described in detail in the following paragraphs.

3.8.5.1 Cost minimisation analysis

This is the most limited type of pharmaco-economic analysis. It is used to compare the costs of alternative treatment and select the least costly alternative based on the assumption that the alternative treatment strategies are equally effective (Bootman *et al.,* 1999: 10). A more sophisticated version of cost minimisation analysis is the ability to try to measure the net cost of alternative treatment by including other health costs that are associated with the treatment decision (McCombs, 1998: 114s).

A cost minimisation study that estimates the benefits of lowering cholesterol using data from the 4S (Scandinavian simvastatin survival study*), simvastatin therapy, produced a 10% decrease in length of hospital stay, a 26% reduction in number of hospitalisation events, a 31% reduction in hospital costs and a 34% reduction in total hospital days. As a result of these savings, though not in South Africa, the cost of simvastatin was reduced (Pedersen *et al.,* 1996: 1796).

3.8.5.2 Cost-effectiveness analysis

Cost-effectiveness analysis is an analysis that compares the clinical effects of alternative therapies (mortality and morbidity to their net costs (McCombs, 1998: 112s). In other words, it is an analysis that helps in the selection of alternative drug therapy that yields the best outcome (Bootman *et al.,* 1999: 11). The limitation of this approach is that all the years of life gained are taken from the quantity of life perspective and quality of life lived is not considered (McCombs, 1998: 114s). In this analysis, input is measured in monetary terms and output is measured in natural units for example mmHg in high blood pressure (Bootman *et al.,* 1999: 11).

Huse *et al.* (1998: 1357) calculated the cost-effectiveness of statins in both primary and secondary prevention of cardiovascular heart diseases. It was found that all statins (simvastatin, fluvastatin, atorvastatin, lovastatin, pravastatin) included in the study were cost-effective in prevention of cardiovascular heart diseases and atorvastatin was the most cost-effective. In the study by Johannesson *et al.* (1997: 332), simvastatin was cost-effective in patients with coronary heart disease among both men and women at the ages (from 35 to 70 years) and cholesterol level studied (<5.2mmol/l to >6.2mmol/l).

3.8.5.3 Cost benefit analysis

According to McCombs (1998: 114s) cost benefit analysis is the most difficult of all the pharmaco-economic methodologies and it requires that both the input and the output of the interventions must be measured in monetary terms. The difficulty is brought by the fact that all the benefits and the costs associated with the intervention should be included in the programme. It is primarily used to help in the allocation of limited health care resources to health care programmes (Bootman *et al.,* 1999: 11).

3.8.5.4 Cost utility analysis

During cost utility analysis the consequence of the intervention is measured in terms of both quality and quantity of life and the input is measured in monetary terms (Bootman *et al.,* 1999: 11) and the cost per quality adjusted life year has to be developed before the approach becomes gold standard in pharmaco-economics (McCombs, 1998: 114s). Cost utility analysis helps in allocation of funds to health care programmes. However; there is unavailability of reliable and sensitive instruments that can detect changes in drug treatment (Bootman *et al.,* 1999: 11). Different methods like visual analogue scale and patient's questionnaires have been invented for measuring health-related quality of life (McCombs, 1998: 116s).

3.8.7 Application of pharmaco-economics in patients with dyslipidemia

Numerous studies on the application of pharmaco-economics with hypolipidemic drugs have been conducted (Hawkins & Jackson, 2001: 179-195; McMurray, 1999: 99-104; Olsson *et al.,* 2004: 1-7). An example of such study was the pharmaco-economic impact of HMG-CoA reductase inhibitors (statins) in type II diabetes mellitus. In that study, the epidemiology, cost and effectiveness of statins in prevention of cardiovascular diseases in patients with type II diabetes mellitus, in both primary and secondary prevention was reviewed. It was found that in the secondary prevention, statins have been shown to be well-tolerated, efficacious and cost-effective means of reducing cardiovascular risk. Recommendations for further studies were made (Chaiyakunapruk *et al.*, 2000: 1-8).

The major concern with HMG-CoA inhibitors is cost. Pharmaco-economic studies can be used in the development of cost-effective treatment strategies to estimate the lipid-lowering efficacy of several of HMG-CoA inhibitors alone or in combination with other hypolipidemic drugs

* Refer to glossary

(Hilleman *et al.*, 1999: 536-562). Based on that, Hilleman *et al.* (1999: 536-562) conducted a study called "*A population - based treat - to - target pharmacoeconomic analysis of HMG-CoA reductase inhibitors in hypercholesterolaemia*". It was found that the most cost-effective treatment approach is to individualise the selection of statins based on coronary risk and it was further stated that atorvastatin and fluvastatin should be available in the national formulary.

3.8.8 Methods for calculating cost

In conducting a pharmaco-economic study, estimates of costs, effects and cost-effectiveness ratios for particular treatment methods are obtained from the clinical trials. The information received from clinical trials is insufficient to calculate the expected value and variance of the cost-effectiveness ratio and confidence intervals. Methods for collecting information about costs, effects, and cost-effectiveness ratios are presented in table 3.2.2 (Rajagopalan *et al.*, 1996: 1300; Hawkins & Jackson, 2001: 191).

Table 3.5 Methods for calculating information about costs and cost-effectiveness ratios

Costs

i) Direct costs

1. Drug costs
    - Statin therapy (acquisition + dispensing + medical management)
    - Related medication (acquisition + dispensing + medical management)
2. Physician costs
    - Outpatient's visits
    - Inpatient care
    - Monitoring
    - Lab tests (lipid profiles, blood test)
3. Health care professional expense
    - Pharmacists
    - Dietician
    - Home nursing
4. Hospital costs
    - Diagnostic procedures
    - Surgery
    - Hospital stay
    - Emergency room
    - Intensive care unit
    - Transportation to hospital
5. Events costs
    - Coronary heart failure
    - Stroke/ TIA
    - Arrhythmias
    - Nonfatal myocardial infarction
    - Angina (coronary insufficiency/ unstable angina)
    - Fatal acute myocardial infarction

6. Procedure costs
   - Heart transplantation
   - Pace maker insertion and replacement

ii) Indirect costs

1. Decrease in labour production
   - From morbidity
   - From mortality
2. Missed work days

Effects (calculated in various ways depending on the treatment or procedure evaluated).
Life years gained
Quality-adjusted life years gained
Event-free survival
Cost effectiveness ratio
Cost per life-year gained
Cost per quality-adjusted life-year gained
Cost per event-free survivor
Costs per level of effectiveness attained (i.e. an index can be created for the entire range of effectiveness and the ratio of costs to the effectiveness index can be calculated).

3.8.9 Barriers to conducting pharmaco-economic research

There are two types of barriers that can impede pharmaco-economic research in managed care organisations namely organisational as well as technical obstacles. The former include areas such as the company's funding priorities, growth objectives, and corporate culture. The latter include data inaccuracy and the other problem with claims data is that patient information is not available on education, socioeconomic status, medical history and ethnicity (Draugalis, 1995: 104).

In dyslipidemia, conclusions drawn from economic studies based on intermediate outcome such as percentage of low-density lipoprotein or the extent to which low-density lipoprotein cholesterol goals are achieved, may be incorrect or misleading, since important outcomes do not necessarily correlate with surrogate end points (Hawkins & Jackson, 2001: 188)

3.8.10 Overcoming barriers of pharmaco-economic studies

Different approaches can be used to overcome the obstacles that are encountered in pharmaco-economic studies. Examples of approaches are; developing trust, recognising common grounds, sharing the risk, promoting communication and understanding within managed care organisations (Rajagopalan *et al.*, 1996: 1300). Designing research sensitive to corporate objectives will be outlined in detail in the following paragraph.

Research projects that are conducted should reflect real world setting modification or real world savings. This will help managed care organisations to translate the results without harming their image. The research must be flexible to the needs of managed care organisations (Draugalis & Coons, 1995: 106). The research must be designed such that it is based on large scale, prospective outcome studies that document the effectiveness of lipid lowering therapy in reducing cardiovascular mortality and morbidity (Hawkins & Jackson, 2001: 188).

3.9 HEALTH CARE IN SOUTH AFRICA

3.9.1 Introduction

In 1994, the newly elected government faced tremendous challenges of transforming a highly inequitable and fragmented health care system (Forman *et al.,* 2004: 13). Though during the past ten years, the national and provincial health ministries successfully integrated many systems that they inherited, much work remains to be undertaken before the health system will be fully functional (Wimble, 2004: 28).

3.9.2 Key pieces of legislation to transform public and private health care in South Africa.

Certain pieces of legislation have served several central functions in the task of transforming health care in South Africa and creating a unified and equitable health care sector. In the area created by the lack of enabling legislative framework, the free provision of primary health care services, the restructuring of every health care financing and delivery, the establishment of the district health care system and the reform of the hospital level services through policies and programmes have been pursued without the benefit of implementing legislation. While much progress has been made under these programmes, the absence of a legislative framework for the creation of a unified health care system throughout this past decade can be considered significant failure of transformation (Forman *et al.,* 2004: 21). The following acts have been shaped to transform health care in South Africa:

3.9.2.1 The Medicines and Related Substances Control Act (101/1965), as amended

The Medicine Act (101/1965) was designed to enable the government to embark on a variety of Acts to provide a supply of more affordable medicines to the South African citizens. These measures include parallel importation of imported medicines, generic substitution of off-patent medicines and the establishment of a pricing committee to introduce a pricing system for all

medicines sold in South Africa through the establishment of the single exit price for medicines (Forman *et al.*, 2004: 21).

3.9.2.1.1 Generic substitution

According to the Medicine and Related Substances Control Amendment Act (101/1965), a pharmacist or any person licensed for dispensing shall inform all the members of the public who visit the pharmacy or any place where dispensing takes place, of the benefits of the substitution for a branded medicine by a generic medicine, and shall in the case of a substitution, take reasonable steps to inform the prescriber of the medicine of such substitution. The pharmacist or any person licensed for dispensing shall dispense a generic medicine instead of an innovator medicine prescribed by the person authorised to prescribe unless expressly forbidden by the patient to do so.

When a generic medicine is dispensed by the pharmacist, he/she shall note the brand name or where no such brand name exists, the name of the manufacturer of that generic medicine shall be noted in the prescription book. A generic medicine shall not be sold in the following cases:

- If the person prescribing medicine has written in his or her own hand on the prescription the words "no substitution" next to the item prescribed.
- If the retail price of the generic medicine is higher than that of the prescribed medicine.
- Where the Medicine Control Council has declared the product not substitutable.

3.9.2.1.2 Introduction of a pricing system for all medicines sold in South Africa through the establishment of the single exit price

According to Blecher and Thomas (2004: 275), the health component of the consumer price index (CPIX) has persistently run above the general index (around 3% on average) (refer to table 3.6). The health component of the consumer price index is also composed of private sector costs and may also (like consumer price index itself) not accurately reflect public sector cost pressures. There has been a great discrepancy between rising per capita expenditure in the public and private sectors (5.7% on average annually), which provides further evidence of the existence of health inflation, although in the private sector, the increased inflation may be brought by about over-provision and excess profit (Blecher & Thomas, 2004: 275).

Based on the above mentioned discussion, the transparent pricing system evolved. According to the Medicines and Related Substances Control Amendment Act (101/1965), the minister may on recommendation of the pricing committee make regulations on (1) the introduction of transparency pricing system for all medicines and scheduled substances sold in the Republic of

South Africa, (2) an appropriate fee to be charged by wholesalers and distributors or any other person selling schedule 0 medicines (3) an appropriate dispensing fee to be charged by a pharmacist or by a person licensed to dispense.

Beaumont (2004: 1) suggested the following as the principles of the transparent pricing system:

- Single exit price for each product to be set by the manufacturer and be printed on the pack.
- Professional fee for dispensing services.
- Theme of disclosure of monetary information.
- Discounting and bonusing prohibited.

The following were set as maximum fees for dispensing:
Pharmacists: 26% for products <R100.00, R26.00 for products greater than R100.00, excluding value added tax.
Licensed dispensers such as: 16% for products less than R100.00, R16.00 for products greater than R100.00, excluding value added tax.
Schedule 0 medicines to be excluded from all pricing restrictions.
In private hospitals, only one dispensing fee can be charged per prescription.

Table 3.6 Health component of CPIX vs. CPIX by financial year (Blecher & Thomas (2004: 275)

	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
CPIX	8.1	7.8	12.3	6.9	7.8	6.6	9.8
CPIX medical	10.3	17.5	12.3	10.2	10.5	10.9	12.1

According to Forman *et al.* (2004: 21) this legislation will play a critical role in ensuring the availability of essential medicines in South Africa.

3.9.2.2 The Medical Schemes Act, Act 131 of 1998

Medical Schemes Act (131/1998) had a specific goal of increasing equitable access to health care in the private sector (Forman *et al.*, 2004: 21). The Act was passed against a background of legally permitted discrimination by medical schemes against older and less healthy members and applicants through risk-rating and denial of membership, permitted by deregulation of the industry in the late 1980's and early 1990 (Harrison, 2004: 291). The Medical Schemes Act (131/1998) include a prescribed set of minimum health care benefits (Forman *et al.*, 2004: 21).

The remaining problem of this environment relate to continuing cost escalation, with related decrease in affordability of medical schemes contribution and growing disparity between health expenditure in the private and public health care sectors (Harrison, 2004: 298). The extent to which this Act will provide a greater unity in the public and private health care sectors in practice however, remains to be seen (Forman *et al.,* 2004: 22).

3.10 CONCLUSION

The concept of pharmaceutical care is part of the health care system. There are important differences between the concept of pharmaceutical care, managed care and disease management, although there are some similarities. The main difference can be observed in the extent of influence of the patient on the process or the concept of care and in the initiator of the concept of care. There is a decreasing chance for the patient to influence his/her own treatment from pharmaceutical care through disease management to managed care (Van Mil *et al.,* 1999: 207).

Pharmaceutical care is not a static, one-day event care, the care is ongoing until the patient physically moves away from your practice, looks out for another practitioner to provide pharmaceutical care, or expires (Cipolle *et al.,* 1998: 124). The main aim of pharmaceutical care is the maintenance of the patient's quality of life. Being a pharmacist is about the provision of pharmaceutical care and helping patients to get the best possible quality of life (Mason, 2000: 4). For a better enhancement of patient care, all systems of the health care must function as a unity.

3.11 CHAPTER SUMMARY

In this chapter the concepts of health care were discussed. The definition, barriers, equation and factors influencing pharmaceutical care were elucidated. The impact of drug-related morbidity and mortality on pharmaceutical care were discussed. The chapter would not have attained its scope if the pharmaceutical care practice and patient care process had not been discussed. A brief lay out of drug utilization review, pharmaco-economics and pharmaco-epidemiology; managed care and managed pharmaceutical care were discussed.

Research methodology will be discussed in Chapter 4.

CHAPTER 4: RESEARCH METHODOLOGY

4.1 INTRODUCTION

In this chapter both the general and the specific research objectives of the research project will be set out as well as the research methodology of the empirical investigation.

Data for this study were obtained from the Medscheme® database. The research is considered retrospective and non-experimental. For more information on retrospective drug utilisation studies refer to paragraph 3.6.5.

4.2 RESEARCH OBJECTIVES

The general as well as the specific research objectives of study will be outlined below.

4.2.1 General research objective

The general research objective of the study was to scrutinise and evaluate the medicine management of dyslipidemia in the private health care sector in South Africa by determining the prevalence and medicine treatment cost of dyslipidemia.

The basic objective was to investigate the effect of the Medscheme® price list,* (MPL) on the cost and prevalence of drugs, specifically hypolipidemic drugs claimed for patients in the private health care sector in South Africa. MPL is a managed reference pricing system whereby a ceiling price has been allocated to a group of drugs, which are similar in terms of composition, clinical efficacy, safety and quality (Medscheme®, 2003: 1).

4.2.2 The specific research objectives

The specific research objectives of the literature review were

- to describe the epidemiology of dyslipidemia;
- to differentiate between the different lipoproteins dyslipidemia;
- to determine the pathophysiology of dyslipidemia;
- to define and differentiate between the different types of dyslipidemia;

* refer to glossary

- to describe possible risk factors for dyslipidemia;
- to describe the diagnosis and test procedures for diagnosing of dyslipidemia;
- to describe the signs and symptoms, candidates for screening as well as the complications of dyslipidemia;
- to describe the treatment protocols and the drugs that are used in the management of dyslipidemia;
- to determine the relationship between dyslipidemia and other diseases such as hypertension, cardiovascular heart disease and diabetes;
- to describe and define the concept of managed pharmaceutical care;
- to investigate the application of managed pharmaceutical care principles in the management of dyslipidemia;
- to investigate the application of pharmaco-economic principles in the medicine management of dyslipidemia;
- to investigate the application of pharmaco-epidemiological principles in the medicine management of dyslipidemia; and
- to investigate the application of drug utilisation principles in the management of drug cost of dyslipidemia.

The specific research objectives of the empirical study were

- to investigate the differences in the utilisation patterns of drugs in general before and after implementation of the Medscheme® price list;
- to investigate the differences in the utilisation patterns of hypolipidemic drugs before and after implementation of the Medscheme® price list;
- to determine the effect of Medscheme® price list on the cost of hypolipidemic drugs;
- to determine and compare the difference in prevalence of innovator products vs. generic products that have been claimed before and after implementation of the Medscheme® price list for drugs in general and and hypolipidemic drugs specifically;
- to determine the difference in cost between the innovator and the generic drugs for both the general data and hypolipidemic drugs;
- to determine the cost savings that could have been incurred if hypolipidemic drugs were sold at MPL prices;
- to determine the cost savings that could have been incurred if generic products were prescribed on behalf of innovator products (provided that the patent protect time on the original drug is over);

- to compare the prescribed daily dose with the defined daily dose of individual hypolipidemic drugs; and
- to formulate recommendations with regard to the medicine management of dyslipidemia.

4.3 DATA SOURCE

Data for this study were extracted with permission from Medscheme® database for a period of twenty-four months (i.e. 2 years) from May 2001 to April 2003. Medscheme® price list (MPL) was implemented in May 2002. Data were analysed and compared from May 2001 to April 2002 (i.e. a year before implementation of MPL) and from May 2002 to April 2003 (after implementation of MPL).

4.4 RESEARCH METHODOLOGY

The research method consisted of two phases, namely the literature study and the empirical investigation

4.4.1 Phase 1: literature study

For comprehensible research to be conducted, the underlying and the background theory should be well understood. In this study, the literature review has served as a foundation of the empirical investigation. The literature review was divided into two chapters, namely the management of dyslipidemia and health care concepts. The former chapter gives the insight of dyslipidemia as a disease, its risk factors and other contributing factors associated with it. The drug therapy and non-drug therapy for the management of dyslipidemia are also discussed in this chapter. The latter chapter describes the concept of managed care, pharmaceutical care, managed pharmaceutical care, drug utilisation review, pharmaco epidemiological and pharmaco-economic principles in the management of dyslipidemia.

4.4.2 Phase 2: the empirical study

The empirical study consists of the following steps:

- Research design.
- Composition of the study population.
- Selection of criteria / measuring instruments for the data analysis.

- Analysis of data.
- Reliability and validity.
- Discussions based on the findings of the empirical investigation.
- Conclusion, recommendations and the way forward based on the result of the empirical investigation.

4.4.2.1 Research design

The research design provides the glue that holds the research project together. It is used to structure the research, to show how all of the major parts of the research project (the samples or groups, measures, treatments or programmes, and methods of assignment) work together to try to address the central research questions (Trochim, 2002: 1).

The variables of this research can be categorised and represented numerically; therefore this research can be classified as quantitative research (Mouton, 1998: 95; Steyn *et al.*, 1994:7). The research can also be graded as a retrospective research because it brings into play information that has been collected and structured before the research was conducted (Kreling & Mott, 1993: 416).

The literature review was conducted to give the underlying theory and the empirical investigation was performed using data from Medscheme®. The prevalence of medicine usage and the cost associated with it was analysed from pre–existing data.

Health care concepts that were applied in the empirical investigation will be outlined in table 4.1

Table 4.1 Health care concepts that were applied in the empirical investigation

DRUG UTILIZATION REVIEW (DUR)	
Concept	Description
DUR study	Aim at facilitating rational use of drugs and reducing needless expenditures (WHO, 2003: 9). Refer to (2.2); (3.6.2); (3.6.3); (4.4)
Quantitative study	It ascertains the quantities of drugs consumed in a specific geographical area. (Baksaas & Lunde, 1981: 5). Refer to: (3.6.4.2); (4.4.2.1); (5.5-5.8)
Retrospective study	It is a DUR study that gathers information and detects problems in a population after they have occurred. This study is done after medications were dispensed (Ferreira, 1999: 1). Refer to (3.6.5); (4.4.2.1); (5.5-5.8)
Prescribed daily dose	It gives the daily amount of drugs that has actually been prescribed (Sacristan and Soto, 1994: 301). Refer to: (3.6.6.2); (4.4.2.3.1.9); (5.8.1.1.3); (5.8.1.3.2); (5.8.1.4.2); (5.8.2.1.3); (5.8.2.2.2); (5.8.2.3.3); (5.8.2.4.3); (5.8.2.5.3); (5.8.3.3).
Defined daily dose	The assumed average maintenance dose per day for a drug used for its main indication in adults (Blackburn, 1993: 17; WHO, 2003: 38). Refer to: (3.6.6.1); (4.4.2.3.1.10); (5.8.1.1.3); (5.8.1.3.2); (5.8.1.4.2) (5.8.2.1.3); (5.8.2.2.2); (5.8.2.3.3); (5.8.2.4.3); (5.8.2.5.3); (5.8.3.3).
Number of prescriptions	Number of prescriptions claimed is used to quantify drug consumption (WHO, 2003: 39). Refer to: (3.6.6.3); (4.4.2.3.1); (5.5-5.8).
Number of medicine items per prescription	Number of medicine items per prescription is used to quantify drugs consumption (WHO, 2003: 39). Refer to: (3.6.6.3); (4.4.2.3.1); (5.5-5.8).
PHARMACEUTICAL CARE	
Concept	Description
Over-dosages	The patient is treated with an excess of the correct drug for his medical condition (Strand *et al.*, 1990: 1095). Refer to: (3.4.5); (5.8.1.1.3).
Sub-therapeutic dosages	The patient is getting the right medication but is being given insufficient dosage (Strand *et al.*, 1990: 1095). Refer to: (3.4.5); (5.8.1.1.3).
PHARMACO-ECONOMICS	
Concept	Description
Cost	The monetary value of resources consumed in its production or delivery (Larson, 1996: 46). Refer to: (1.1); (2.16.5.4.3); (3.8.1); (4.4.2.3.3); (5.5.1) (5.5.3) (5.6); (5.7); (5.8)
Average cost	Average cost is the resources consumed per unit of output. Refer to: (3.8.1); (4.4 2.3.3); (5.5); (5.6); (5.7); (5.8).

4.4.2.2 Composition of the study population

The study population was selected according to prescriptions analysed on the medicine claims (as mentioned in paragraph 4.3) database for a period of two consecutive years (1 May 2001 to

31 April 2003). This study focused specifically on prescriptions prescribed for patients who received hypolipidemic drugs.

To conduct this study, the pharmacological classification system according to MIMS™ was used to classify the medicines (Snyman, 2003: 12a). According to the pharmacological classification of MIMS™ (Snyman, 2003: 12a-14a) hypolipidemic drugs are classified under cardiovascular agents and sub classified in sub-classes fibrates (e.g. fenofibrate- Lipsin 300mg®, gemfibrozil- Lopid 600mg® etc.), statins (e.g. atorvastatin- Lipitor 10mg®, and "other" hypolipidemic drugs (e.g. acipimox- Olbetam®, cholestyramine- Questran lite sac®.

4.4.2.3 Selection of research instrument

The following concepts were used as the measuring instruments for data analysis:

4.4.2.3.1 Medicine items

Medicine items are defined according to the Medicines and Related substances Control Act (101/1965) as "*substance intended for use in the diagnosis, cure, mitigation, treatment, modification or prevention of disease, abnormal physical or mental state or the symptoms thereof in man*". In this research the word medicine items is used interchangeably with the word "drugs". Medicine items are used in this study, as a research instrument to give the idea of the total number of medicine items that were prescribed as well as the total number of medicine items prescribed per prescription in general (total database) as well as for hypolipidemic drugs. It also shows the distribution and utilisation patterns of hypolipidemic drugs. For the purpose of this study, the total number of medicine items prescribed per prescription for both the general as well as for hypolipidemic drugs will be compared for the year before the implementation of MPL and the year after the implementation of the MPL.

4.4.2.3.2 Prevalence

Prevalence is defined according to Waning and Montagne (2001: 21) as the "*probability that a condition exists in a specified population or the probability of the occurrence of a condition*". When used for this study, it shows the utilisation patterns of different drugs in different pharmacological groups but specifically the hypolipidemic drugs. It helps with the identification

of problem areas with regard to drug utilisation. Medicine usage patterns (or prevalence) is an important factor to consider during analysis of medicine usage data because it gives the idea of the number of drugs that are being prescribed and the percentages of people within the population that suffer from certain diseases, e.g. cardiovascular diseases, etc. It also helps medical schemes with budgeting for medical expenditure of their members.

In this study the prevalence of the following drugs will be analysed as follows:

- The prevalence of all medicine items claimed during the study period.
- The prevalence of the top 5-main-pharmacological groups, e.g. cardiovascular drugs, analgesics, etc.
- The prevalence of all medicine items according to generic and innovator products.
- The prevalence of the different sub-pharmacological groups of the cardiovascular agents, e.g. hypolipidemic drugs, antihypertensive drugs, etc.
- The prevalence of the different pharmacological groups of hypolipidemic drugs, e.g. fibrates, statins, etc.
- The prevalence of individual hypolipidemic drugs (e.g. Lipsin 300mg®, Lipitor 20mg® etc.) containing different active ingredients (e.g. fenofibrate, atorvastatin, etc.).

4.4.2.3.3 Medicine cost

Medicine cost is defined as the monetary value of resources consumed in the production or delivery of medicines (Larson, 1996: 46). On an annual basis, health care inflation* that is greater than the consumer price index* (CPI) is a critical concern to everyone (Medscheme®, 2003: 1). Private health care insurance will become unaffordable for most South African citizens unless careful management is implemented (Medsheme®, 2002: 1). It is for this reason that cost was employed in the analyses of data during this study.

The total medicine cost, the average medicine cost per prescription, the average medicine cost per item as well as the cost-prevalence index (calculations associated with cost values) were analysed as follows:

- The total cost of all medicine items claimed during the two consecutive study years were compared for different time periods (four-months periods).

* Refer to glossary

- The total cost of all medicine items claimed according to generic or innovator products for the two consecutive study years were compared for different time periods (four-months periods).
- The cost difference between generic and innovator products claimed.
- The total cost represented by and the cost-prevalence index of the main pharmacological groups (e.g. cardiovascular drugs, respiratory drugs, etc.).
- The total cost of medicine items according to the different sub-pharmacological groups (e.g. positive inotropic drugs, hypolipidemic drugs etc.).
- The cost of all hypolipidemic agents claimed during the two consecutive years.
- The cost of all hypolipidemic agents according to generic or innovator products claimed for the two consecutive study years were compared for different time periods (four-months periods).
- The cost difference of innovator and generic hypolipidemic drugs.
- The cost of the different pharmacological groups of hypolipidemic drugs (e.g. statins).
- The cost of all individual hypolipidemic drugs (e.g. Bezalip retard 400mg®).
- The cost difference between the total cost that the pharmacist or dispensing doctor is asking for and the calculated cost that the Medscheme® is prepared to pay according to the MPL.

4.4.2.4 Data analysis

The statistical analysis system, SAS (SAS institute, 2002) was used to analyse data under the guidance of the Statistical Consultation Services of the North-West University, Potchefstroom Campus. Data analysis was divided into two sections. The first section was the analysis of the general database and the second was the analysis of the hypolipidemic agents. The organogram of the analysis of both the general and the hypolipidemic drugs will be outlined at the end of this chapter.

4.4.2.4.1 Statistical analysis

For the purpose of this research, the following descriptive statistical concepts were utilised to analyse the data according to the measuring instruments/criteria as discussed in paragraph 4.4.2.3.

4.4.2.4.1.1 Percentage (%)

Percentage is the quotient obtained when the magnitude of a part is divided by the magnitude of the whole multiplied by hundred. The term per cent comes from the Latin phrase *per centum* which means per hundred (Glosser, 1999: 1).

4.4.2.4.1.2 Average value (mean)

According to Steyn *et al.* (1994: 90), the mean is the best-known single numerical value used to indicate the central position/location of the numbers. It is also referred to as the average value; it is the sum of the values divided by the number of values (Huysamen, 1998: 44). In terms of statistical presentation, the mean may be defined algebraically as

$$\bar{x} = \frac{\sum x}{N}$$

Where

$\bar{x}$ = the mean

$\sum$ = the sum of

N = the number of observation

x = any value in the data set

4.4.2.4.1.3 The standard deviation

The variance is a measure of how spread out (a variable's spread is the degree to which the variables differ from each other) a distribution is. It is calculated as the average squared deviation of each number from its mean (Steyn *et al.,* 1994: 132). The standard deviation is the positive square root of the variance (Huysamen, 1998: 56). It measures variability to the original units of measurement (Mendenhall *et al.,* 1993: 51).

Statistically the standard deviation may be obtainable as follows:

$$s = \sqrt{\frac{\sum(x-\bar{x})^2}{N-1}}$$

Where

s = the standard deviation

N = the number of observation

Σ = the sum of

$\overline{X}$ = the mean

X = any value in the data set

4.4.2.4.1.4 Weighted average

The weighted average was used in the appendix (table A.20 and table A.22) to calculate the average cost of the "*other*" main pharmacological groups. The weighted mean is used in the computation of the joint mean of various sets of data. It is primarily used to calculate the average value from the different average values (Steyn *et al.*, 1994: 102).

$$\overline{x}_w = \frac{\sum n_i \overline{x}_i}{\sum n_i}$$

Where:

$\overline{x}_w$ = the joint arithmetic mean

$\overline{x}_i$ = the arithmetic mean of data set

n_i = the size of the data set

i= 1, 2,....., k, (the data set)

4.4.2.4.1.7 Effect sizes

The effect size (d-value) is defined according to Cohen (1988: 9) as "*the degree to which a phenomenon is present in a population*". The d-value can be classified as small, medium and large (see below). The terms small, medium and large are relative, not only to each other, but to the specific content and research method being employed in any given investigation (Cohen, 1988: 25).

/ d/ $\leq$0.2 (small effect with no practical significant difference).

/ d/ ~ 0.5 (medium effect size with an effect that is perceived which may be significant).

/ d/ $\geq$0.8 (large effect that is significant and of practical importance).

The d-value can be presented algebraically as follows

$$d = \frac{\overline{x}_a - \overline{x}_b}{S_{max}}$$

Where: $\overline{x}_a$ = the average value of population a.

$\overline{x}_b$ = the average value of population b.

S_{max} = the maximum standard deviation between a and b.

The d-value will be used in this study to see whether differences of practical significance exist between the average medicine costs.

4.4.2.3.1.8 Cost index

Serfontein (1989:180) calculated the cost index as follows:

$$\text{Cost index} = \frac{Cost\ \%}{Prevalence\ \%}$$

For the purpose of this study, cost prevalence values can be interpreted as follows (Serfontein, 1989:180):

Cost index < 1: consumed treatment is relatively inexpensive.

Cost index = 1: cost of treatment is symmetric to the prevalence.

Cost index > 1: consumed treatment is relatively expensive.

4.4.2.4.1.9 Prescribed daily dose (PDD)

The prescribed daily dose is the average daily amount of a drug that is actually prescribed (refer paragraph 3.6.6.2). This clinical measure can be calculated as follows:

PDD = total quantity *strength / total days supplied.

Where quantity is the quantity of drugs dispensed, strength is the strength of the drug under study and the total day supply is the number of days that the drug was consumed (Burchill, 1999a: 1).

4.4.2.4.1.10 Defined daily dose (DDD)

The defined daily dose is the assumed average maintenance dose per day for a drug used for its main indication in adults (refer paragraph 3.6.6.1). This is a technical unit of measurement and

does not necessarily reflect the actual amount or dose used. The number of DDDs used per day per resident or the number of DDDs used per year per resident can be calculated as follows:

{Quantity/ (DDD / strength)}/ The number of days supplied (Burchill, 1999b: 1)

Where quantity is the amount of drugs dispensed, DDD is the DDD assigned by the World Health Organization (WHO, 2002: 60-61), and the strength is the strength of the drugs in the same unit as the DDD. The number of day supplies is the total number of days that the drug was consumed (Burchill, 1999b: 1).

4.4.2.5 Reliability and validity of the research instrument

The study was conducted using information extracted directly from the Medscheme® database. Direct manipulation of the data by the researcher was therefore impossible. The only changes that were made were the arrangement and classification of the drugs according to MIMS™ pharmacological classification. The research was conducted under the impression that all data attained from the database were precise and correct. The data obtained and analysed from the data source can only be generalised to the database and the specific study population.

4.4.2.6 Discussion of the results of the empirical investigation

The discussion and the results of the empirical investigation will be laid out profoundly in chapter 5.

4.4.2.7 Conclusions, recommendations, limitations and way forward

The wrapping up, suggestions, limitations will be fully outlined in Chapter 6. In addition to that, the relationship between the literature review and the empirical investigation will be presented.

4.5 CHAPTER SUMMARY

In this chapter the research methodology was elucidated. The discussion included amongst others, both the general and specific research objectives of the literature and empirical investigation, data source and the research methodology.

The results of the empirical investigation will be discussed in chapter five. Below is the organogram of the analysis of the general database followed by the organogram of the analysis of hypolipidemic drugs.

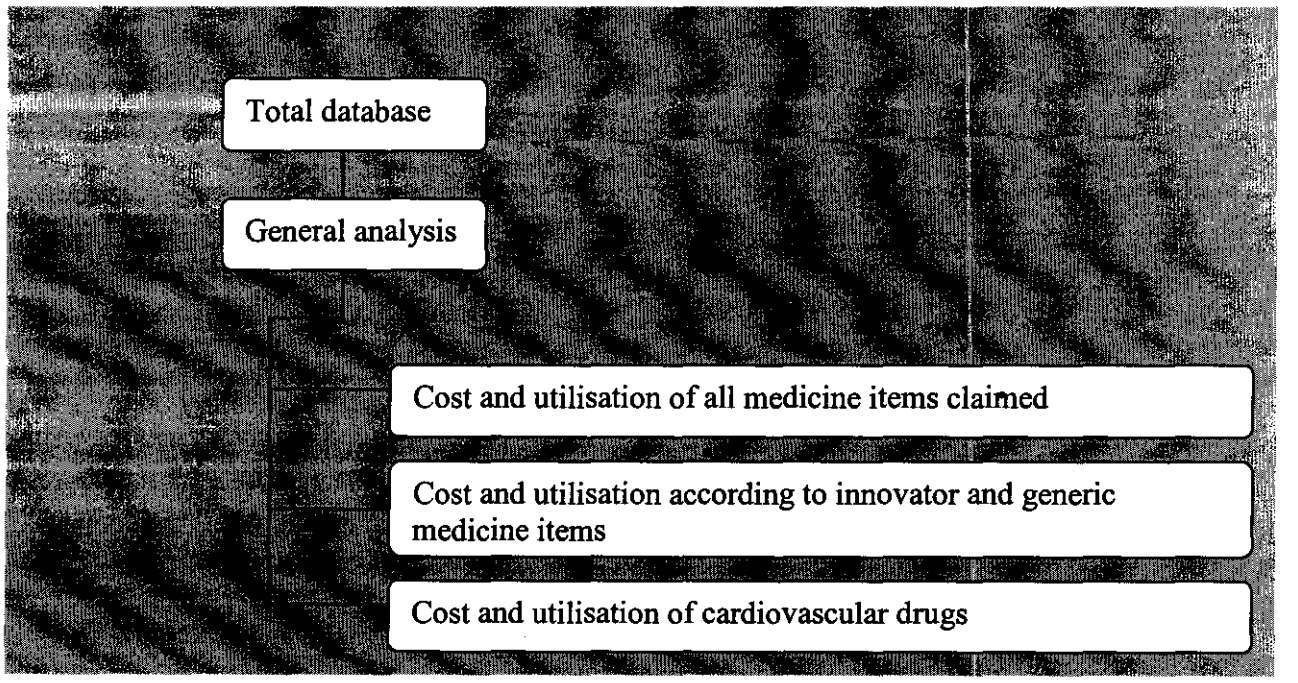


Figure 4.1 Analysis of the general database

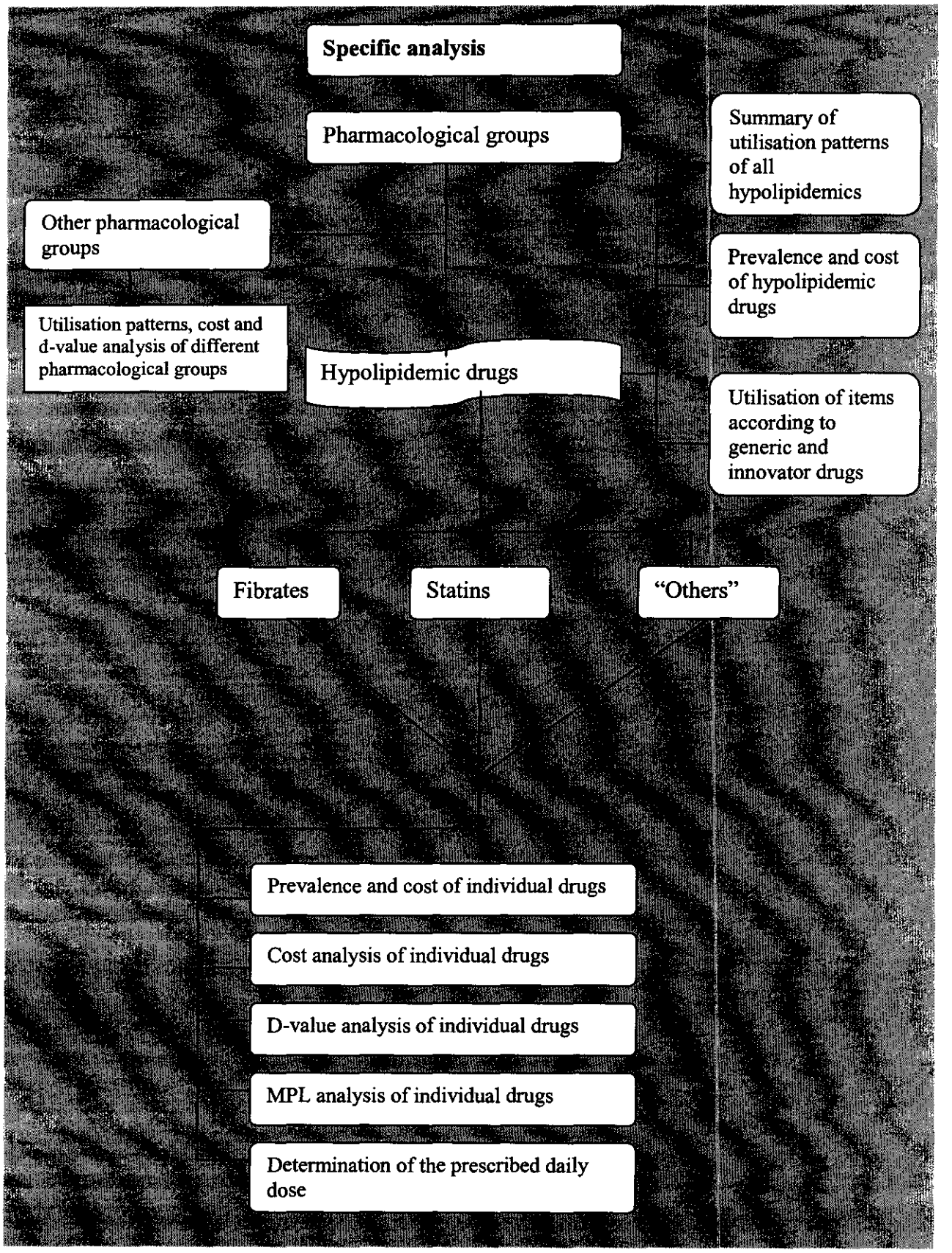


Figure 4.2 General overview of the analysis of hypolipidemic drugs

CHAPTER 5: RESULTS AND DISCUSSION

5.1 INTRODUCTION

In this chapter, the results of the empirical investigation of the usage patterns and cost of hypolipidemic drugs for the study period of two consecutive years (1st May 2001 to 30th April 2003) will be outlined and conferred.

The results will be analysed in sections, namely:

5.2 GENERAL ANALYSIS OF ALL MEDICINES

All medicines on the medicine claims database were analysed as follows

- Cost and utilisation patterns of all medicine items claimed during the study period.
- Cost and utilisation patterns of all medicine items claimed according to generic and innovator medicine items.
- Cost and utilisation patterns of the main pharmacological groups such as the cardiovascular medicine items claimed.

5.3 ANALYSIS OF HYPOLIPIDEMIC DRUG ITEMS

The analysis of hypolipidemic drugs was carried out as follows:

5.3.1 Pharmacological group (e.g. hypolipidemic drugs)

The pharmacological groups (e.g. hypolipidemic drugs) were analysed as follows:

- Prevalence of the pharmacological group (e.g. hypolipidemic drugs).
- Cost analysis of different pharmacological groups.
- d-value analysis of different pharmacological groups.
- Summary of the utilisation patterns of all hypolipidemic drugs on the database.
- Prevalence and cost aspects of hypolipidemic drugs.
- Utilisation of all hypolipidemic drugs according to generic and innovator products.

5.3.2 Sub-pharmacological group (e.g. statins)

- Prevalence and cost of sub-pharmacological groups (e.g. fibrates) of hypolipidemic drugs.
- Cost analysis of the different classes of sub-hypolipidemic drugs.
- d-value analysis of different classes of sub-hypolipidemic drugs.

5.3.3 Active ingredients

Individual hypolipidemic drugs will be analysed under the headings of their active ingredients as follows:

The fibrates will be analysed first then followed by the statins and "others" hypolipidemic drugs will be analysed in one table.

5.3.3.1 Fibrates (e.g. bezafibrate, clofibrate, fenofibrate and gemfibrozil)

- Prevalence and cost aspects of individual drugs under the sub-pharmacological group fibrates
- Cost analysis of individual drugs under the sub-pharmacological group fibrates
- d-value analysis of individual drugs containing fibrates
- MPL analysis of individual drugs containing fibrates
- Determination of the prescribed daily dose of the individual drugs containing fibrates

5.3.3.2 Statins (e.g. atorvastatin, cerivastatin, fluvastatin, pravastatin and simvastatin)

- Prevalence and cost aspects of individual drugs under the sub-pharmacological group statins
- Cost analysis of individual drugs under the sub-pharmacological group statins
- d-value analysis of individual drugs under the sub-pharmacological group statins
- MPL analysis of individual drugs under the sub-pharmacological group statins
- Determination of the prescribed daily dose of the individual drugs containing statins

5.3.3.3 Other hypolipidemic drugs (e.g. acipimox, cholestyramine, essential phospholipids, nicotinic acid, probucol)

- Prevalence and cost aspects of individual drugs under the sub-pharmacological group "other hypolipidemic drugs"
- Cost analysis of individual drugs under the sub-pharmacological group "other hypolipidemic drugs"
- d-value analysis of individual drugs under the sub-pharmacological group "other hypolipidemic drugs"
- Determination of the prescribed daily dose of the individual drugs under the sub-pharmacological group "other hypolipidemic drugs"

5.4 IMPORTANT CLARIFICATION WITH REGARD TO THE INTERPRETATION OF THE RESULTS

- For the purpose of this study, the following time periods will be denoted in the discussion: May 2001 to August 2001 = P1; September 2001 to December 2001 = P2; January 2002 to April 2002 = P3; May 2002 to August 2002 = P4; September 2002 to December 2002 = P5; January 2003 to April 2003 = P6. Each study year is displayed in its own table. It should be noted that each study year consists of three periods. P1, P2 and P3 are denoted the first study year and P4, P5 and P6 are denoted the second study year. These study periods can be illustrated as follows:

Table 5 (i) The first study year.

May 2001 to Aug 2001	P1
Sep 2001 to Dec 2001	P2
Jan 2002 to Apr 2002	P3

Table 5 (ii) The second study year.

May 2002 to Aug 2002	P4
Sep 2002 to Dec 2002	P5
Jan 2003 to Apr 2003	P6

- Medscheme® Price List (MPL) was implemented on 1 May 2002; the period from May 2001 to April 2002 will be compared with the period from May 2002 to April 2003 to perceive the difference in prescribing and utilisation patterns as well as drug expenditure differences. The basic principle is to witness the impact of the MPL on prescribing and drug utilisation patterns.
- For the purpose of this study, drugs of the cardiovascular system have been referred to as drugs of the main pharmacological group. The hypolipidemic drugs and the different groups of hypolipidemic drugs have been referred to as the pharmacological and the sub-pharmacological groups respectively.
- Hypolipidemic drugs have three sub-pharmacological groups according to MIMS™ classification (i.e. fibrates, statins and others). The sub-pharmacological group "others"

as indicated above and in tables of this chapter, contains the following active ingredients: acipimox, cholestyramine, essential phospholipids, nicotinic acid and probucol.

- MPL comparison can only be made with bezafibrate and simvastatin because they are the only hypolipidemic drugs that have generic substitutes and both appear on the MPL list. The patent life of most of the hypolipidemic drugs have not yet expired.
- The word "quantity" as appears in tables in appendix E refers to the number of tablets per prescription for a one-month supply.
- The prescribed daily dosage has been calculated for hypolipidemic drugs whose defined daily dosages have been assigned by the World Health Organization.
- The d-value has been calculated and compared between consecutive periods of the two study years.
- For the purpose of this study a d-value of ≤ 0.2 will be regarded as having a small effect with no practical significance, a d-value of >0.2 and/or ≤ 0.5 will be regarded as having a medium effect size with an effect that is perceived to be significant and a d-value of ≥ 0.8 shows a large effect that is significant and of practical importance (Cohen, 1998: 25).
- For the purpose of this study, MIMS™ refers to the Monthly Index of Medical Specialties of 2003 and MDR refers to the MIMS desk reference of 2002. The two books are quoted as Snyman 2003 and Snyman 2002 respectively in the bibliography.
- For the purpose of this study, Sweetman refers to the Martindale the complete drug reference, 33rd edition of 2002.
- For the purpose of this study, the word drug and medicine item have been used interchangeably.
- The percentages have been rounded off to the nearest 0.01 and may not add up exactly to 100 on some tables.
- The abbreviations G and I (in some tables) stand for generic products and innovator or original products respectively.
- Surgical equipments, non-medicinal items (e.g. syringes, needles, etc.) and mixtures (with unidentifiable active ingredients) were excluded from all analyses of these data.
- In mathematics, zero divided by any number is zero (0/1 = 0); every number divided by itself is one (1/1 =1). For the purpose of this study, the rule that was used is that of every number divided by itself being one. In tables where zero is divided by zero, the answer is one taking into consideration that zero is a number.

5.5 GENERAL ANALYSIS OF ALL MEDICINE ITEMS CLAIMED

5.5.1 Utilisation and cost of all medicine items claimed

Table 5.1 and table 5.2 give the summarised utilisation patterns of all medicine items claimed during May 2001 to April 2002 and May 2002 to April 2003 respectively. The total number of prescriptions increased from 11060996 during the first study year to 14347442 during the second study years. The total number of all medicine items claimed increased from 21820911 to 27277825 during the first and second study year. This amounted to a 25.01% increase in the total number of medicine items claimed. The increase in the use of drugs in any population is due to the growth in the size of population, the ageing process, and changing attitudes towards the use of drugs (de Joncheere *et al.*, 2003: 10). In this study, an increase in medical aid claims through the clearinghouse or an increase in number of members and dependents could have contributed to the increase in the number of medicine items claimed.

Although there was an increase in the total number of medicine items claimed between the first and the second year, there were no practically significant differences between the average numbers of medicine items claimed per prescription between the different four-months periods ($d < 0.8$).

Though the total cost of all medicine items claimed from P1 to P3 and P4 to P6 increased from R3 097 064 602 to R4 053 280 295 respectively, the average cost of medicine items claimed per prescription was fluctuating. It increased from R269.56±306.44 to R288.73±314.51 in the first study year. In the second study year it was R279.47±306.09, R287.16±406.40 and R281.56±325.12 for P4, P5 and P6 respectively. The results further revealed that there was no practically significant difference between the average costs of medicine items claimed per prescription between the different four-months periods ($d < 0.8$). A similar trend was observed for the average cost per medicine item. See Appendix A table A.17 and table A.18 as well as table 5.1 and table 5.2.

There was a 30.87% (n = R956 215 693) increase in the total cost of all medicine items claimed from the first to the second study years. From this discussion it can be concluded that both the cost of drug therapy and prevalence have increased from P1 to P6. From these above mentioned results, it can then be deduced that the total cost and total number of medicine items claimed the

year before the implementation of the MPL were relatively lower than the total cost and total number of medicine items claimed the year after the implementation of the MPL.

Table 5.1 Summary of the utilisation patterns of all medicine items claimed from May 2001 to April 2002 (period P1 to P3).

[illegible]	[illegible]	[illegible]	[illegible]
Total number of medicine items	6036149	6427511	9357251
Total number of prescriptions	2951703	3295200	4814093
Average number of medicine items per prescription	2.04 ± 1.25	1.95 ± 1.21	1.94 ± 1.20
Minimum number of medicine items per prescription	1.00	1.00	1.00
Maximum number of medicine items per prescription	19.00	20.00	19.00
Total cost of all medicine items (R)	795670612	911431143	1389962847
Average cost of medicine items per prescription (R)	269.56 ± 306.44	276.59 ± 309.75	288.73 ± 314.51
Maximum cost of medicine items per prescription (R)	38942.21	24531.06	24552.01
Average cost per medicine item (R)	131.82 ● 160.41	141.80 ± 164.14	148.54 ± 167.09
Maximum cost per medicine item (R)	38793.12	19248.28	21837.88

As shown in table 5.1 and table 5.2 the maximum cost per medicine item was relatively higher than the average cost per medicine item for both the first and second study years respectively. The maximum cost per medicine item was 294.29, 135.74, & 147.02 times higher than the average cost per medicine item for P1, P2 and P3 respectively. During the second study year, the maximum cost per medicine item was 230.51, 549.13 and 487.27 times higher than the average cost per medicine item for P4, P5 and P6 respectively (refer to table 5.2).

Table 5.2 Summary of the utilisation patterns of all medicine items claimed from May 2002 to April 2003 (period P4 to P6)

Description	May 2002 to Aug 2002 (P4)	Sept 2002 to Dec 2002 (P5)	Jan 2003 to April 2003 (P6)
Total number of medicine items	9776243	8113959	9387623
Total number of prescriptions	5020895	4310511	5016036
Average number of medicine items per prescription	1.95±1.18	1.88±1.14	1.87±1.13
Minimum number of medicine items per prescription	1.00	1.00	1.00
Maximum number of medicine items per prescription	17.00	20.00	18.00
Total cost of all medicine items (R)	1403168759	1237803191	1412308345
Average cost of medicine items per prescription (R)	279.47±306.09	287.16±406.40	281.56±325.12
Maximum cost of medicine items per prescription (R)	33084.05	129490.32	129490.32
Average cost per medicine item (R)	143.53±166.40	152.55±224.02	150.44±180.52
Maximum cost per medicine item (R)	33084.05	83769.48	73304.28

5.5.2 Utilisation patterns of all medicine items claimed according to generic and innovator medicine items.

The present economic and health care environment in South Africa has made it unavoidable for administrators managing the health care budget to adopt strict measures to practise cost effective health care (Raal, 2004: 118). Cutting the cost of health care becomes probable when generics are encouraged as parallel substitution (Bredesen, 2003: 351). In South Africa, the more immediate accessible initiatives have been to encourage medical practitioners and pharmacists to substitute original products with generic equivalents once the patent on the original product has expired (Raal, 2004: 118). According to the Medicines and Related Substances Control Act (101/1965), a pharmacist must inform all the members of the public who visit the pharmacy of the benefit of the substitution of the branded medicine by an interchangeable multi-source medicine and must inform the prescribers provided such substitution takes place. This could have been the reason for the increase in utilisation of generic medicines.

The total number of innovator products claimed from P1 to P3 was 73.4 % (n=21820911) compared to 68.92% (n=27277825) claimed from P4 to P6. From Tables 5.3 and 5.4 it can be seen that the prevalence of innovator products decreased gradually in percentages from 74.13% (n=6036149) to 67.53% (n=9387564) of the total number of medicine items claimed during P1 and P6 respectively.

Generic prescribing on the other hand has increased from 25.87% to 32.47% for P1 and P6 correspondingly. The total cost of generic products augmented from 12.9% (n=R 795 670 612) of the total cost of all medicine items claimed during P1 to 16.78% (n=R1 412 308 345) of the total cost of medicine items claimed during P6 accordingly (refer to table 5.3 and 5.4).

The d-value of 0.50 for P1, 0.54 for P2 and 0.56 for P3 as classified according to Cohen (1998:25) (refer to paragraph 4.4.2.3.1.7) illustrates an observable medium effect and it shows that there may be significant differences between the average cost of innovator and generic products for the different time periods. A similar trend was observed during the second study year (refer to table 5.3 and 5.4).

The average cost of all innovator products claimed was on average calculated to be 2.3 times higher than that of generic products during the two-year study period. The d-value between the average costs of innovator products between the different study periods is of no practical significance ($d < 0.8$) (refer to Table 5.3 and 5.4). From appendix A table A.23 and table A.24 it can be observed that the average cost of innovator products escalated from May 2001 and climaxed during December 2002 and it then started declining. On the other hand, the average cost of generic drugs increased from P1 to P3 during the first study year and from P4 to P6 during the second study year. The d-value between the average costs of generic products between the different study periods was of no practical significance. The d-values were 0.10, 0.10 and 0.04 between P1and P4, P2 and P5 and P3 and P6 respectively.

The cost-prevalence index of the innovator products was higher than one for the duration the study periods from P1 to P6. This shows that the cost of the innovator products is relatively expensive in comparison with that of the generic products (cost-prevalence index is 0.5 for each period from P1 to P3 and it increased slightly from 0.51(P4), 0.51(P5) to 0.52 (P6)). This is an indication that the generic products are relatively inexpensive. Based on the above mentioned discussion, a cost saving can be attained if prescriptions with innovator products (whose generic substitutes are available) are substituted with an interchangeable multi-source medicine.

Table 5.3 Utilisation of all medicine items claimed according to generic (G) and innovator (I) medicine items from May 2001 to April 2002 (period P1 to P3)

Month	Origin	Total no of medicine items	%*	Average cost per item (R)	Standard deviation	Minimum cost per item (R)	Total cost (R)	%#	Cost prescribing index	id#
May 2001 to Aug 2001 (P1)	I	4474402	74.13	154.87	176.89	38793.12	692946182.00	87.09	1.17	0.50
	G	1561747	25.87	65.77	62.64	1649.07	102724429.00	12.91	0.50	
Sep 2001 to Dec 2001(P2)	I	4757927	72.02	166.90	180.05	19248.28	794110336.00	87.13	1.21	0.54
	G	1669584	25.98	70.27	66.55	4733.59	117320807.00	12.87	0.50	
Jan 2002 to Apr 2002 (P3)	I	6798665	72.66	176.40	183.45	21837.88	1199268474.0	86.28	1.19	0.56
	G	2558586	27.34	74.53	71.69	2742.61	190694373.00	13.72	0.50	

%*I is the total number of innovator items claimed for that particular period divided by the total number of all medicine items claimed for that period, G is the total number of generic items for that particular period divided by the total number of all medicine items claimed for that particular period.
%# I is the total cost of innovator items divided by the total cost of all medicine items claimed for that particular period. G is the total cost of generic items on the database for that particular period divided by the total cost of all medicine items claimed for that particular period.

Table 5.4 Utilisation of all medicine items on the database according to generic and innovator medicine items from May 2002 to April 2003 (period P4 to P6)

Month	Origin	Total no of medicine items	%*	Average cost per item (R)	Standard deviation	Minimum cost per item (R)	Total cost (R)	%#	Cost prescribing index	id#
May 2002 to Aug 2002* (P4)	I	6848238	70.05	173.87	185.55	33084.05	1190729185.0	84.85	1.21	0.55
	G	2928005	29.95	72.55	68.78	3417.20	212439574.00	15.15	0.51	
Sep 2002 to Dec 2002 (P5)	I	5612312	69.17	186.10	258.06	83769.48	1044451856.0	84.40	1.22	0.42
	G	2501647	30.83	77.30	72.02	5304.06	193351335.00	15.60	0.51	
Jan 2003 to Apr 2003 (P6)	I	6339266	67.53	185.40	204.48	73304.28	1175311498.0	83.22	1.23	0.53
	G	3048298	32.47	77.74	74.58	5916.62	236969451.00	16.78	0.52	

%*I is the total number of innovator items claimed for that particular period divided by the total number of all medicine items claimed for that period, G is the total number of generic items on the database for that particular period divided by the total number of all medicine items for that particular period.
%# I is the total cost of innovator items claimed divided by the total cost of all medicine items claimed for that particular period. G is the total cost of generic items claimed for that particular period divided by the total cost of all medicine items claimed for that particular period. *Frequency missing 59

5.5.3 Cost and prevalence of the main pharmacological groups

Table 5.5 Prevalence and cost of the top 5 main pharmacological groups claimed from May 2001 to April 2002 (period P1 to P3)

Months	Main pharmacological groups	Prevalence	%*	Cost	%#	Cost per item
May 2001 to Aug 2001 (P1)	Analgesics	524549	8.69	31328209.34	3.94	0.45
	Anti-microbials	713307	11.82	120118583.00	15.10	1.28
	Cardiovascular drugs	716130	11.86	154904474.00	19.47	1.64
	Endocrine system drugs	527341	8.74	75014613.58	9.43	1.08
	Respiratory system drugs	1008679	16.71	83483450.10	10.49	0.63
	Other drugs	2546143	42.18	464849330.00	58.42	1.39
Sep 2001 to Dec 2001 (P2)	Analgesics	497404	7.74	29996373.98	3.29	0.43
	Anti-microbials	629139	9.79	115901857.00	12.72	1.30
	Cardiovascular drugs	9355261	14.55	204301758.00	22.42	1.54
	Endocrine system drugs	648199	10.08	94177389.96	10.33	1.02
	Respiratory system drugs	810908	12.62	82860660.00	9.09	0.72
	Other drugs	3520911	45.22	527238038.9	57.85	1.28
Jan 2002 to Apr 2002 (P3)	Analgesics	805679	8.61	56412777.34	4.06	0.47
	Anti-microbials	1013988	10.84	183923140.00	13.23	1.22
	Cardiovascular drugs	1258650	13.45	285027117.00	20.51	1.52
	Endocrine system drugs	897839	9.60	142515715.00	10.25	1.07
	Respiratory system drugs	1105272	11.81	118587699.00	8.53	0.72
	Other drugs	4275823	45.70	786466448.30	56.58	1.24

%* Prevalence of the specific main pharmacological group divided by the prevalence of the total number of medicine items claimed multiplied by hundred. Refer to table 5.1 for the total number of medicine items claimed for the specific period. %# Total cost of the specific main pharmacological group divided by the total cost of all medicine items claimed for the specific period multiplied by hundred

Table 5.5 and table 5.6 give the summary of the prevalence and cost of the top 5 main pharmacological groups from P1 to P3 and from P4 to P6 respectively. Of the top 5 main pharmacological groups listed (excluding other drugs) in tables 5.5 and 5.6, cardiovascular drugs were the most frequently claimed drugs on the database except during winter season (May to August of the two study years) where respiratory drugs had the highest prevalence. It should be borne in mind that respiratory drugs could be seasonal drugs because they are used more often in winter (when coughs, colds and fever are more prevalent).

Table 5.6 Prevalence and cost of the top 5 main pharmacological groups claimed from May 2002 to April 2003 (period P4 to P6)

Months	Main pharmacological group	Prevalence	%*	Cost	%#	Cost per item
May 2002 to Aug 2002 (P4)	Analgesics	847115	8.67	52621833.92	3.75	0.43
	Anti-microbials	1140958	11.67	206624524.00	14.73	1.26
	Cardiovascular drugs	1276088	13.05	288571782.00	20.57	1.58
	Endocrine system drugs	907555	9.28	142219734.00	10.14	1.09
	Respiratory system drugs	1612420	16.49	151071613.00	10.77	0.65
	Other drugs	3992107	40.83	841109486.9	59.94	1.47
Sep 2002 to Dec 2002 (P5)	Analgesics	671269	8.27	43882182.07	3.55	0.43
	Anti-microbials	880239	10.85	182059712.00	14.71	1.36
	Cardiovascular drugs	1167991	14.39	264549670.00	21.37	1.49
	Endocrine system drugs	812201	10.01	127505854.00	10.30	1.03
	Respiratory system drugs	1004092	12.37	113108340.00	9.14	0.74
	Other drugs	3578167	44.10	731105758.10	59.06	1.34
Jan 2003 to Apr 2003 (P6)	Analgesics	872617	9.30	59322471.78	4.20	0.45
	Anti-microbials	1086445	11.57	216655246.00	15.34	1.33
	Cardiovascular drugs	1249395	13.31	286299561.00	20.27	1.52
	Endocrine system drugs	856150	9.12	139182315.00	9.85	1.08
	Respiratory system drugs	1187011	12.64	129085353.00	9.14	0.72
	Other drugs	4136005	44.06	830544946.80	58.81	1.33

%* Prevalence of the specific main pharmacological group divided by the prevalence of the total number of medicine items claimed multiplied by hundred. Refer to table 5.2 for the total number of medicine items claimed for the specific period. %# Total cost of the specific main pharmacological group divided by the total cost of all items claimed for the specific period multiplied by hundred.

The prevalence of cardiovascular drugs increased from 11330041 to 3693474 during the first and second study years respectively. As seen on appendix A table A.9 and table A.10, the prevalence percentages of cardiovascular drugs were more or less the same for corresponding months. The prevalence percentages for the two study years climaxed in December 2001 (15.15%) and again in December 2002 (15.20%) and stabilised from January to April (13.00% on average) of the two study years. This increase in prevalence of cardiovascular drugs support the statement of the World Health Organization (2002: 1) which states that cardiovascular diseases are the leading cause of death worldwide responsible for a third of global fatality. It should be noted that there

was a similar trend of prevalence and cost of cardiovascular drugs during different study periods of the second study year.

Cardiovascular drugs represented 20.80 % (n =R 3 097 064 602) of the total cost of all medicine items claimed from P1 to P3 compared to 20.71 % (n= R 4 053 280 295) of the total cost of all medicine items claimed from P4 to P6. "Lipitor", one of the cardiovascular drugs, was among the top 10 medicine items claimed for both study years. It accounted for more than 1% (n = 49098736) of all medicine items claimed during both study years. Of the other four main pharmacological groups, the anti-microbials presented as the second relatively expensive group of drugs, which accounted for 13.68% and 14.92% of the total cost of all medicine items claimed during the first and second study years respectively. The least expensive of the four pharmacological groups was the group analgesics, which accounted for 3.76% and 3.83% of the total cost of all medicine items claimed in the first and second study years respectively. Unlike the total cost of other main pharmacological groups, the total cost of cardiovascular drugs was relatively the same throughout the first and second study years.

Though the cost-prevalence index of cardiovascular drugs was higher than one for all periods, it generally declined from P1 to P6. The decrease in the cost-prevalence index could have been brought about by an increase in generic prescribing of the cardiovascular drugs. tables A.11 and A.13 (appendix A) confirm that generic prescribing of cardiovascular medicine items increased from 19.49 % (May 2001) to 26.93% (April 2003).

It is clear from table 5.5 and table 5.6 that the cost-prevalence index of cardiovascular drugs was relatively higher compared to the cost-prevalence index of the other main pharmacological groups. This is an indication that cardiovascular drugs are relatively expensive compared to drugs of other main pharmacological groups. From the above-mentioned figures, it can be seen that the prevalence of cardiovascular drugs increased from P1 to P6 whereas the cost decreased from P1 to P6 though not at the same rate as the increase in prevalence. It can then be concluded that generic prescribing contributed to the slight decrease in cost percentages of cardiovascular drugs for all study periods.

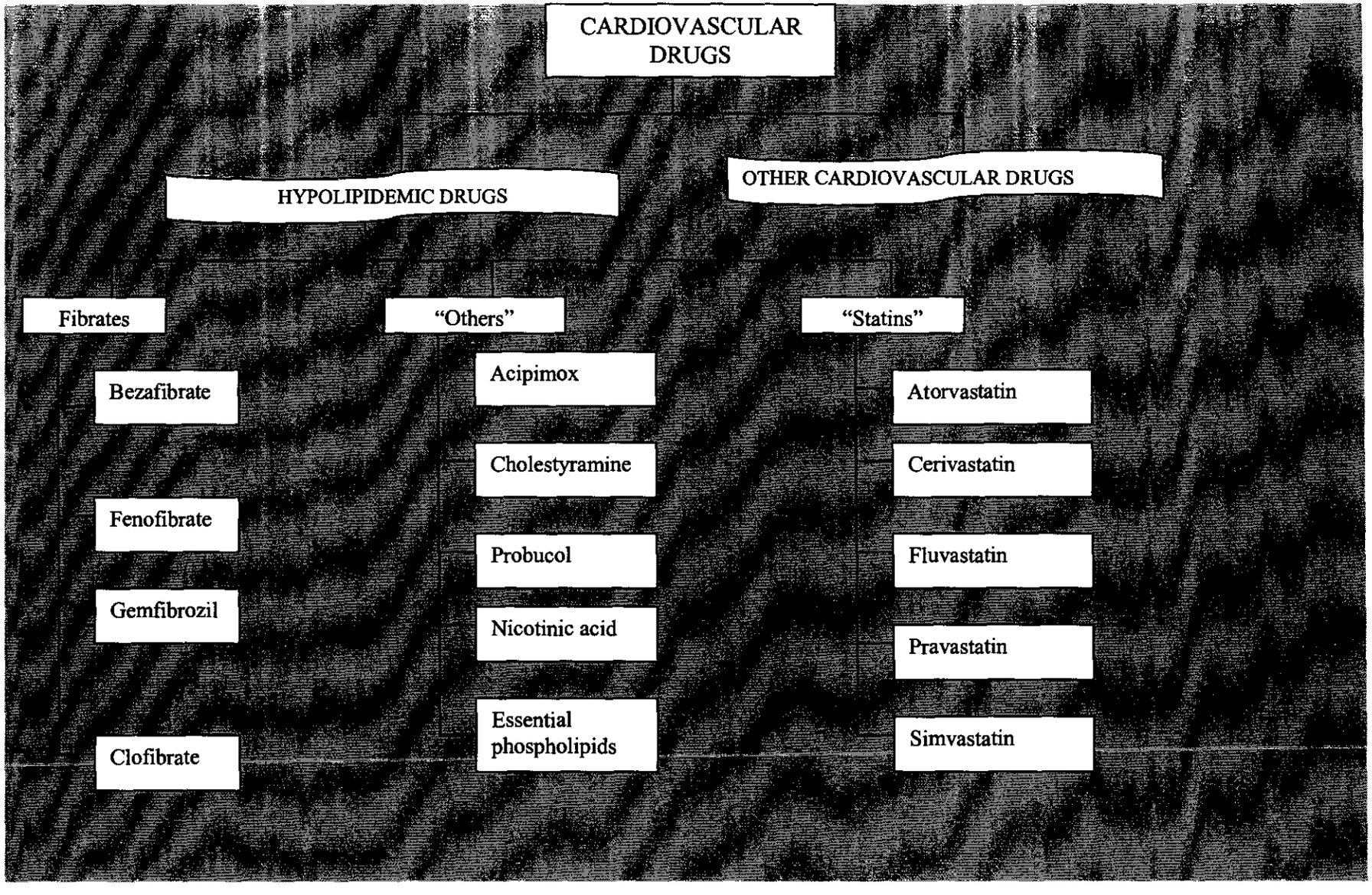


Figure 5.1 Overview of different active ingredients in the pharmacological group hypolipidemic drugs

5.6 ANALYSIS OF THE PHARMACOLOGICAL GROUP: HYPOLIPIDEMIC DRUGS.

The analysis of hypolipidemic drugs will be outlined in this section.

5.6.1 Pharmacological groups in the main pharmacological group: cardiovascular drugs.

The utilisation patterns as well as the cost of the pharmacological groups in the main pharmacological group cardiovascular agents will be discussed.

5.6.1.1 General overview of the utilisation patterns of the pharmacological groups of the cardiovascular drugs.

Of all the cardiovascular drugs claimed, anti-hypertensive drugs had the highest prescription rate and accounted for 61.01% and 61.84% of the total number of cardiovascular drugs (n=11330041 and n=3693474) during the first and second study years respectively. Hypolipidemic drugs were the second most prescribed pharmacological group of the cardiovascular drugs, which accounted for 20.16% and 20.57% for the first and second study years respectively. The least prescribed pharmacological group of the cardiovascular drugs was the positive inotropic drugs, which accounted for 0.28% and 0.20 % for the two study years respectively (refer to table 5.7).

As described in paragraph 5.5.3 it was clear that generic prescribing of the cardiovascular drugs increased. As shown in table B.15, table B.16, table B.17 and table B.18 (refer to appendix B) vasoconstrictors and other vasodilators are groups of cardiovascular drugs without generic substituents. It can be seen that more than 75% of the prescribed anti-anginal drugs were generic agents towards the end of the second study year. In May 2001 generic prescribing of the anti-anginal drugs accounted for 68.12% and it increased to 79.34% in April 2003 (refer to appendix B, table B.15). Generic prescribing of anti-arrhythmic drugs doubled from 24.15% (indicated for May 2001) to 51.29% (indicated for April 2003). Generic prescribing of other drugs of the main pharmacological group: cardiovascular drugs increased from P1 to P6, however, that of positive inotropic drugs was stabilised at 21.00% on average for the two study years.

The cost of anti-hypertensive drugs accounted for more than half of the cost of cardiovascular drugs. It increased from 58.69% (n=R 644 233 349) to 59.55% (n=R 839 421 013) of the total cost of cardiovascular drugs during the first and second study years respectively. Hypolipidemic drugs were the second group (that claimed the highest proportion of cost) of drugs of the

cardiovascular drugs, which accounted for 30.35% and 30.14% of the total cost of cardiovascular drugs during the first and second study years respectively. Other pharmacological groups of the cardiovascular drugs accounted for less than 20% of the total cost of cardiovascular drugs (refer to tables 5.7 and 5.8).

The cost-prevalence index of the other vasodilator drugs was on average the largest of all the cardiovascular drugs. It was calculated to be on average 1.58 and 1.94 for the first and the second study years respectively. Hypolipidemic drugs had the third largest cost-prevalence index (1.52 and 1.46 during the first and the second study years respectively). Based on the above-mentioned discussion, it can be concluded that drugs of the "other vasodilator" pharmacological group are relatively expensive compared to the rest of the drugs of the cardiovascular system (refer to table 5.7 and table 5.8). On the other hand, hypolipidemic drugs are the third relatively expensive drugs of the cardiovascular system.

The average cost of the different pharmacological groups increased in the first study year except that of anti-arrhythmic drugs which fluctuated between different periods of the first study year and the second study year. The average cost of different pharmacological groups continued to grow throughout the second study year. However, the average cost of hypolipidemic drugs and anti-anginal drugs declined in the second study year (refer to table 5.7 and table 5.8). The decline in average cost of both anti-anginal and hypolipidemic drugs could have been brought about by the increased utilisation of generic drugs of these pharmacological groups of the cardiovascular drugs (refer to appendix B, tables B.17 and table B.18)

Table 5.7 Cost analysis of the pharmacological groups in the main pharmacological group cardiovascular drugs from May 2001 to April 2002 (period P1 to P3)

[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Total number of items	Anti-anginal drugs	110985	15.50	140149	14.99	188781	15.00
	Anti-arrythmic drugs	5572	0.78	7314	0.78	11088	0.88
	Antihypertensives	437470	61.09	572699	61.23	764184	60.71
	Hypolipidemic drugs	140962	19.68	189652	20.28	258422	20.53
	Other vasodilators	2769	0.39	1959	0.21	3105	0.25
	Positive inotropics	14064	1.96	18357	1.96	23787	1.89
	Vasoconstrictors	4308	0.60	5129	0.55	9283	0.74
Average cost/ item and standard deviation (R)	Anti-anginal drugs	121.43 ± 79.99		124.09 ± 81.01		129.33 ±90.08	
	Anti-arrythmic drugs	369.68 ± 248.50		352.97 ± 225.35		379.90 ±213.45	
	Antihypertensives	209.57 ± 90.70		209.28 ± 89.41		217.18 ±90.99	
	Hypolipidemic drugs	326.20 ± 94.73		330.96 ± 87.94		337.93 ±89.26	
	Other vasodilators	316.66 ± 197.25		345.11 ± 201.53		395.01 ±237.19	
	Positive inotropics	13.76 ± 7.74		13.72 ±7.34		14.30 ±8.93	
	Vasoconstrictors	147.25 ± 76.65		152.24 ± 75.11		165.51 ±86.41	
			%#		%#		%#
Total cost (R)	Anti-anginal drugs	13476482.0	8.70	17391387	8.51	24415181	8.57
	Anti-arrythmic drugs	2059860.73	1.33	2581641. 2	1.26	4212362.7	1.48
	Antihypertensives	91682324.5	59.19	119852512	58.66	165968208	58.23
	Hypolipidemic drugs	45981144.6	29.68	62766748	30.72	87328156	30.64
	Other vasodilators	876826.05	0.57	676072.17	0.33	1226518.1	0.43
	Positive inotropics	193474.40	0.12	251945.80	0.12	340247.2	0.12
	Vasoconstrictors	634361.37	0.41	780844.32	0.38	1536442.8	0.54
Cost -prevalence index	Anti-anginal drugs	0.56		0.57		0.57	
	Anti-arrythmic drugs	1.70		1.62		1.68	
	Antihypertensives	0.97		0.96		0.96	
	Hypolipidemic drugs	1.51		1.51		1.49	
	Other vasodilators	1.46		1.57		1.72	
	Positive inotropics	0.06		0.06		0.06	
	Vasoconstrictors	0.68		0.69		0.73	

%* Is the quotient of the frequency of the individual pharmacological group and total number of all cardiovascular drugs claimed for the corresponding study period multiplied by hundred

%# Is the quotient of the total cost of the individual pharmacological group and the total cost of all cardiovascular drugs claimed for the corresponding study period multiplied by hundred

Table 5.8 Cost analysis of the pharmacological groups in the main pharmacological group cardiovascular drugs from May 2002 to April 2003 (period P4 to P6)

Total number of items	Anti-anginal drugs	187656	14.71	164473	14.08	177347	14.19
	Anti-arrythmic drugs	10381	0.81	8616	0.74	9961	0.80
	Antihypertensives	783139	61.37	726419	62.19	774268	61.97
	Hypolipidemic drugs	262405	20.56	240826	20.62	256444	20.53
	Other vasodilators	3170	0.25	1977	0.17	2170	0.17
	Positive inotropics	23311	1.83	19649	1.68	20742	1.66
	Vasoconstrictors	6026	0.47	6031	0.52	8463	0.68
Average cost/ item and standard deviation (R)	Anti-anginal drugs	128.52 ±85.15		125.33 ±80.35		124.96 ±80.27	
	Anti-arrythmic drugs	410.48 ±174.38		412.93 ±172.43		409.50 ±190.96	
	Antihypertensives	215.22 ±91.00		216.71 ±91.29		224.63 ±95.57	
	Hypolipidemic drugs	338.97 ±85.33		335.12 ±84.61		324.69 ±104.89	
	Other vasodilators	414.89 ±239.88		441.27 ±243.55		461.62 ±246.03	
	Positive inotropics	15.10 ±10.73		15.46 ±12.06		16.28 ±11.13	
	Vasoconstrictors	170.95 ±89.62		178.20 ±94.89		180.80 ±94.91	
			%#		%#		%#
Total cost (R)	Anti-anginal drugs	24117185.5	8.36	20614073.	7.79	22160577	7.74
	Anti-arrythmic drugs	4261240.25	1.48	3557779.0	1.34	4079034	1.42
	Antihypertensives	168547376	58.41	157421830	59.51	173924891	60.75
	Hypolipidemic drugs	88948672.3	30.82	80705053.	30.51	83265559	29.08
	Other vasodilators	1315218.84	0.46	872381.91	0.33	1001722.0	0.35
	Positive inotropics	351934.37	0.12	303814.72	0.11	337682.76	0.12
	Vasoconstrictors	1030154.69	0.36	1074738.0	0.41	1530095.1	0.53
Cost -prevalence index	Anti-anginal drugs	0.57		0.55		0.55	
	Anti-arrythmic drugs	1.83		1.81		1.78	
	Antihypertensives	0.95		0.96		0.98	
	Hypolipidemic drugs	1.50		1.48		1.42	
	Other vasodilators	1.84		1.94		2.06	
	Positive inotropics	0.07		0.07		0.07	
	Vasoconstrictors	0.77		0.79		0.78	

%* Is the quotient of the frequency of the individual pharmacological group and total number of all cardiovascular drugs claimed for the corresponding study period multiplied by hundred
%# Is the quotient of the total cost of the individual pharmacological group and the total cost of all cardiovascular drugs claimed for the corresponding study period multiplied by hundred

Though there was an increase in average cost of drugs of the pharmacological group between the different study periods, the d-value of less than 0.2 (small effect with no practical significance) was calculated for anti-anginal drugs, antihypertensive drugs and positive inotropic drugs of the main pharmacological group: cardiovascular drugs between different periods (refer to table 5.11, table 5.13, and table 5.15). On the other hand, the d–value of less than 0.5 greater than 0.2 (medium effect size with an effect that may be significant) was calculated for anti-arrhythmic drugs, other vasodilators, and vasoconstrictors between different periods (refer to table 5.12, table 5.14 and table 5.16).

Table 5.9 d-value analysis of the average cost of drugs for the different pharmacological groups from May 2001 to April 2002 (period P1 to P3)

May 2001 to Aug 2001 (P1)	Anti-arrythmic drugs	1.00					
	Antihypertensive drugs	0.97	0.64				
	Hypolipidemic drugs	2.16	0.17	1.26			
	Other vasodialators	0.99	0.21	0.54	0.05		
	Positive inotropic drugs	1.35	1.43	2.16	3.30	1.54	
	Vasoconstrictors	0.32	0.89	0.69	1.89	0.85	1.74
Sep 2001 to Dec 2001 (P2)	Anti-arrythmic drugs	1.02					
	Antihypertensive drugs	0.95	0.64				
	Hypolipidemic drugs	2.33	0.10	1.36			
	Other vasodialators	1.10	0.03	0.67	0.07		
	Positive inotropic drugs	1.36	1.51	2.19	3.61	1.64	
	Vasoconstrictors	0.35	0.89	0.64	2.03	0.96	1.84
Jan 2002 to Apr 2002 (P3)	Anti-arrythmic drugs	1.17					
	Antihypertensive drugs	0.97	0.76				
	Hypolipidemic drugs	2.32	0.20	1.33			
	Other vasodialators	1.12	0.06	0.75	0.24		
	Positive inotropic drugs	1.28	1.71	0.17	3.63	1.61	
	Vasoconstrictors	0.40	1.00	0.57	1.93	0.97	1.75

d-values of > 0.8 shows a practical significant value.

It is clear from table 5.9 and table 5.10 that there was a conspicuous variation in d-values calculated between the average costs of medicine items in the different pharmacological groups of the cardiovascular drugs during different study periods. These differences in d-value are an indication of the variation in the average cost of drugs within different pharmacological groups of the cardiovascular drugs.

Table 5.10 d-value analysis of the average cost of drugs for the different pharmacological groups from May 2002 to April 2003 (period P4 to P6)

May 2002 to Aug 2003 (P4)	Anti-arrythmic drugs	1.62					
	Antihypertensive drugs	0.95	1.12				
	Hypolipidemic drugs	2.47	0.41	1.36			
	Other vasodialators	1.19	0.02	0.83	0.32		
	Positive inotropic drugs	1.33	2.27	2.20	3.80	1.67	
	Vasoconstrictors	0.47	1.37	0.49	1.87	1.02	1.73
Sep 2002 to Dec 2003 (P5)	Anti-arrythmic drugs	1.67					
	Antihypertensive drugs	1.00	1.14				
	Hypolipidemic drugs	2.48	0.45	1.30			
	Other vasodialators	1.30	0.12	0.92	0.44		
	Positive inotropic drugs	1.37	2.31	2.21	3.78	1.75	
	Vasoconstrictors	0.56	1.36	0.41	1.65	1.08	1.72
Jan 2003 to Apr 2003 (P6)	Anti-arrythmic drugs	1.49					
	Antihypertensive drugs	1.04	0.97				
	Hypolipidemic drugs	1.90	0.44	0.95			
	Other vasodialators	1.37	0.21	0.96	0.56		
	Positive inotropic drugs	1.35	2.06	2.18	2.94	1.81	
	Vasoconstrictors	0.59	1.20	2.46	1.37	1.14	1.73

d-values of > 0.8 shows a practical significant value.

As seen in table 5.9 and table 5.10, the d-value between hypolipidemic drugs and drugs of other pharmacological groups of the cardiovascular drugs was large (d > 0.8) and of practical significance with the exception of the d-value between hypolipidemic drugs and anti-arrhythmic drugs and hypolipidemic drugs and other vasodilators. This shows that there is substantial variation in prices of hypolipidemic drugs and drugs of other pharmacological groups (except anti-arrhythmic drugs and other vasodilators).

Table 5.11 d-value analysis of the average cost of anti-anginal drugs for the different time periods

May 2002 to Aug 2002 (P4)	0.05		
Sep 2002 to Dec 2002 (P5)		0.02	
Jan 2003 to Apr 2003 (P6)			0.05

Table 5.12 d-value analysis of the average cost of anti-arrhythmic drugs for the different time periods

May 2002 to Aug 2002 (P4)	0.16		
Sep 2002 to Dec 2002 (P5)		0.27	
Jan 2003 to Apr 2003 (P6)			0.14

Table 5.13 d-value analysis of the average cost of antihypertensive drugs for the different time periods

May 2002 to Aug 2002 (P4)	0.06		
Sep 2002 to Dec 2002 (P5)		0.08	
Jan 2003 to Apr 2003 (P6)			0.08

Table 5.14 d-value analysis of the average cost of other vasodilators for the different time periods

May 2002 to Aug 2002 (P4)	0.41		
Sep 2002 to Dec 2002 (P5)		0.39	
Jan 2003 to Apr 2003 (P6)			0.27

Table 5.15 d-value analysis of the average cost of positive inotropic drugs for the different time periods

	May 2002 to Aug 2002 (P4)	Sep 2002 to Dec 2002 (P5)	Jan 2003 to Apr 2003 (P6)
May 2002 to Aug 2002 (P4)	0.12		
Sep 2002 to Dec 2002 (P5)		0.14	
Jan 2003 to Apr 2003 (P6)			0.18

Table 5.16 d-value analysis of the average cost of vasoconstrictors for the different time periods

	May 2002 to Aug 2002 (P4)	Sep 2002 to Dec 2002 (P5)	Jan 2003 to Apr 2003 (P6)
May 2002 to Aug 2002 (P4)	0.26		
Sep 2002 to Dec 2002 (P5)		0.27	
Jan 2003 to Apr 2003 (P6)			0.16

5.6.2 General overview of utilisation patterns of hypolipidemic drugs

Lipid-lowering drugs are considered as the first choice drugs in control of dyslipidemias and they are well tolerated by most patients (Carvalho *et al.,* 2004: 257). Hypolipidemic drugs constituted 2.70% (n = 21820911) and 2.78% (n =27277825) for the first study year and the second study year respectively of the total number of all medicine items claimed per study year. As depicted in table 5.11 and table 5.12 it can be seen that the total number of hypolipidemic drugs claimed increased during the first study year and reached a maximum value (n= 262405) in P4 then it was regulated from P5 to P6. It was 589036 in the first study year compared to 759675 in the second study year.

The average number of all hypolipidemic drugs claimed per prescription stayed the same for all study periods (refer to table 5.17 and table 5.18). Due to a standardised average number of hypolipidemic drugs per prescription, the d-value of 0.00 was obtained between (P1 and P4), (P2 and P5) and P3 and P6). This shows that there was on average, only one hypolipidemic drug dispensed per prescription for all study periods.

The total cost of all hypolipidemic drugs claimed from P1 to P3 constituted 6.33% (n= R3 097 604 602) of the total cost of all medicine items claimed whereas during the second study year the cost of hypolipidemic drugs decreased to 6.23 % (n= R 4 053 280 295) of the total cost of all medicine items claimed. Though this shows a decrease in percentage of disbursement of

hypolipidemic drugs, the actual cost of all hypolipidemic drugs claimed increased from R196 076 050 during the first study year to R252 919 285 during the second study year. In South Africa, this increase in drug cost could have been brought about by the weak performance of the economy towards the end of the 1990's; this was followed by an insignificant economic expansion (South African Revenue Services, 2001: 2). International economic recession has also contributed to capital outflows and weaknesses in developing countries (South Africa) putting the rand under considerable pressure in 2000, depreciating to about 9½ per cent in real terms during 2000 (Manuel, 2001: 4).

The rand went into freefall late in 2001; however, it turned out to be the economy's discount grace (ABSA, 2004: 4). Monetary policy was tightened during 2002 (Manuel, 2004: 11). The strong performance of the rand during 2002 and the initial stages of 2003 contributed to the moderation in inflation (ABSA, 2004: 4). Consumer price index (CPIX) inflation declined significantly from its peak (11.3% in October). CPIX is now firmly within the target range of 3% to 6% and it will average 4.8% this year (2004) and will remain within the target band over the medium term (Manuel, 2004: 11). This could have brought the increase in prices of medicine items from 2001 to 2003.

It is clear from table 5.17 that the average cost per hypolipidemic drug increased from P1 (R326.20 ± 94.73) to P3 (R337.93± 89.26), it reached a peak in March 2002 (341.98 ± 90.16) from there it declined right through to the end of the second study year (refer to table C.9 and C.10 of Appendix C). The d-value of the average cost per hypolipidemic agent between the different time periods was small (d $\leq$0.2) with no practical significance.

Table 5.17 General overview of the utilisation patterns of hypolipidemic drugs from May 2001 to April 2002 (period P1 to P3)

Total number of hypolipidemic drugs claimed	140962	189652	258422
Average cost per hypolipidemic drug (R)	326.20 ± 94.73	330.96 ± 87.94	337.93 ± 89.26
Maximum cost per hypolipidemic drug (R)	3466.82	1932	3276.40
Number of prescriptions with hypolipidemic drugs	139542	187906	256160
Average number of hypolipidemic drugs per prescription	1.01 ± 0.10	1.01 ± 0.09	1.01 ± 0.10
Minimum number of hypolipidemic drugs per prescription	1.00	1.00	1.00
Maximum number of hypolipidemic drugs per prescription	3.00	3.00	3.00
Average cost of hypolipidemic drugs per prescription (R)	329.51±102.76	334.03 ± 95.98	340.91 ±98.18
Maximum cost of hypolipidemic drugs per prescription (R)	3466.82	2043.77	3276.40
Total cost of all hypolipidemic drugs (R)	45981144.59	62766748.93	87328156.44

The average cost of hypolipidemic drugs claimed per prescription increased during the first study year from P1 to P3. The second study year was witnessed by a decline in average cost of hypolipidemic drugs per prescription. The d-value of the average cost of hypolipidemic drugs per prescription between different time periods was small ($d \leq 0.2$) and insignificant (refer to table 5.20). The maximum cost per hypolipidemic drug was relatively higher than the average cost per hypolipidemic drug during the two study years.

Table 5.18 General overview of the utilisation patterns of hypolipidemic drugs from May 2002 to April 2003 (period P4 to P5)

[illegible]	[illegible]	[illegible]	[illegible]
Total number of hypolipidemic drugs claimed	262405	240826	256444
Average cost per hypolipidemic drug	338.97±85.33	335.11±84.61	324.69±104.89
Maximum cost per hypolipidemic drug	1893.78	1744.49	4184.04
Number of prescriptions with hypolipidemic drugs	260363	239046	254733
Average number of hypolipidemic drugs per prescription	1.01 ± 0.09	1.01 ● 0.09	1.01 ± 0.08
Minimum number of hypolipidemic drugs per prescription	1.00	1.00	1.00
Maximum number of hypolipidemic drugs per prescription	3.00	3.00	3.00
Average cost of hypolipidemic drugs per prescription	341.63±92.79	337.61±91.62	326.87±111.09
Maximum cost of hypolipidemic drugs per prescription	2179.01	1744.49	4184.04
Total cost of all hypolipidemic drugs	88948672.84	80705052.84	83265559.41

It is evident from table 5.18 that the maximum cost per hypolipidemic drug was 10.63, 5.84 and 9.70 times the average cost per hypolipidemic drug for P1, P2 and P3 during the first study year respectively. During the second study year, it was 5.59, 5.21 and 12.89 times the average cost per hypolipidemic drug for P4, P5 and P6 respectively (See table 5.19).

Table 5.19 d-value analysis of the average cost per hypolipidemic drugs claimed for the different time periods.

[illegible]	[illegible]	[illegible]	[illegible]
May 2002 to Aug 2002 (P4)	0.13		
Sep 2002 to Dec 2002 (P5)		0.05	
Jan 2003 to Apr 2003 (P6)			0.13

Table 5.20 d-value analysis of the average cost of hypolipidemic drugs claimed per prescription for the different time periods.

May 2002 to Aug 2002 (P4)	0.11		
Sep 2002 to Dec 2002 (P5)		0.04	
Jan 2003 to Apr 2003 (P6)			0.13

Table 5.21 d-value analysis of the average number of hypolipidemic drugs claimed per prescription for the different time periods.

May 2002 to Aug 2002 (P4)	0.00		
Sep 2002 to Dec 2002 (P5)		0.00	
Jan 2003 to Apr 2003 (P6)			0.00

As indicated on table 5.22 and table 5.23, hypolipidemic agents constituted on average 20.16% for P1 to P3 (n= 11330041) and 20.57% (n= 3693474) for P4 to P6 of the total number of cardiovascular drugs claimed per study year respectively. This slight deviation in the prevalence percentage of hypolipidemic drugs shows that for all study years, the proportion of hypolipidemic drugs in relation to cardiovascular drugs was stable regardless of the increase in number of cardiovascular drugs claimed (refer to table 5.22 and table 5.23).

The total cost of hypolipidemic drugs accounted on average 30.34% and 30.13% of the total cost of cardiovascular drugs claimed for P1 to P3 (n = R 644 233 349) and P4 to P6 (n = R 839421013) respectively. Unlike the prevalence percentage, the cost percentage was stabilised at a decreasing rate. Though the cost-prevalence index declined from P1 to P6, it was higher than one for both study years (refer to table 5.22 and table 5.23).

Table 5.22 Prevalence and cost of all hypolipidemic drugs claimed from May 2001 to April 2002 (period P1 to P3)

Months	Prevalence	Prevalence [%*]	Cost (R)	Cost [%#]	Cost-prevalence index
May 2001 to Aug 2001 (P1)	140962	19.68	45981144.59	29.68	1.51
Sep 2001 to Dec 2001 (P2)	189652	20.28	62766748.93	30.72	1.51
Jan 2002 to Apr 2002 P3)	258422	20.53	87328156.44	30.63	1.49

%* Frequency of hypolipidemic drugs divided by frequency of cardiovascular drugs (see table 5.5) for the corresponding study period multiplied by hundred
%# Total cost of hypolipidemic drugs divided by total cost of cardiovascular drugs (see table 5.5) for the corresponding study period multiplied by hundred

Table 5.23 Prevalence and cost of all hypolipidemic drugs claimed from May 2002 to April 2003 (period P4 to P6)

Months	Prevalence	Prevalence [%*]	Cost (R)	Cost [%#]	Cost-prevalence index
May 2002 to Aug 2002 (P4)	262405	20.56	88948672.84	30.82	1.50
Sep 2002 to Dec 2002 (P5)	240826	20.62	80705052.84	30.50	1.48
Jan 2003 to Apr 2003 (P6)	256444	20.53	83265559.41	29.08	1.42

%* Frequency of hypolipidemic drugs divided by frequency of cardiovascular drugs (see table 5.6) for the corresponding study period multiplied by hundred
%# Total cost of hypolipidemic drugs divided by total cost of cardiovascular drugs (see table 5.6) for the corresponding study period multiplied by hundred

5.6.3 Utilisation of hypolipidemic drugs according to generic and innovator medicine items

At the beginning of this study, only one of the hypolipidemic drugs (bezafibrate) was available as a generic equivalent. Adco-simvastatin® was introduced into the South African market as a generic equivalent of Zocor® in October 2002 (see table B.9 and B.10 of Appendix B). That is shortly after the expiry of the innovator-patented life. Looking at table 5.15 and table 5.16, the prevalence of generic drugs increased slightly from P1 to P5 and a marked increased can be clearly seen between P5 and P6. The noticeable increase in generic utilisation is largely due to the introduction of Adco- simvastatin®.

The prevalence of hypolipidemic generic medicine items augmented from 5236 in the first study year to 37079 in the second study year. This increase in generic prescribing was accompanied by a 4% decrease in utilisation of innovator drugs. Innovator drugs constituted 99.11% (n=589036)

and 95.11% (n=759675) of the total number of hypolipidemic drugs for the first and second study years respectively (refer to table 5.26 and tables 5.17 and 5.18).

As seen in table 5.26 and table 5.27, the cost of innovator drugs declined from 99.60% to 97.60% of the total cost of hypolipidemic drugs from P1 to P6 respectively. The difference between the average costs of innovator drugs and generic drugs is evident. The average cost of innovator drugs was on average 1.54 times higher than that of generic products during the two study periods. Because of that, the d-value between the average cost of innovator drugs and generic drugs for all the study periods was more than 0.8 and of practical significance.

There was no practical significant difference between the average costs of innovator drugs between the different four-months periods (refer to table 5.24). The average cost of generic drugs increased from P1 to P3. It then reached a peak during P4 and it started levelling down from P5 to P6 (refer to table 5.26 and table 5.27). The decrease in average cost of generic products from P4 to P6 could have been brought about by the addition of another generic product (Adco-simvastatin®) into the South African market. The d-value of 1.28, 0.41 and 0.94 between the average cost of generic hypolipidemic drugs for the time periods P1 and P4, P2 and P5 and P3 and P6 respectively was evident for generic drugs (refer to table 5.25). The d-value of 1.28 and 0.94 ($d > 0.8$) had a large effect that is significant and of practical importance. This d-value explains the variation in average costs of generic hypolipidemic drugs between different study periods.

Table 5.24 d-value analysis of the average cost of innovator hypolipidemic drugs for the different time periods

	May 2001 to Aug 2001 (P1)	Sep 2001 to Dec 2001 (P2)	Jan 2002 to Apr 2002 (P3)
May 2002 to Aug 2002 (P4)	0.14		
Sep 2002 to Dec 2002 (P5)		0.07	
Jan 2003 to Apr 2003 (P6)			0.02

Table 5.25 d-value analysis between the average costs of generic hypolipidemic drugs for the different time periods

May 2002 to Aug 2002 (P4)	1.28		
Sep 2002 to Dec 2002 (P5)		0.41	
Jan 2003 to Apr 2003 (P6)			0.94

The cost-prevalence index of innovator hypolipidemic drugs was on average 1.00 and 1.02 for the first and second study years respectively. This shows that equilibrium exists between the cost and the prevalence of innovator hypolipidemic drugs. On the other hand, the cost-prevalence index of generic hypolipidemic drugs was on average 0.64 and 0.67 for the first and second study years respectively. This shows that generic hypolipidemic drugs are relatively inexpensive compared to innovator hypolipidemic drugs (refer to table 5.26 and table 5.27)

From the above discussion, it can be concluded that generic prescribing patterns of hypolipidemic drugs increased during the second study year. It is clearly indicated that the increase in generic prescribing goes hand in hand with the decrease in cost of drug therapy. This can further indicate that the cost of hypolipidemic drugs can further be reduced if more of the generic drugs are prescribed instead of innovator drugs.

Table 5.26 Summary of the usage of hypolipidemic drugs according to generic and innovator medicine items from May 2001 to April 2002 (period P1 to P3)

Months	I or G	Total no of items	%*	Average cost/ item(R)	Standard deviation (R)	Maximum cost/item (R)	Total Cost(R)	Cost %#	Cost-prevalence index	d-values
May to Aug 2001 (P1)	I	140068	99.37	326.98	94.47	3466.82	45799492.87	99.60	1.00	1.31
	G	894	0.63	203.19	37.44	394.90	181651.72	0.39	0.62	
Sep 1 to Dec 2001 (P2)	I	187993	99.13	332.00	87.57	1932.80	62414194.52	99.48	1.00	1.36
	G	1659	0.87	212.51	30.33	444.04	352554.41	0.52	0.60	
Jan to Apr 2002 (P3)	I	255739	98.96	338.97	89.05	3276.40	86687489.75	99.27	1.00	1.12
	G	2683	1.04	238.79	40.32	506.46	640666.69	0.73	0.70	

%*I is the total number of innovator hypolipidemic drugs claimed for the particular period divided by the total number of all hypolipidemic drugs (see table 5.7) claimed for that period, G is the total number of generic hypolipidemic drugs claimed for the particular period divided by the total number of all hypolipidemic drugs (see table 5.7) claimed for that particular period. %# I is the total cost of innovator hypolipidemic drugs claimed divided by the total cost of all hypolipidemic drugs (see table 5.7) claimed for that particular period. G is the total cost of generic hypolipidemic drugs claimed for the particular period divided by the total cost of all hypolipidemic drugs (see table 5.7) for that particular period

Table 5.27 Summary of the usage of hypolipidemic drugs according to generic and innovator medicine items from May 2002 to April 2003 (period P4 to P6)

Months	I or G	Total no of items	%*	Average cost/ item(R)	Standard deviation (R)	Maximum cost/item (R)	Total Cost(R)	Cost %#	Cost-prevalence index	d-values
May to Aug 2002 (P4)	I	258877	98.66	340.17	85.20	1893.78	88063279.17	99.00	1.00	1.05
	G	3528	1.34	250.96	33.55	758.24	885393.17	1.00	0.75	
Sep to Dec 2002 (P5)	I	234303	97.29	337.88	83.59	1744.49	79166044.14	98.09	1.01	1.22
	G	6523	2.71	235.94	56.92	580.34	1539008.70	1.91	0.70	
Jan to Apr 2003 (P6)	I	229416	89.46	341.15	96.67	4184.04	78266393.43	94.00	1.05	1.62
	G	27028	10.54	184.96	57.03	626.44	4999165.98	6.00	0.57	

%*I is the total number of innovator hypolipidemic drugs claimed for that particular period divided by the total number of all hypolipidemic drugs (see table 5.7) claimed for that period (see table 5.8), G is the total number of generic hypolipidemic drugs claimed for the particular period divided by the total number of all hypolipidemic drugs (see table 5.8) claimed for that particular period. %# I is the total cost of innovator hypolipidemic drugs claimed divided by the total cost of all hypolipidemic drugs (see table 5.7) claimed for that particular period. G is the total cost of generic hypolipidemic drugs claimed for that particular period divided by the total cost of all hypolipidemic drugs (see table 5.7) claimed for that particular period (see table 5.7)

5.7 SUB-PHARMACOLOGICAL GROUPS OF THE HYPOLIPIDEMIC DRUGS

The prevalence and cost of the different sub-pharmacological groups of the hypolipidemic drugs will be compared and discussed.

As described above, the total number of hypolipidemic drugs generally increased from the first study year to the second study year (refer to paragraph 5.6.2). Statins were the most frequently utilised hypolipidemic drugs. They accounted for 95.77% (n=589036) to 96.26% (n=759675) of the total number of hypolipidemic drugs prescribed in the first and second study years respectively. Fibrates were the second most prescribed sub-pharmacological group of the hypolipidemic drugs. The prevalence of fibrates decreased from 2.93% (n=589036) to 2.78% (n=759675) during the first study year and the second study year respectively. On the other hand, other hypolipidemic drugs accounted for 1.28% (n=589036) and 0.95% (n=759675) of the total number of hypolipidemic drugs during the first and second study years respectively (refer to table 5.28 and table 5.29).

Clinical evidence has shown that statins prevent or delay ischemic events in patients at risk for atherosclerotic coronary disease (Lazar, 2004: 730). In addition to that, statins have the most licensed indications and are widely championed by the authors of the evidence-based guidelines (Pittard, 2004: 1). Based on that, they are usually the starting drugs of choice (Dujovne, 2004: 269). The above-mentioned discussions might be the reason for the increase in utilisation of statins compared to other hypolipidemic drugs. From table 5.28 and table 5.29, it can be concluded that the statins and fibrates are the two sub-pharmacological groups of hypolipidemic drugs that increased in prevalence during the second study year.

More than 95% of the total cost of hypolipidemic drugs (n =R 196 076 050 (first study year) and (n=R 252 919 285 (second study year) was allocated to statins during both study years. The cost percentage was rather stabilised compared to the cost percentage of other sub-pharmacological groups. As indicated on table 5.17 and table 5.18, the cost of fibrates continued to grow from the first study year through to the second study year though prevalence decreased. It was R5 759 714.77 in the first study year and R7 430 172.47 during the second study year. However, the cost of the sub-pharmacological groups "others" declined with a decline in prevalence of the sub-pharmacological group "others". The cost of the sub-pharmacological group "others" accounted for 0.78% and 0.49% of the total cost of all hypolipidemic drugs in the first and second study years respectively. On average the cost-prevalence index of fibrates was 0.98 during the first study year, compared to 1.06 during the second study year. This shows that fibrates were

relatively expensive during the second study year in comparison with the first study year. The cost-prevalence index of statins was on average 1.00 for all study years. This indicates that both the cost and prevalence of statins were stable during both study years (refer to table 5.28 and table 5.29)

Table 5.28 Prevalence and cost of the different sub-pharmacological groups of the hypolipidemic drugs from May 2001 to April 2002 (period P1 to P3)

Sub-pharmacological group	Description	May 2001 to Aug 2001 (P1)	Sept 2001 to Dec 2001 (P2)	Jan 2002 to April 2002 (P3)
Fibrates	Prevalence	4107	5563	7680
	Prevalence %*	2.91	2.93	2.97
	Cost (R)	1295126.85	1768878.49	2695709.43
	Cost %#	2.82	2.82	3.01
	Cost-prevalence index	0.97	0.96	1.04
Statins	Prevalence	134811	181978	247373
	Prevalence %*	95.63	95.95	95.72
	Cost (R)	44295425.50	60550005.90	83944807.90
	Cost %#	96.33	96.47	96.13
	Cost-prevalence index	1.01	1.01	1.00
Others	Prevalence	2044	2111	3369
	Prevalence %*	1.45	1.11	1.30
	Cost (R)	390592.24	447864.54	687639.11
	Cost %#	0.85	0.71	0.78
	Cost-prevalence index	0.59	0.64	0.61

%* Is the quotient of the prevalence of the sub-pharmacological group and total number of hypolipidemic drugs for the corresponding period (as indicated on table 5.17) multiplied by hundred.
%# Is the total cost of the different sub-pharmacological group divided by the total cost of hypolipidemic drugs for the corresponding period (as indicated on table 5.17) multiplied by hundred.

Table 5.29 Prevalence and cost of different sub-pharmacological groups from May 2002 to April 2003 (period P4 to P6)

Sub-pharmacological group	Information	May 2002 to Oct 2002 (P4)	Nov 2002 to Jan 2003 (P5)	Feb 2003 to Apr 2003 (P6)
Fibrates	Prevalence	7607	6641	6933
	Prevalence %*	2.90	2.75	2.70
	Cost (R)	2545100.32	2322128.76	2562943.39
	Cost %#	2.86	2.88	3.08
	Cost-prevalence index	0.99	1.05	1.14
Statins	Prevalence	252149	232184	246889
	Prevalence %*	96.09	96.41	96.27
	Cost (R)	85918618.31	78022535.94	80305661.00
	Cost %#	96.59	96.68	96.45
	Cost-prevalence index	1.01	1.00	1.00
Others	Prevalence	2649	2001	2622
	Prevalence %*	1.00	0.83	1.02
	Cost (R)	484953.71	360388.14	396955.02
	Cost %#	0.55	0.45	0.47
	Cost-prevalence index	0.55	0.54	0.46

%* Is the quotient of the prevalence of sub-pharmacological group and total number of hypolipidemic drugs for the corresponding period (as indicated on table 5.18) multiplied by hundred.
%# Is the total cost of the different sub-pharmacological group divided by the total cost of hypolipidemic drugs for the corresponding period (as indicated on table 5.18) multiplied by hundred.

The maximum cost per medicine item of the sub-pharmacological group statins was relatively higher than the maximum cost per item of the other sub-pharmacological groups of the hypolipidemic drugs during both study years. The maximum cost per medicine item of fibrates, statins, and "others" was on average 4.51, 8.56 and 5.60 times the average cost per medicine items of the different sub-pharmacological groups respectively during the first study year. During the second study year, the maximum cost per medicine items of fibrates, statins and "others" was on average 3.37, 7.87 and 5.89 times the average cost per medicine items of the different sub-pharmacological groups of the hypolipidemic drugs respectively (refer to table 5.30 and table 5.31).

Table 5.30 Summary of the cost analysis of individual sub-pharmacological groups from May 2001 to April 2002 (period P1 to P3)

Sub-pharmacological group	Explanation	[illegible] (P1)	[illegible] (P2)	[illegible] (P3)
Fibrates	Total number of medicine items	4107	5563	7680
	Average cost per item (R)	315.35 ± 132.00	317.97±116.69	351.00 ± 135.08
	Maximum cost per item (R)	1546.68	1932.80	892.24
	Total cost (R)	1295126.85	1768878.49	2695709.43
Statins	Total number of medicine items	134811	181978	247373
	Average cost per item (R)	328.57 ± 89.45	332.73±84.14	339.35 ± 83.45
	Maximum cost per item (R)	3466.82	1821.15	3276.40
	Total cost (R)	44295425.50	60550005.90	83944807.90
Others	Total number of medicine items	2044	2111	3369
	Average cost per item (R)	191.09 ± 193.15	212.16±183.63	204.11 ± 199.47
	Maximum cost per item (R)	1518.65	726.62	842.62
	Total cost (R)	390592.24	447864.54	687639.11

During the second study year, the average cost of fibrates was higher than that of the first study year. It was R334.54±128.57 and R315.34±132 for P4 and P1 respectively, R349.67±135.41 and R317.97±116.69 for P5 and P2 respectively and R369.67±144.09 and 351.00±135.08 for P6 and P3 respectively. This could have been brought about by an increase in the prices of fibrates as witnessed above. The average cost of statins increased from P1 to P3 and it started to decline from P4 to P6 (this could have been brought about by an increase in utilisation of generic simvastatin drugs). The average cost of "others" increased in the first two study periods and it started to decline from P2 to P6 (refer to table 5.30 and 5.31).

The d-value of the average cost of all sub-pharmacological groups of the hypolipidemic drugs was small and insignificant between different time periods (refer to table 5.34, table 5.35 and table 5.36). This shows that even though the average cost of statins and "others" increased, the increase was not conspicuous. On the other hand, the decline in average cost of fibrates was also insignificant.

Table 5.31 Summary of the cost analysis of individual sub-pharmacological groups from May 2002 to April 2003 (period P4 to P6)

Sub-pharmacological group	Information	May 2002 - Aug 2002 (P4)	Sept 2002 - Dec 2002 (P5)	Jan 2003 - April 2003 (P6)
Fibrates	Total number of medicine items	7607	6641	6933
	Average cost per item (R)	334.57±128.57	349.67±135.41	369.67±144.09
	Maximum cost per item (R)	1427.35	1047.62	1047.62
	Total cost (R)	2545100.32	2322128.76	2562943.39
Statins	Total number of medicine items	252149	232184	246889
	Average cost per item (R)	340.75±80.65	336.04±80.43	325.27±100.91
	Maximum cost per item (R)	1893.78	1744.49	4184.04
	Total cost (R)	85918618.31	78022535.94	80305661.00
Others	Total number of medicine items	2649	2001	2622
	Average cost per item (R)	183.07±173.36	180.10±159.49	151.39±164.17
	Maximum cost per item (R)	842.62	712.53	1378.37
	Total cost (R)	484953.71	360388.14	396955.02

Only one relatively large d-value (1.0 for P1) was experiential between the average cost of fibrates and statins (during the first study year). The d-value between average cost of fibrates and statins, though insignificant, increased from P4 to P5 (during the second study year). As seen in table 5.32 and table 5.33 the d-value calculated for the differences between the average cost of fibrates and "others" was on average 0.65 (medium and might be significant) in the first study year. It increased throughout the second study year to more than 0.8. This shows that there was a relatively large variation between the average cost of fibrates and the average cost of the "others". The same trend was observed between the d-values calculated for the differences in the average cost of statins and "others". According to the above discussion, it shows that the prices of fibrates and statins varied slightly between the different study years. However, both the cost of fibrates and statins were relatively higher than the prices of "others" during the second study year.

Table 5.32 d-value analysis of the average cost of medicine items for the different sub-pharmacological groups from May 2001 to April 2002 (period P1 to P3)

Statins	1.0		0.13		0.09	
Others	0.64	0.71	0.58	0.66	0.74	0.68

Table 5.33 d-value analysis of the average cost of medicine items for the different sub-pharmacological groups from May 2002 to April 2003 (period P4 to P6)

Statins	0.05		0.10		0.30	
Others	0.87	0.91	1.06	0.98	1.33	1.01

Table 5.34 d-value analysis of the average cost of fibrates per item for the different time periods

May 2002 to Aug 2002 (P4)	0.15		
Sep 2002 to Dec 2002 (P5)		0.23	
Jan 2003 to Apr 2003 (P6)			0.13

Table 5.35 d-value analysis of the average cost of statins per item for the different time periods

May 2002 to Aug 2002 (P4)	0.14		
Sep 2002 to Dec 2002 (P5)		0.04	
Jan 2003 to Apr 2003 (P6)			0.14

Table 5.36 d-value analysis of the average cost of "others" per item for the different time periods

May 2002 to Aug 2002 (P4)	0.04		
Sep 2002 to Dec 2002 (P5)		0.17	
Jan 2003 to Apr 2003 (P6)			0.26

5.8 INDIVIDUAL HYPOLIPIDEMIC MEDICINE ITEMS

The utilisation patterns and the cost of individual hypolipidemic drugs will be discussed in this section. Individual drugs of the sub-pharmacological group fibrates will be discussed first, followed by individual drugs of the sub-pharmacological group statins and "others".

5.8.1 Fibrates

The utilisation patterns and cost of individual drugs containing bezafibrate, clofibrate, fenofibrate and gemfibrozil as an active ingredient will be discussed in this section.

5.8.1.1 Bezafibrates

The usage patterns and cost of medicine items containing bezafibrate, as an active ingredient will be discussed under this paragraph

5.8.1.1.1 Prevalence and cost of medicine items containing bezafibrate as an active ingredient

The total number of individual medicine items containing bezafibrate as an active ingredient increased from 9542 to 12942 during the first and second study years respectively. Bezalip 200mg®, Bezalip retard 400mg® and Rolab-bezafibrate 400mg® constituted 12.35%, 32.78% and 54.87% respectively of the total number of bezafibrates (n = 9542) containing drugs prescribed in the first study year.

Prescribing patterns changed in the second study year. As witnessed in the table below, the prevalence percentage of Bezalip retard 400mg® decreased by more than half of what it had been in the first study year. It constituted 8.77% (n = 12942) of the total number of bezafibrates drugs prescribed during the second study year. Though the prevalence percentage of Bezalip 200mg® decreased, it accounted for 10.96% (n = 12942) of the total number of bezafibrates drugs prescribed during the second study year. The prevalence percentage of Rolab-bezafibrate 400mg® accounted for 80.27% (n = 12942) of the total number of bezafibrate drugs prescribed during the second study year. The actual prevalence increased by more than half of what it had been during the first study year. The prevalence of Rolab-bezafibrate 400mg® was 10389 and 5236 during the second and first study years respectively.

As seen in table B.11 to table B.14 (refer to Appendix B), individual medicine items containing bezafibrate as an active ingredient, were drugs with the highest prescription rate of the sub-pharmacological group fibrates. All individual medicine items containing bezafibrate as an

active ingredient accounted for on average 1.59% of the total number of hypolipidemic drugs claimed during both study years. The rate of decline of both Bezalip 200mg® and Bezalip retard 400mg® was the same as the rate of increase in utilisation of Rolab-bezafibrate 400mg®. This shows that patients on Bezalip 200mg® and Bezalip retard 400mg® could have been therapeutically switched to Rolab-bezafibrate 400mg®.

As indicated in table 5.37, the cost percentage of Rolab-bezafibrate 400mg® increased from P1 to P3, however, the cost percentage of Bezalip retard 400mg® declined from P1 to P3. During the second study year, the same trend of the cost percentages of individual medicine items containing bezafibrate as an active ingredient was witnessed (refer to table 5.38). Bezalip 200mg® Bezalip retard 400mg® and Rolab-bezafibrate 400mg® accounted for 10.18 %, 44.95% and 44.88% of the total expenditure (n=R2 618 038.90) of all bezafibrates claimed during the first study year. During the second study year, Bezalip 200mg®, Bezalip retard 400mg® and Rolab-bezafibrate 400mg® accounted for 10.29%, 11.60% and 78.11% of the total cost (n= R3 597 023) of bezafibrates claimed. All medicine items containing bezafibrate as an active ingredient accounted for 45.45% (n= R5 759 714.77) and 48.41% (n= R 7 430 172.47) of the total cost of fibrates during the first and second study years respectively.

Table 5.37 Prevalence and cost of individual medicine items containing bezafibrate as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Month	Individual bezafibrate	Prevalence	Prevalence %	Cost	Cost %	Cost to prevalence index
May 2001 to Aug 2001 (P1)	Bezalip 200mg®	316	0.22	65167.95	0.14	0.64
	Bezalip retard 400mg®	920	0.65	302038.00	0.66	1.02
	Rolab-bezafibrate 400mg®	894	0.63	181651.72	0.40	0.63
Sep 2001 to Dec 2001 (P2)	Bezalip 200mg®	364	0.19	82818.34	0.13	0.68
	Bezalip retard 400mg®	1023	0.54	374566.04	0.60	1.11
	Rolab-bezafibrate 400mg®	1659	0.87	352554.41	0.56	0.64
Jan 2002 to April 2002 (P3)	Bezalip 200mg®	498	0.19	118489.48	0.14	0.74
	Bezalip retard 400mg®	1185	0.46	500086.27	0.57	1.24
	Rolab-bezafibrate 400mg®	2683	1.04	640666.69	0.73	0.70

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs for the corresponding period (calculated from table 5.22) multiplied by hundred.
%# Is the total cost of individual hypolipidemic drugs divided by the total cost of all hypolipidemic drugs for the corresponding period (calculated from table 5.22) multiplied by hundred.

During the first study year, the cost-prevalence index of all individual items containing bezafibrate as an active ingredient increased from P1 to P3 (refer to table 5.37). Bezalip retard 400mg® was the only bezafibrate with the cost-prevalence index of more than one during the first study year. This shows that the cost of Bezalip retard 400mg® was relatively higher compared to the cost of Rolab bezafibrate 400mg®. During the second study year, the cost-prevalence index of Bezalip retard 400mg® had no definite trend. It increased from P4 (CPI = 1.05) to P5 (CPI = 1.21) and then decreased during P6 (CPI = 1.00) whereas, the cost-prevalence index of the other two bezafibrates increased. The cost-prevalence index of Rolab-bezafibrate 400mg® increased to the point where it reached one towards the end of the second study year. It is apparent from table 5.37 and table 5.38 that the more Rolab-bezafibrate 400mg® is prescribed, the more its cost-prevalence index is increasing and hence it becomes relatively expensive compared to Bezalip retard 400mg®.

Table 5.38 Prevalence and cost of individual medicine items containing bezafibrate as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Month	Bezafibrate	Prevalence	Prevalence per %*	Cost (Rs)	Cost %#	Cost-prevalence index
May 2002 to Aug 2002 (P4)	Bezalip 200mg®	520	0.20	131204.37	0.15	0.75
	Bezalip retard 400mg®	571	0.22	202570.85	0.23	1.05
	Rolab-bezafibrate 400mg ®	3528	1.34	885393.17	1.00	0.75
Sep 2002 to Dec 2002 (P5)	Bezalip 200mg®	407	0.17	103664.38	0.13	0.76
	Bezalip retard 400mg®	344	0.14	137662.92	0.17	1.21
	Rolab-bezafibrate 400mg®	3233	1.34	880446.26	1.09	0.81
Jan 2003 to April 2003 (P6)	Bezalip 200mg®	491	0.19	135116.12	0.16	0.84
	Bezalip retard 400mg®	220	0.09	77119.37	0.09	1.00
	Rolab-bezafibrate 400mg®	3628	1.14	1043845.67	1.25	1.10

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs for the corresponding period (calculated from table 5.23) multiplied by hundred.
%# Is the total cost of individual hypolipidemic drugs divided by the total cost of all hypolipidemic drugs for the corresponding period (calculated from table 5.23) multiplied by hundred.

5.8.1.1.2 Cost analysis of individual medicine items containing bezafibrate as an active ingredient

It is apparent from table 5.39 that the average cost of all individual medicine items containing bezafibrate as an active ingredient increased during the first study year. Though the average cost of all bezafibrates drugs increased during the first study year, the rate of increase of Bezalip retard 400mg® was higher than the rate of increase in average cost of the other two bezafibrates. The average cost of Bezalip retard 400mg® increased from R328.30 to R422.01 (with a difference of R94, 00). This represents 29% (422.01-328.30/328.30*100) increase in average cost of Bezalip retard 400mg® during the first study year. The second study year (refer to table 5.40) is witnessed by continued increase in average cost of Rolab-bezafibrate 400mg® and Bezalip 200mg®. As opposed to the first study year, the average cost of Bezalip retard 400mg® decreased towards the end of the second study year. This could have been brought about by the decrease in the prevalence of this group of drugs. It can be concluded that though the number of drugs containing bezafibrate as an active ingredient increased (during the second study year), prescriptions of the innovator drugs decreased as opposed to the generic drugs.

Table 5.39 Cost analysis of individual medicine items containing bezafibrate as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Months	Bezafibrate	No. of items	Average cost/ item	Standard deviation	Maximum cost/ item	Total cost
May 2001 to Aug 2001 (P1)	Bezalip 200mg®	316	206.23	78.37	320.73	65167.95
	Bezalip retard 400mg®	920	328.30	41.73	655.36	302038.00
	Rolab-bezafibrate 400mg®	894	203.19	37.44	394.90	181651.72
Sep 2001 to Dec 2001 (P2)	Bezalip 200mg®	364	227.52	91.80	386.95	82818.36
	Bezalip retard 400mg®	1023	366.14	65.11	792.34	374566.04
	Rolab-bezafibrate 400mg®	1659	212.51	30.32	444.04	352554.41
Jan 2002 to April 2002 (P3)	Bezalip 200mg®	498	237.93	101.66	425.49	118489.48
	Bezalip retard 400mg®	1185	422.01	69.80	871.38	500086.27
	Rolab-bezafibrate 400mg®	2683	238.79	40.32	506.46	640666.69

Table 5.40 Cost analysis of individual medicine items containing bezafibrate as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Months	Bezafibrate	Number of items	Average cost per item (RM)	Standard deviation	Minimum cost (RM)	Total cost (RM)
May to Aug 2002 (P4)	Bezalip 200mg®	520	252.32	111.61	446.70	131204.37
	Bezalip retard 400mg®	571	354.77	110.88	459.02	202570.85
	Rolab-bezafibrate 400mg®	3528	250.96	33.55	758.24	885393.17
Sep 2002 to Dec 2002 (P5)	Bezalip 200mg®	407	254.70	104.46	482.32	103664.38
	Bezalip retard 400mg®	344	400.18	107.63	495.52	137662.92
	Rolab-bezafibrate 400mg®	3233	272.33	48.73	569.64	880446.26
Jan 2003 to April 2003 (P6)	Bezalip 200mg®	491	275.19	108.65	482.32	135116.12
	Bezalip retard 400mg®	220	350.54	104.79	569.98	77119.37
	Rolab-bezafibrate 400mg®	3628	287.72	40.28	626.44	1043845.67

The d-value of the average cost between Rolab-bezafibrate 400mg® and Bezalip retard 400mg® as shown on table 5.41 was more than 0.8 (large and of practical significance) during the first study year. This shows that there was much deviation in average cost of the two products during the first study year. It can be concluded from the values below that the average cost of Bezalip retard 400mg® was relatively higher than the average cost of Rolab-bezafibrate 400mg® during the first study year.

During the second study year, the d-value took the trend of the average cost of Bezalip retard 400mg®. The d-value of 0.94, 1.19, and 0.60 was evident for P4, P5 and P6 respectively. This d-value trend opposes that of the first study year (increased d-value throughout the study year). It shows that the average cost of Bezalip retard 400mg started levelling down towards the end of the second study year.

Table 5.41 d-value analysis of the average cost of individual medicine items containing bezafibrate as an active ingredient for the different time periods

Rolab-bezafibrate 400mg®	3.00	2.4	2.62

as sub-therapeutic as it is below the maintenance dose of bezafibrate as described according to Sweetman (2002: 8495).

By virtue of their strength, both Bezalip retard 400mg® and Rolab-bezafibrate 400mg® can only conform to the defined dose if one and half tablets are given for 30 days supply. According to the Martindale, both Bezalip retard 400mg® and Rolab-bezafibrate 400mg® are modified release tablets (Sweetman, 2002: 849) and the whole tablet must be administered to achieve the daily maintenance dose of 400mg. If one tablet is given daily then the dose is below the DDD (dose=0.4g). On the other hand, if two tablets are given daily then the dose will be above that of the defined daily dose (dose=0.8g). The two bezafibrates can only conform to the maintenance dose of bezafibrate if the good standards of dispensing are adhered to.

As depicted in table 5.43 and table 5.44, the number of prescriptions that conformed to the DDD was very low. The prescriptions of Bezalip retard 400mg® that conformed to the DDD constituted 0.13% (n = 3128) and 0.00% (n = 1135) during the first and the second study years respectively whilst those of Rolab-bezafibrate 400mg® constituted 0.08% (n = 5236) and 0.04% (n = 10389) during the first and second years respectively. The prescriptions with the DDD of less than the maintenance dose decreased for both Bezalip retard 400mg® and Rolab-bezafibrate 400mg® from the first study year through to the second study year. Those prescriptions accounted for 2.77% (n =3128) and 2.03% (n = 1135) as well as 2.39% (n =5236) and 1.57% (n =10389) for Bezalip retard 400mg® and Rolab-bezafibrate 400mg® during the first and second study years respectively.

More than 95% (n=19888, the total number of all prescriptions of Bezalip retard 400mg® and Rolab-bezafibrate 400mg® during both study years) of prescriptions for Bezalip retard 400mg® and Rolab-bezafibrate 400mg® conformed to the maintenance dose for both study years. Those prescriptions were fewer in the first study year compared to the second study year. The prescriptions that were above the defined daily dose for Bezalip retard 400mg® decreased from the first study year to the second study year. The prescriptions for Bezalip retard 400mg® above the DDD accounted for 2.11% (n = 3128) and 0.79% (n = 1135) during the first and the second study years respectively; on the other hand, those for Rolab-bezafibrate 400mg® accounted for 2.08% (n = 5236) and 2.18% (n = 10389) in the first and second study years respectively.

Table 5.43 The prescribed daily dose of individual medicine items containing bezafibrate as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Bezafibrate	PDD	May to Aug 2001 (P1)		Sept to Dec 2001 (P2)		Jan to Apr 2002 (P3)	
		P	%*	P	%*	P	%*
Bezalip 200mg®	<0.4g	125	39.56	162	44.51	260	52.21
	=0.4g	127	40.19	131	35.99	169	33.94
	=0.6g	64	20.26	71	19.51	69	13.86
	>0.6g	0	0	0	0	0	0
Bezalip retard 400mg®	<0.4g	60	0.65	11	1.07	17	1.43
	=0.4g	887	96.41	988	96.58	1148	96.88
	=0.6g	4	0.43	0	0	0	0
	>0.6g	23	2.50	24	2.35	20	1.69
Rolab-bezafibrate 400mg®	<0.4g	25	2.8	37	2.23	63	2.35
	=0.4g	836	93.51	1601	96.50	2561	95.45
	=0.6g	4	0.45	0	0	0	0
	>0.6g	29	3.24	21	1.27	59	2.20

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table
%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table (per study period e.g. P1) divided by the total number of prescriptions of the individual medicine item whose PDD is calculated multiplied by hundred.

Table 5.44 The prescribed daily dose of individual medicine items containing bezafibrate as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Bezafibrate	PDD	May to Aug 2002 (P4)		Sept to Dec 2002 (P5)		Jan to Apr 2003 (P6)	
		P	%*	P	%*	P	%*
Bezalip 200mg®	<0.4g	262	50.38	233	57.25	256	51.14
	=0.4g	186	35.77	133	32.68	187	38.09
	=0.6g	72	13.85	41	10.07	48	9.78
	>0.6g	0	0	0	0	0	0
Bezalip retard 400mg®	<0.4g	9	1.58	10	2.91	4	1.82
	=0.4g	556	97.37	334	97.09	213	96.82
	=0.6g	0	0	0	0	0	0
	>0.6g	6	1.05	0	0	3	1.36
Rolab-bezafibrate 400mg®	<0.4g	64	1.81	42	1.30	57	1.57
	=0.4g	3386	95.98	3096	95.76	3514	96.86
	=0.6g	1	0.03	0	0	3	0.08
	>0.6g	77	2.18	95	2.94	54	1.49

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table
%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table (per study period e.g. P5) divided by the total number of prescriptions of the individual medicine item whose PDD is calculated multiplied by hundred.

It can be concluded from the discussion above that more than 95% (n=22484) of the prescription of bezafibrate did not conform to the defined daily dose during both study years. This indicates that the prescribed daily dose of bezafibrate in South Africa is not in line with the defined daily dose as set by the World Health Organization.

5.8.1.1.4 MPL analysis of bezafibrates.

The MPL analysis is conducted on drugs that appear on the Medscheme® price list. Bezalip retard 400mg® and Rolab-bezafibrate 400mg® are the two bezafibrates that appear on the price list (refer to appendix D, table D5 and table D6 for calculations of the cost per unit). It is evident from table 5.45 that the total cost of Bezalip retard 400mg® was higher than the calculated cost for all the quantities prescribed (with the exception of Bezalip retard 400mg® with a packaging size of 60 tablets). The total cost that is higher than the calculated cost indicates that the cost paid to the provider (pharmacy or dispensing doctor) is actually higher than the cost that the medical administrator or medical scheme is prepared to pay. According to Medical Scheme Act (131/1998), if the total cost that the pharmacist or dispensing doctor is asking for, is more than the cost that the medical administrator or medical scheme is prepared to pay then the patient will have to pay the remaining balance.

The cost difference shows the actual balance that the patient is expected to co-pay the provider. Generally, the total cost of Rolab-Bezafibrate 400mg® was higher than the calculated cost. It was apparent for all study periods that the calculated cost of Rolab-Bezafibrate 400mg® with a package size of 60 tablets was higher than the total cost for all periods. As seen on table 5.45, the cost difference for Bezalip retard 400mg® and Rolab-bezafibrate 400mg® for May 2002 to the end of August 2002 was R57 743.45 and (-) R20 941.42 respectively. This shows that there was no patient expected co-payment for Rolab-bezafibrate 400 mg® whereas on the other hand, 28.51% (n=R202 570.85) of the total cost of Bezalip retard 400mg® was expected to be co-paid by the patients for May 2002 to the end of August 2002.

It is apparent from table 5.46 and table 5.47 that the total cost of Bezalip retard 400mg® was greater than the calculated cost for the periods September 2002 to December 2002 (P5) and for January 2003 to April 2003 (P6). The cost difference was R 46 999.42 and R 14 598.43 for P5 and P6 respectively. The above discussion shows that the cost difference of Bezalip retard 400mg® was declining from P4 to P6. The total cost of Rolab-bezafibrate 400 mg® was greater than the calculated cost during P5; however, during P6 the calculated cost was greater than the total cost of Rolab-bezafibrate 400 mg®. The cost difference was (-) R7 814.39 and R5 061.33 during P5 and P6 respectively. There was no patient expected co-payment during P5 for Rolab-bezafibrate 400 mg®, however, patient expected co-payment accounted for 0.48% (n=R1 043 845.67) of the total cost of Rolab-bezafibrate 400 mg® during P6.

It can be concluded, based on the above mentioned discussion, that the use of generic products results in little or no patients expected co-payments. As indicated, the use of Rolab-bezafibrate 400 mg® was relatively inexpensive when compared to the utilisation of Bezalip retard 400mg® during P4 to P5, Therefore generic prescribing should be encouraged.

Table 5.45 MPL analysis of Bezalip retard® 400mg and Rolab-bezafibrate® 400mg from May 2002 to August 2002 (P4)

Product name	Quantity	Number of prescriptions	Number of tablets	Average cost/ item (R) ±	Total cost (R)	Medschemepricelist				
						Reimbursement limit (R)	Calculated cost (R)	Effect +/-	Cost difference	Cost saving %
Bezalip retard 400mg®	10	1	10	169.29 ± 0	169.29	8.43	84.30	+	84.99	50.20
	15	6	90	141.18 ± 0	847.08	8.43	758.70	+	88.38	10.43
	20	2	40	187.53 ± 0	375.06	8.43	337.20	+	37.86	10.09
	30	556	16680	361.78±102.96	201148.94	8.43	140612.40	+	60536.54	30.10
	60*	6	360	5.08 ± 0*	30.48	8.43	3034.80	-	-3004.32	-9856.69
Rolab-bezafibrate 400 mg®	6	1	6	57.48 ± 0	57.48	8.43	50.58	+	6.9	12.00
	15	36	540	140.66 ± 0.14	5063.58	8.43	4552.20	+	511.38	10.10
	20	3	60	186.97 ± 0.01	560.92	8.43	505.80	+	55.12	9.83
	22	3	66	205.47 ± 0	616.41	8.43	556.38	+	60.03	9.74
	23	3	69	214.69 ± 0	644.07	8.43	581.67	+	62.4	9.69
	28	18	504	253.74 ± 0	4567.32	8.43	4248.72	+	318.6	6.98
	30	3386	101580	252.16 ±12.18	853825.46	8.43	856319.40	-	-2493.94	-0.29
	38	1	38	328.19 ± 0	328.19	8.43	320.34	+	7.85	2.39
	60	76	4560	249.63 ± 189.74	18971.50	8.43	38440.80	-	-19469.3	-102.62
	90	1	90	758.24 ± 0	758.24	8.43	758.70	-	-0.46	-0.06

*The information for Bezalip retard 400mg® with a packaging size of 60 tablets is copied directly from the database. The cost saving was calculated according to the information on the database. Refer to chapter 4 for validity and reliability of data.

Calculated cost is the cost that the medical administrator or medical scheme is prepared to pay; the total cost is the total cost claimed by the provider; Cost difference is the cost in excess of what the medical administrator or medical scheme is prepared to pay, it is the expected cost to be paid by the patient to the provider. This patient co-payment results when the calculated cost is less than the total cost. Cost saving % is the expected percentage co-paid by the patient. Effect (+) = the total cost is more than the cost that the medical administrator or medical scheme is prepared to pay. Effect (-) = the calculated cost is more than the total cost; this indicated the savings incurred by the medical administrator or medical scheme or patient.

Table 5.46 MPL analysis of Bezalip retard® 400mg and Rolab-bezafibrate® 400mg from September 2002 to December 2002 (P5)

Product name	Quantity	Number of scripts	Number of tablets	Average cost per item (R)	Total cost (R)	Medscheme price list				
						Cost per unit (R)	Calculated cost (R)	+/-	Cost difference	Cost saving %
Bezalip retard 400mg®	5	1	5	26.54 ± 0	26.54	8.95	44.75	-	-18.21	-68.61
	8	4	32	141.19 ± 6.18	564.76	8.95	286.40	+	278.36	49.29
	10	2	20	94.78 ± 0	189.56	8.95	179.00	+	10.56	5.57
	15	2	30	252.99 ± 0	505.98	8.95	268.50	+	237.48	46.93
	23	1	23	386.89 ± 0	386.89	8.95	205.85	+	181.04	46.79
	30	334	10020	407.15 ± 99.84	135989.19	8.95	89679.00	+	46310.19	34.05
Rolab-bezafibrate 400 mg®	7	4	28	66.93 ± 0	267.72	8.95	250.60	+	17.12	6.39
	9	1	9	95.68 ± 0	95.68	8.95	80.55	+	15.13	15.81
	13	3	39	137.25 ± 0	411.75	8.95	349.05	+	62.7	15.23
	14	1	14	147.74 ± 0	147.74	8.95	125.30	+	22.44	15.19
	15	26	390	146.76 ± 8.41	3815.64	8.95	3490.50	+	325.14	8.52
	25	3	75	262.14 ± 0	786.42	8.95	671.25	+	115.17	14.64
	28	4	112	285.33 ± 0	1141.32	8.95	1002.40	+	138.92	12.17
	30	3096	92880	269.63 ± 19.92	834477.77	8.95	831276.00	+	3201.77	0.38
	60	95	5700	413.71 ± 202.13	39302.22	8.95	51015.00	-	-11712.8	-29.80

Calculated cost is the cost that the medical administrator or medical scheme is prepared to pay; the total cost is the total cost claimed by the provider; Cost difference is the cost in excess of what the medical administrator or medical scheme is prepared to pay, it is the expected cost to be paid by the patient to the provider. This patient co-payment results when the calculated cost is less than the total cost. Cost saving % is the expected percentage co-paid by the patient. Effect (+) = the total cost is more than the cost that the medical administrator or medical scheme is prepared to pay. Effect (-) = the calculated cost is more than the total cost; this indicated the savings incurred by the medical administrator or medical scheme or patient.

Table 5.47 MPL analysis of Bezalip retard® 400mg and Rolab bezafibrate® 400mg from January 2003 to April 2003 (P6)

Product name	Quantity	Number of scripts	Number of tablets	Average cost per unit (R)	Total cost (R)	Medscheme price list (R)				
						Cost per unit (R)	Calculated cost (R)	+/-	Cost difference	Cost saving %
Bezalip retard 400mg®	8	4	32	85.28 ± 0	341.12	9.47	303.04	+	38.08	11.16
	30	213	6390	352.44 ● 96.60	75068.81	9.47	60513.30	+	14555.51	19.39
	60	3	180	569.81 ± 0.28	1709.44	9.47	1704.60	+	4.84	0.28
Rolab-bezafibrate 400 mg®	5	3	15	54.03 ± 0	162.09	9.47	142.05	+	20.04	12.36
	15	44	660	158.10 ± 0.03	6955.49	9.47	6250.20	+	705.29	10.14
	20	6	120	210.09 ± 0	1260.54	9.47	1136.40	+	124.14	9.85
	25	4	100	262.14 ± 0	1048.56	9.47	947.00	+	101.56	9.69
	30	3514	105420	285.67 ± 15.80	1003853.28	9.47	998327.40	+	5525.88	0.55
	45	3	135	441.97 ± 0	1325.91	9.47	1278.45	+	47.46	3.58
	60	54	3240	541.48 ± 97.28	29239.80	9.47	30682.80	-	-1443	-4.94

Calculated cost is the cost that the medical administrator or medical scheme is prepared to pay; the total cost is the total cost claimed by the provider; Cost difference is the cost in excess of what the medical administrator or medical scheme is prepared to pay, it is the expected cost to be paid by the patient to the provider. This patient co-payment results when the calculated cost is less than the total cost. Cost saving % is the expected percentage co-paid by the patient. Effect (+) = the total cost is more than the cost that the medical administrator or medical scheme is prepared to pay. Effect (-) = the calculated cost is more than the total cost, this indicated the savings incurred by the medical administrator or medical scheme or patient

5.8.1.2 Clofibrate

5.8.1.2.1 Prevalence and cost of individual medicine items containing clofibrate as an active ingredient

Lipaten® is the only medicine item that contains clofibrate as an active ingredient. It was only prescribed once (January 2002) during this study. No d-value calculation was carried out. It does not appear in the Medscheme price list® as a result MPL analysis was not carried out. Since it was only prescribed in January, there was no comparison between its utilisation patterns a year before and a year after the implementation of Medscheme price list®. The cost-prevalence index of Lipaten® shows that the cost of Lipaten® outweighs the prevalence.

Table 5.48 Prevalence and cost of Lipaten® (P3)

Period	Prevalence	Prevalence percentage*	Cost (R)	Cost percentage#	Cost-prevalence index
January 2002 to April 2002 (P3)	8	0.0031	3256.16	0.0037	1.19

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs for the corresponding period (calculated from table 5.22) multiplied by hundred
%# Is the total cost of individual hypolipidemic drugs divided by the total cost of all hypolipidemic drugs for the corresponding period (calculated from table 5.22) multiplied by hundred.

5.8.1.3 Fenofibrate

The utilisation patterns and cost of drugs containing fenofibrate, as an active ingredient will be discussed under this paragraph.

5.8.1.3.1 Prevalence and cost of medicine items containing fenofibrate as an active ingredient

The total number of individual medicine items containing fenofibrate as an active ingredient increased from 5397 to 5456 during the first and second study years respectively. Though there was an increase in the actual number of drugs containing fenofibrate as an active ingredient, the prevalence percentages decreased and fenofibrates accounted for 31.12% (n=17350) and 25.76% (n= 21181) of the total number of fibrates and hence 0.92% (n=589036) and 0.72% (n=759675) of the total number of hypolipidemic drugs claimed during the first and second study years respectively.

Lipsin 300mg® accounted for 40.72% (n=R5 759 714.77) and 37.70% (n=R7 430 172.47) of the total cost of all fibrates and 1.20% (n=R 196 076 050.00) and 1.11% (n=R252 919 285.00) of the

total cost of all hypolipidemic drugs claimed during the first and the second study years respectively. The total cost of Lipsin 300mg® increased with an increase in prevalence during the first study year. The trend was rather erratic during the second study year. The cost-prevalence index was higher than one for all study years and it increased from P4 to P6 during the second study year. This indicates that Lipsin 300mg® is relatively expensive compared to Lopid 600mg® (CPI is on average less than one during the first study year).

Table 5.49 Prevalence and cost of individual medicine items containing fenofibrate as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Months	Fenofibrate	Prevalence	Prevalence percentage %*	Cost (R)	Cost percentage %#	Cost-prevalence index
May to Aug 2001 (P1)	Lipsin 300mg®	1436	1.02	592583.51	1.29	1.26
Sep to Dec 2001 (P2)	Lipsin 300mg®	1745	0.92	708674.90	1.13	1.23
Jan to Apr 2002 (P3)	Lipsin 300mg®	2216	0.86	1044367.74	1.20	1.40

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs for the corresponding period (calculated from table 5.23) multiplied by hundred
%# Is the total cost of individual hypolipidemic drugs divided by the total cost of all hypolipidemic drugs for the corresponding period (calculated from table 5.23) multiplied by hundred.

Table 5.50 Prevalence and cost of individual medicine items containing fenofibrate as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Months	Fenofibrate	Prevalence	Prevalence percentage %*	Cost (R)	Cost percentage %#	Cost-prevalence index
May to Aug 2002 (P4)	Lipsin 300mg®	1931	0.74	933204.66	1.05	1.42
Sep to Dec 2002 (P5)	Lipsin 300mg®	1716	0.71	880137.22	1.09	1.54
Jan to Apr 2003 (P6)	Lipsin 300mg®	1809	0.71	988179.58	1.19	1.68

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs for the corresponding period (calculated from table 5.23) multiplied by hundred.
%# Is the total cost of individual hypolipidemic drugs divided by the total cost (n= R 252 919 285) of all hypolipidemic drugs for the corresponding period (calculated from table 5.23) multiplied by hundred.

As seen in table 5.51, the average cost of Lipsin 300mg® had an irregular trend. It was R412.66±142.98, R406.12±104.34 and R471.29±119.62 for P1, P2 and P3 respectively. The average cost of Lipsin 300mg® increased from P4 to P6 during the second study year. The

maximum cost per medicine item was 3.47 and 2.30 times the average cost of Lipsin 300mg® during the first and second study years respectively. The d-value of 0.49, 0.95 and 0.58 was evident between P1 and P4, P2 and P5 and P3 and P6. The d-value of 0.95 (large and practically significant) was the largest of all d-values of Lipsin 300mg®. It shows that there was much variation in prices of Lipsin 300mg® between September 2001 to October 2001 and September 2002 and October 2002.

Table 5.51 Cost analysis of individual medicine items containing fenofibrate as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Months	Fenofibrate	Number of items	Average cost/item (R)	Standard deviation	Maximum cost/ item (R)	Total cost (R)
May 2001 to Aug 2001	Lipsin 300mg®	1436	412.66	142.98	1546.68	592583.51
Sep 2001 to Dec 2001	Lipsin 300mg®	1745	406.12	104.34	1932.80	708674.90
Jan 2002 to Apr 2002	Lipsin 300mg®	2216	471.29	119.62	892.24	1044367.74

Table 5.52 Cost analysis of individual medicine items containing fenofibrate as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Months	Fenofibrate	Number of items	Average cost/item (R)	Standard deviation	Maximum cost/ item (R)	Total cost (R)
May 2002 to Aug 2002	Lipsin 300mg®	1931	483.28	105.49	1427.35	933204.66
Sep 2002 to Dec 2002	Lipsin 300mg®	1716	512.90	111.64	1047.62	880137.22
Jan 2003 to Apr 2003	Lipsin 300mg®	1809	546.26	128.96	1047.62	988179.58

Table 5.53.The d-value analysis of the average cost of Lipsin 300mg® for the different time periods

	May 2001 to Aug 2001 (P1)	Sep 2001 to Dec 2001 (P2)	Jan 2002 to Apr 2002 (P3)
May 2002 to Aug 2002 (P4)	0.49		
Sep 2002 to Dec 2002 (P5)		0.95	
Jan 2003 to Apr 2003 (P6)			0.58

5.8.1.3.2 The prescribed daily dose of individual medicine items containing fenofibrate as an active ingredient.

The World Health Organization (2002: 61) allocated 0.2g orally as the defined daily dose of fenofibrate. It should be noted that the World Health Organization's defined daily dose is for micronised fenofibrate. In this study, Lipsin 300mg® was the only fenofibrate that was claimed and it is again the only fenofibrate that is registered in South Africa. By virtue of its strength, Lipsin 300mg® capsule cannot produce a defined daily dose of 0.2g. Taking one capsule of Lipsin 300mg® gives the strength of 0.3g which is above the DDD if taken for a month supply (assuming that one month is 30 days). Based on the above-mentioned discussion, the prescriptions that were in line with the defined daily dose were those in which Lipsin 300mg® was given once daily for 20 days.

On average, 90.03% (n= 5397) of all prescriptions for Lipsin 300mg® during the first study year were in line with the manufacturer's recommended dosage compared to 92.65% (n=5455) of all prescriptions for Lipsin 300mg® during the second study year. Only a smaller insignificant proportion conformed to the defined daily dose.

Table 5.54. The prescribed daily dose of individual medicine items containing fenofibrate as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Month	DDD	Lipsin 300mg® <0.2g	<0.3g	=0.3g	>0.3g
May 2001 to Aug 2001 (P1)	P	42	7	1285	102
	%*	2.92	0.49	89.48	7.10
Sep 2001 to Dec 2001 (P2)	P	58	3	1575	109
	%*	3.32	0.17	90.26	6.25
Jan 2002 to Apr 2002 (P3)	P	46	6	1999	165
	%*	2.08	0.27	90.21	7.45

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table

%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table (per study period e.g. P1) divided by the total number of prescriptions of the individual medicine item whose PDD is calculated multiplied by hundred.

Table 5.55. The prescribed daily dose of individual medicine items containing fenofibrate as an active ingredient from May 2002 to April 2003 (period P2 to P6)

Mont					
	PDD	0.2g	0.3g	0.6g	0.9g
May 2002 to Aug 2002 (P4)	P	37	5	1799	89
	%*	1.92	0.26	93.21	4.61
Sep 2002 to Dec 2002 (P5)	P	46	1	1594	75
	%*	2.68	0.06	92.89	4.37
Jan 2003 to Apr 2003 (P6)	P	42	3	1661	103
	%*	2.32	0.17	91.82	5.69

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table
%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table (per study period e.g. P4) divided by the total number of prescriptions of the individual medicine item whose PDD is calculated multiplied by hundred.

5.8.1.4 Gemfibrozil

The utilisation patterns and cost of medicine items containing gemfibrozil, as an active ingredient will be discussed under this paragraph.

5.8.1.4.1 Prevalence and cost of medicine items containing gemfibrozil as an active ingredient

As indicated in table 5.56, the total number of medicine items containing gemfibrozil as an active ingredient increased from P1 to P3. This trend was unpredictable during the second study year as prevalence decreased from P4 to P5 and then picked up at P6 (refer to table 5.57). It is apparent from table 5.56 and table 5.57 that the total number of drugs containing gemfibrozil as an active ingredient accounted for 13.85% (n=17350) and 12.32% (n=21181) of the total number of fibrates and 0.41% (n=589036) and 0.34% (n=759675) of the total number of hypolipidemic drugs claimed during the first and the second study years respectively.

Lopid 600mg® accounted for 13.76% (n=R5 759 714.77) and 13.41% (n=R 7 430 172.47) of the total cost of fibrates and 0.40% (n=R196 076 050) and 0.39% (n=R252 919 285) of the total cost of all hypolipidemic drugs claimed during the first and second study years respectively. The results revealed that there was a slight decrease in the total cost percentage of Lopid 600mg® during the second study year (refer to table 5.57). The cost-prevalence index increased from the first study year to the second study year. The cost-prevalence index shows that the cost of Lopid 600mg® was relatively inexpensive during the first study year in comparison with the second study year. On average it was 0.97 and 1.14 for the first and second study years respectively.

Table 5.56 Prevalence and cost of individual medicine items containing gemfibrozil as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Months	Gemfibrozil	Prevalence	Prevalence percentage	Cost (R)	Cost percentage	Cost-prevalence
May to Aug 2001 (P1)	Lopid 600mg®	541	0.38	153685.67	0.33	0.87
Sep to Dec 2001 (P2)	Lopid 600mg®	772	0.41	250264.78	0.40	0.98
Jan to Apr 2002 (P3)	Lopid 600mg®	1090	0.42	388843.09	0.44	1.05

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs for the corresponding period (calculated from table 5.22) multiplied by hundred
%# Is the total cost of individual hypolipidemic drugs divided by the total cost of all hypolipidemic drugs for the corresponding period (calculated from table 5.22) multiplied by hundred.

Table 5.57 Prevalence and cost of individual medicine items containing gemfibrozil as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Months	Gemfibrozil	Prevalence	Prevalence percentage %*	Cost (R)	Cost percentage %#	Cost-prevalence
May to Aug 2002 (P4)	Lopid 600mg®	1057	0.40	392727.27	0.44	1.10
Sep to Dec 2002 (P5)	Lopid 600mg®	767	0.32	285244.86	0.35	1.09
Jan to Apr 2003 (P6)	Lopid 600mg®	785	0.31	318682.65	0.38	1.23

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs for the corresponding period (calculated from table 5.23) multiplied by hundred
%# Is the total cost of individual hypolipidemic drugs divided by the total cost of all hypolipidemic drugs for the corresponding period (calculated from table 5.23) multiplied by hundred.

It is noticeable from table 5.58 and table 5.59 that the average cost of Lopid 600mg® augmented from P1 to P3 during the first study year and it was stabilised between P4 and P5 and later increased to R405.97± 131.21 during P6. Although there was a divergence in the cost of Lopid 600mg® during the different time periods, the difference was insignificant as the d-value was less than 0.8. This shows that the cost of Lopid 600mg® was contained throughout the study years. There was a relatively smaller difference between the maximum cost per medicine item and the average cost per medicine item of Lopid 600mg® during the two study years. The maximum cost per medicine item of Lopid 600mg® was 1.82 and 1.93 times the average cost of Lopid 600mg® during the first and second study years respectively (see table 5.58).

Table 5.58 Cost analysis of individual medicine items containing gemfibrozil as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Months	Gemfibrozil	Number of items	Average cost/item (R)	Standard deviation	Maximum cost/item (R)	Total cost (R)
May to Aug 2001 (P1)	Lopid 600mg®	541	284.08	122.70	418.10	153685.67
Sep to Dec 2001 (P2)	Lopid 600mg®	772	324.18	116.38	646.84	250264.78
Jan to Apr 2002 (P3)	Lopid 600mg®	1090	356.74	117.04	712.96	388843.09

Table 5.59 Cost analysis of individual agents containing gemfibrozil as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Months	Gemfibrozil	Number of items	Average cost/item (R)	Standard deviation	Maximum cost/item (R)	Total cost (R)
May to Aug 2002 (P4)	Lopid 600mg®	1057	371.55	116.20	712.95	392727.27
Sep to Dec 2002 (P5)	Lopid 600mg®	767	371.90	114.45	712.94	285244.86
Jan to Apr 2003 (P6)	Lopid 600mg®	785	405.97	131.21	791.14	318682.65

Table 5.60 The d-value analysis of the average cost of Lopid 600mg® for the different time periods

	May 2001 to Aug 2001 (P1)	Sep 2001 to Dec 2001 (P2)	Jan 2002 to Apr 2002 (P3)
May 2002 to Aug 2002 (P4)	0.71		
Sep 2002 to Dec 2002 (P5)		0.41	
Jan 2003 to Apr 2003 (P6)			0.37

5.8.1.4.2 The prescribed daily dose of individual medicine items containing gemfibrozil as an active ingredient.

According to the World Health Organization (2002:61), the defined daily dose of gemfibrozil (Lopid 600mg®) is 1.2g taken orally. This means that the patient must take two tablets each containing 600mg of gemfibrozil daily in divided doses. Table 5.61 indicates that the number of prescriptions with PDD of less than 1.2g for Lopid 600mg® decreased percentage wise from P1 to P3. Less than half of the prescriptions for Lopid 600mg® had a PDD of less than 1.2g during

the first study year. During the second study year, more than half of the prescriptions for Lopid 600mg® had a PDD of 1.2g.

On average, 48.24% (n=2403) and 58.33% (n=2609) were calculated for prescriptions with the prescribed daily dose of 1.2g during the first and second study years respectively. On the other hand, the prescribed daily dose of more than 1.2g of gemfibrozil accounted for on average 0.90% (n=2403) and 0.41% (n=2609) of the total number of prescriptions containing Lopid 600mg® during the first and second study years respectively. It can then be concluded that the prescription patterns of Lopid 600mg® changed during the second study year. It was during the second study year that most of the prescriptions with Lopid 600mg® were in line with the defined daily dose as set by the WHO.

Table 5.61 The prescribed daily dose of individual medicine items containing gemfibrozil as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Months	PDD	Lopid 600mg®		
		<1.2g	=1.2g	>1.2g
May 2001 to Aug 2001 (P1)	P	295	246	0
	%*	54.53	45.47	0
Sep 2001 to Dec 2001 (P2)	P	353	410	9
	%*	45.72	53.11	1.17
Jan 2002 to Apr 2002 (P3)	P	485	594	11
	%*	44.49	54.49	1.01

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table
%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table (per study period e.g. P1) divided by the total number of prescriptions of the individual medicine item whose PDD is calculated multiplied by hundred.

Table 5.62 The prescribed daily dose of individual medicine items containing gemfibrozil as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Months	PDD	Lopid 600mg®		
		<1.2g	=1.2g	>1.2g
May 2002 to Aug 2002 (P4)	P	427	624	6
	%*	40.40	59.04	0.58
Sep 2002 to Dec 2002 (P5)	P	328	436	3
	%*	42.76	56.84	0.39
Jan 2003 to Apr 2003 (P6)	P	319	424	2
	%*	40.64	59.11	0.25

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table
%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table (per study period e.g. P4) divided by the total number of prescriptions of the individual medicine item whose PDD is calculated multiplied by hundred.

5.8.2 Statins

The utilisation patterns and the cost of drugs of the pharmacological group statins will be discussed under this section.

5.8.2.1 Atorvastatin

Under this section, the utilisation patterns and cost of medicine items containing atorvastatin as an active ingredient will be discussed.

5.8.2.1.1 Prevalence and cost of individual medicine items containing atorvastatin as an active ingredient

It is evident from table 5.63 and table 5.64 that the total number of individual medicine items containing atorvastatin as an active ingredient increased from 393386 to 524213 during the first and second study years respectively. This accounted for 69.73% (n=564162) and 71.69% (n=731222) of the total number of statins and 66.78% (n=589036) and 69.00% (n=759675) of the total number of all hypolipidemic drugs and 1.80% (n=21820911) and 1.92% (n=27277825) of the total number of all medicine items claimed from the database during the first and second study years respectively. It is clear from table 5.63 and table 5.64 that, apart from the general increase in numbers of atorvastatin, the prevalence percentages increased as well.

Looking through a wider perspective, this increase in utilisation of drugs containing atorvastain as an active ingredient can be influenced by many factors. Below are some of the studies that have shown the benefit of statins over other drugs. The results of the following studies might have influenced the prescribing patterns of hypolipidemic drugs. According to a study that was conducted by Pasceri *et al.* (2004: 10), it was found that pretreatment of atorvastatin 40mg/d for 7 days significantly reduces procedural myocardial injury in elective coronary intervention. In a single centre retrospective study whose objective was to evaluate the change in total cholesterol and LDL cholesterol in hyperlipidemic patients, switched from atorvastatin to simvastatin, Raal (2004: 120) found that there was a worsening trend in total cholesterol in patients who had been switched from atorvastatin to simvastatin. Raal (2004: 118) stated that the high intra-patient variation seen in that study strongly suggested that therapeutic substitution is associated with an unpredictable response in plasma lipid levels and their control. It was then pointed out in that study that the results would have practical implications for physicians who are considering a switch of that nature.

Nissen (2003: 1) conducted another study that could have led to increased utilisation of atorvastatin. In that study, the effects of two powerful cholesterol-lowering drugs (atorvastatin and pravastatin) were compared. It was found that atorvastatin appeared to be more effective than pravastatin. It was reported that atherosclerosis worsened slowly over 18 months in patients taking pravastatin and halted in those taking atorvastatin. The above-mentioned discussion could have been the reason for the increased utilisation of atorvastatin.

As shown on table 5.63 Lipitor 10mg®, Lipitor 20mg® and Lipitor 40mg® constituted 76.58%, 22.48% and 0.94 % of the total number of medicine items containing atorvastatin as an active ingredient during the first study year respectively. The prevalence of Lipitor 10mg® and Lipitor 40mg® increased during the second study year, on the other hand that of Lipitor 20mg® decreased. The three medicine items accounted for 76.65%, 2.34% and 21.01% of the total number of drugs containing atorvastatin as an active ingredient respectively. It is evident from table 5.63 and table 5.64 that the prevalence of Lipitor 40mg® increased by more than 100% of what it was during the first study year.

Not only is Lipitor 10mg® the drug that drives the hypolipidemic market, it was also one of the top ten medicine items claimed according to prevalence during both the study years. It was the second or first most prescribed drug on the market (refer to appendix A, table A.5 to table A.8) for most months. Lipitor 10mg® accounted for more than 1% of all drugs claimed during both study years.

It is apparent from table 5.63 and table 5.64 that the total cost of all individual medicine items containing atorvastatin as an active ingredient augmented from R136 681 475.20 to R186 606 548.00 during the first and second study years respectively. This accounted for 72.40% (n = R 188 790 239.3) and 76.40% (n =R 244 246 815.3) of the total cost of all statins, 69.71% (n = R 196 076 050) and 73.78% (n =R 252 919 285) of the total cost of all hypolipidemic drugs and 4.41% (n = R 3 097 604 602) and 4.60% (n = R 4 053 280 295) of the total cost of all medicine items claimed during the first and second study years respectively. It should, however, be noted that the total cost of individual medicine items is influenced by volume of drugs sold and cost per unit of drugs. As explained above, some studies substantiated the effectiveness of atorvastatin over other hypolipidemic drugs. This resulted in increased utilisation of these medicine items and hence increased cost of this class of drugs. The patent life of atorvastatin expires in 2011 (Willis *et al.*, 2003; 9). The introduction of generic atorvastatin might have a

great impact on the cost of hypolipidemic drugs; maybe then the cost of hypolipidemic drugs might reduce.

Lipitor 10mg®, Lipitor 20mg® and Lipitor 40mg® constituted 68.67%, 29.83% and 1.50% respectively of the total cost of medicine items (n = R 136 681 475.2) containing atorvastatin as an active ingredient during the first study year. The trend of the total cost of individual medicine items containing atorvastatin as an active ingredient was similar to that of the prevalence. The total cost percentage of Lipitor 10mg® and Lipitor 40mg® increased during the second study year. That of Lipitor 40mg® increased by more than hundred per cent of what it had been during the first study year (refer to table 5.63 and table 5.64).

Lipitor 10mg® and Lipitor 40mg® accounted for 70.04% and 3.22% respectively of the total cost (n= R 186 606 548) of medicine items containing atorvastatin as an active ingredient during the second study year. Lipitor 20mg®, on the other hand, constituted 26.75% of the total cost of medicine items containing atorvastatin as an active ingredient during the second study year. The above discussions apparently state that all individual medicine items containing atorvastatin as an active ingredient had the highest prescription rate in comparison to other drugs belonging to the sub-pharmacological group: statins and to the pharmacological group: hypolipidemic drugs.

The cost-prevalence index of less than one was apparent for Lipitor 10mg®. The other remaining two drugs had a cost-prevalence index of more than one (refer to table 5.63 and table 5.64). During the second study year, the cost-prevalence index of Lipitor 10mg® increased and reached 1.03 during P6. The cost-prevalence index of the other two remaining atorvastatins fluctuated during the second study year. The cost-prevalence indeces of 2.45 and 2.40 were calculated for atorvastatin (as a percentage of total data) during the first and second study years respectively.

Table 5.63 Prevalence and cost of individual medicine items containing atorvastatin as an active ingredient from May 2001 to April 2002 (period P1 to P3)

[illegible]	Atorvastatin	Prevalence	Prevalence percentage %*	Cost (Rs)	Cost percentage %#	Unit cost per prescription
May 2001 to Aug 2001 (P1)	Lipitor 10mg®	67188	47.66	20688671.12	44.99	0.94
	Lipitor 20mg®	20497	14.54	9489475.21	20.64	1.42
	Lipitor 40mg®	295	0.21	171819.73	0.37	1.76
Sep 2001 to Dec 2001 (P2)	Lipitor 10mg®	98759	52.07	30442133.57	48.50	0.93
	Lipitor 20mg®	28778	15.17	13162802.89	20.97	1.38
	Lipitor 40mg®	1050	0.55	606337.93	0.97	1.76
Jan 2002 to April 2002 (P3)	Lipitor 10mg®	135292	52.35	42725391.12	48.93	0.93
	Lipitor 20mg®	39183	15.16	18123353.96	20.75	1.37
	Lipitor 40mg®	2344	0.91	1271489.70	1.46	1.60

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs for the corresponding period (calculated from table 5.22) multiplied by hundred
%# Is the total cost of individual hypolipidemic drugs divided by the total cost of all hypolipidemic drugs for the corresponding period (calculated from table 5.22) multiplied by hundred.

Table 5.64 Prevalence and cost of individual medicine items containing atorvastatin as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Months	Atorvastatin	Prevalence	Prevalence percentage %	Cost (R)	Cost percentage %	Cost-prevalence index
May 2002 to Aug 2002 (P4)	Lipitor 10mg®	141303	53.85	45278896.16	50.90	0.95
	Lipitor 20mg®	38206	14.56	17592396.19	19.78	1.36
	Lipitor 40mg®	3161	1.20	1620911.63	1.82	1.52
Sep 2002 to Dec 2002 (P5)	Lipitor 10mg®	131307	54.52	42231080.84	52.33	0.96
	Lipitor 20mg®	34631	14.38	15560601.33	19.28	1.34
	Lipitor 40mg®	3694	1.53	1760874.96	2.18	1.42
Jan 2003 to April 2003 (P6)	Lipitor 10mg®	129216	50.39	43180104.20	51.86	1.03
	Lipitor 20mg®	37263	14.53	16757093.21	20.12	1.38
	Lipitor 40mg®	5432	2.12	2624589.51	3.15	1.49

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs for the corresponding period (calculated from table 5.23) multiplied by hundred
%# Is the total cost of individual hypolipidemic drugs divided by the total cost of all hypolipidemic drugs for the corresponding period (calculated from table 5.23) multiplied by hundred.

5.8.2.1.2 The analysis of cost of individual medicine items containing atorvastatin as an active ingredient.

It is perceptible from table 5.65 and table 5.66 that the average cost of Lipitor 10mg® increased from P1 to P6. The trend of the average cost of Lipitor 20mg was unpredictable during the first study year. Like the prevalence, the second study year was typified by a decline in the average cost of Lipitor 20mg®. This shows that the cost and prevalence of Lipitor 20mg® are directly proportional. On the other hand, the average cost of Lipitor 40mg® generally declined from P1 to P6. As seen in table 5.65 and table 5.66, the average cost of Lipitor 40mg® was R582.44 ± 165.33 at the beginning of the first study year during P1 and it reached R483.17 ± 184.83 at the end of the second study year during P6. It is evident that the cost and prevalence of Lipitor 40mg® are inversely proportional. It can then be concluded that the more Lipitor 40mg® is prescribed the less costly it becomes.

The d-value analysis of the average cost of Lipitor 10mg®, Lipitor 20mg® and Lipitor 40mg® between the different time periods was of practical insignificance ($d > 0.8$) (refer to table 5.67,

5.68 and table 5.69). The maximum cost per item of Lipitor 20mg® was relatively higher than the maximum cost per item of other medicine items containing atorvastatin as an active ingredient during the first study year. However, during the second study year, the maximum cost of Lipitor 10mg® was on average relatively higher than the maximum cost of other medicine items containing atorvastatin as an active ingredient.

Table 5.65 Cost analysis of individual medicine items containing atorvastatin as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Months	Atorvastatin	Number of items	Average cost/item (R)	Standard deviation	Maximum cost/item (R)	Total cost (R)
May 2001 to Aug 2001 (P1)	Lipitor 10mg®	67188	307.92	33.15	959.45	20688671.12
	Lipitor 20mg®	20497	462.97	124.08	3466.82	9489475.21
	Lipitor 40mg®	295	582.44	165.33	1170.61	171819.73
Sep 2001 to Dec 2001 (P2)	Lipitor 10mg®	98759	308.25	34.38	1776.91	30442133.57
	Lipitor 20mg®	28778	457.39	97.69	1821.15	13162802.89
	Lipitor 40mg®	1050	577.46	163.05	1170.61	606337.93
Jan 2002 to April 2002 (P3)	Lipitor 10mg®	135292	315.80	34.75	1847.83	42725391.12
	Lipitor 20mg®	39183	462.53	87.98	2193.96	18123353.96
	Lipitor 40mg®	2344	542.44	173.58	1170.74	1271489.70

Table 5.66 Cost analysis of individual medicine items containing atorvastatin as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Months	Atorvastatin	Number of items	Average cost/ item (R)	Standard deviation	Maximum cost/ item (R)	Total cost (R)
May 2002 to Aug 2002 (P4)	Lipitor 10mg®	141303	320.44	36.61	1848.32	45278896.16
	Lipitor 20mg®	38206	460.46	81.40	1893.78	17592396.19
	Lipitor 40mg®	3161	512.78	182.41	1170.64	1620911.63
Sep 2002 to Dec 2002 (P5)	Lipitor 10mg®	131307	321.62	37.60	1744.49	42231080.84
	Lipitor 20mg®	34631	449.33	82.85	1420.78	15560601.33
	Lipitor 40mg®	3694	476.69	180.31	1240.78	1760874.96
Jan 2003 to April 2003 (P6)	Lipitor 10mg®	129216	334.17	43.21	4184.04	43180104.20
	Lipitor 20mg®	37263	449.70	95.30	1988.34	16757093.21
	Lipitor 40mg®	5432	483.17	184.83	1240.79	2624589.51

Table 5.67 The d-value analysis of the average cost of Lipitor 10mg® for the different time periods

Periods	May 2001 to Aug 2001 (P1)	Sep 2001 to Dec 2001 (P2)	Jan 2002 to Apr 2002 (P3)
May 2002 to Aug 2002 (P4)	0.34		
Sep 2002 to Dec 2002 (P5)		0.35	
Jan 2003 to Apr 2003 (P6)			0.43

Table 5.68 The d-value analysis of the average cost of Lipitor 20mg® for the different time periods

Periods	May 2001 to Aug 2001 (P1)	Sep 2001 to Dec 2001 (P2)	Jan 2002 to Apr 2002 (P3)
May 2002 to Aug 2002 (P4)	0.02		
Sep 2002 to Dec 2002 (P5)		0.08	
Jan 2003 to Apr 2003 (P6)			0.13

Table 5.69 The d-value analysis of the average cost of Lipitor 40mg® for the different time periods

Periods	May 2001 to Aug 2001 (P1)	Sep 2001 to Dec 2001 (P2)	Jan 2002 to Apr 2002 (P3)
May 2002 to Aug 2002 (P4)	0.38		
Sep 2002 to Dec 2002 (P5)		0.56	
Jan 2003 to Apr 2003 (P6)			0.32

5.8.2.1.3 The prescribed daily dose of individual medicine items containing atorvastatin as an active ingredient.

According to the World Health Organization (2002: 61), atorvastatin was assigned a defined daily dose of 10mg orally. On the other hand as described in the Martindale, according to Sweetman, (2002: 842), the initial dose of atorvastatin is 10mg/d, which may be adjusted at intervals of four weeks up to a maximum of 80mg daily. In South Africa the maximum recommended dosage according to the manufacturer is 40mg daily (MIMS™). Atorvastatin is available in three strengths in South Africa, i.e. Lipitor 10mg®, Lipitor 20mg® and Lipitor 40mg®.

By virtue of its strength, Lipitor 10mg® will conform to the defined daily dosage when given once daily. For the dosage of both Lipitor 20mg® and Lipitor 40mg® to be in line with the defined daily dosage, Lipitor 20mg must be given either half a tablet daily for thirty days or 1 tablet daily for 15 days (for a month supply assuming that 1 month consists of 30 days). The dosage of Lipitor 40mg® can also be adjusted accordingly for the defined daily dose to be in line with the prescribed daily dose.

As seen in table 5.70, 31.35% (n=301239) of the prescriptions for Lipitor 10mg® during the first study year were below the defined daily dose of 10mg orally. It is evident that 68.47% (n=301239) of the prescriptions for Lipitor 10mg were in line with the defined daily dose during the first study year. Only an insignificant 0.18% (n=301239) of the prescriptions for Lipitor 10mg® were above the defined daily dose. Only 1.37% (n = 88458) of the prescriptions of Lipitor 20mg® were in line with the defined daily dose during the first study year. On the other hand, 26.97% (n = 88458) of the prescriptions had a prescribed daily dose of greater than 10mg and less than 20mg during the first study year. More than 50% (n = 88458) of the prescriptions had a prescribed daily dose of 20mg. This means that more than 50% (n = 88458) of the

prescriptions for Lipitor 20mg® were given as a once daily dosing for a month supply. None of the prescriptions for Lipitor 40mg® (n = 3689) was in line with the defined daily dose during the first study year. As indicated in table 5.70, most of the prescriptions of Lipitor 40mg® had a prescribed daily dose of 40mg (i.e. 1 tablet once daily) which is line with the MIMS™ (2003: 158).

Table 5.70 The prescribed daily dose of individual medicine items containing atorvastatin as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Atorvastatin	PDD (mg)	May 2001 to Aug 2001 (P1)		Sep 2001 to Dec 2001 (P2)		Jan 2002 to Apr 2002 (P3)	
		P	%*	P	%*	P	%*
Lipitor 10mg® (P1)	<10mg	19091	28.41	32517	32.93	42841	31.67
	=10mg	47951	71.37	66067	66.90	92238	68.18
	>10 <20	83	0.12	113	0.11	135	0.10
	=20mg	57	0.08	49	0.05	68	0.05
	>20 <80	6	0.01	13	0.01	10	0.01
	= 80mg	0	0	0	0	0	0
	>80mg	0	0	0	0	0	0
Lipitor 20mg® (P2)	<10mg	85	0.41	206	0.72	386	0.99
	=10mg	205	1.00	322	1.12	686	1.75
	>10mg <20	5032	24.55	8495	29.52	10334	26.37
	= 20mg	14170	69.13	18758	65.18	26784	68.36
	>20 <80	971	4.74	974	3.38	978	2.50
	=80mg	31	0.15	23	0.08	14	0.04
	>80mg	3	0.01	0	0	1	0
Lipitor 40mg® (P3)	<10mg	2	0.68	0	0	19	0.81
	=10mg	0	0	0	0	0	0
	>10mg <20	3	1.02	25	2.48	93	3.97
	=20	6	2.03	19	1.88	272	11.60
	>20 <40	119	40.34	409	40.50	842	35.92
	=40	147	49.83	495	49.01	988	42.15
	>40 <80	8	2.71	22	2.18	52	2.22
	= 80mg	10	3.39	40	3.96	78	3.33
	>80mg	0	0	0	0	0	0

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table
%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table (per study period e.g. P1) divided by the total number of prescriptions of the individual medicine item whose PDD is calculated multiplied by hundred.

Table 5.71 The prescribed daily dose of individual medicine items containing atorvastatin as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Atorvastatin	PDD	May 2002 - Jul 2002		Sep 2002 - Nov 2002		Jan 2003 - Mar 2003	
		P	%	P	%	P	%
Lipitor 10mg® (P4)	<10mg	43678	30.91	41797	31.83	44265	34.26
	=10mg	97387	68.92	89323	68.03	84814	65.64
	>10 <20	162	0.11	112	0.09	86	0.07
	=20mg	51	0.04	63	0.05	43	0.03
	>20 <80	25	0.02	12	0.01	8	0.01
	= 80mg	0	0	0	0	0	0
	>80mg	0	0	0	0	0	0
Lipitor 20mg® (P5)	<10mg	605	1.58	890	2.57	1425	3.82
	=10mg	1275	3.34	2555	7.38	5184	13.91
	>10mg <20	9681	25.34	8654	24.99	9330	25.04
	= 20mg	26033	68.14	22198	64.10	21076	56.56
	>20 <80	605	1.58	334	0.96	246	0.66
	=80mg	7	0.02	0	0	2	0.01
	>80mg	0	0	0	0	0	0
Lipitor 40mg® (P6)	<10mg	26	0.82	36	0.97	46	0.85
	=10mg	0	0.00	0	0.00	0	0
	>10mg <80	241	7.62	384	10.40	581	10.70
	=20	616	19.49	1114	30.16	2100	38.66
	>20 <40	945	29.90	929	25.15	1094	20.14
	=40	1160	36.70	1063	28.78	1397	25.72
	>40 <80	90	2.85	106	2.87	141	2.60
	= 80mg	83	2.63	62	1.68	73	1.34
	>80mg	0	0	0	0	0	0

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table
%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table (per study period e.g. P4) divided by the total number of prescriptions of the individual medicine item whose PDD is calculated multiplied by hundred.

During the second study year, 32.29% (n=401826) of the prescriptions for Lipitor 10mg® were below the defined daily dose of 10mg compared to 67.57% (n=401826) of the prescriptions, which had a prescribed daily dose of 10mg. Only 0.14% (n=401826) of the prescriptions of Lipitor 10mg® had a prescribed daily dose of more than 10mg during the second study year. The trend of the prescribed daily dose for Lipitor 20mg® that was observed during the first study year was similar to the trend observed during the second study year (refer to table 5.71). As in the first study year, none of the prescriptions for Lipitor 40mg® was in line with the defined daily dose. Based on the above discussion, it can then be concluded that more than 50% of the drugs containing atorvastatin as an active ingredient were prescribed as a once daily dosing regardless of their strength for both study years. These drugs were prescribed according to the

Monthly Index of Medical Specialty (MIMS) and the Martindale rather than the World Health Organization.

5.8.2.2 Cerivastatin

Under this section, the utilisation patterns and cost of medicine items containing cerivastatin as an active ingredient will be discussed

5.8.2.2.1 Prevalence and cost of individual medicine items containing cerivastatin as an active ingredient

On 8 August 2001, Bayer's pharmaceutical division voluntarily withdrew Baycol® from the United States and other worldwide markets (including South Africa) (FDA, 2001: 1; Grady, 2001: 1). Baycol® was withdrawn from the markets because of reports of fatal rhabdomyolysis, a severe muscle adverse reaction from this cholesterol-lowering product (Farmer, 2001: 1383). The above-mentioned discussion rules out Baycol® as a drug under study for the second study year. As a result, utilisation and cost analysis of cerivastatin will only be limited to the first study year.

After the announcement by Bayer pharmaceutical company, the prevalence and cost of medicine items containing cerivastatin as an active ingredient declined from P1 to P3. As witnessed on table 5.72 above, Baycol 0.1mg® and Baycol 0.3mg® were already out of the market at the end of the first study year. Both the prevalence and cost percentages were below one during P2 and P3. This class of drugs had an insignificant contribution to the prevalence and cost of hypolipidemic drugs during this study. As indicated in table 5.73, the average cost of Baycol 0.1mg® and Baycol 0.3mg® increased, but showed a decrease in prevalence. On the other hand, the average cost of Baycol 0.2mg® and Baycol 0.4mg® decreased from P1 to P2 and later picked up during P3.

Table 5.72 Prevalence and cost of individual medicine items containing cerivastatin as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Months	Cerivastatin	Prevalence	Prevalence percentage %*	Cost	Cost percentage %#	Cost prevalence index
May 2001 to Aug 2001 (P1)	Baycol 0.1mg®	571	0.41	140118.82	0.30	0.73
	Baycol 0.2mg®	5229	3.71	1296790.26	2.82	0.76
	Baycol 0.3mg®	2178	1.55	584905.40	1.27	0.82
	Baycol 0.4mg®	1938	1.37	517495.37	1.13	0.82
Sep 2001 to Dec 2001 (P2)	Baycol 0.1mg®	39	0.02	9930.07	0.02	1.00
	Baycol 0.2mg®	265	0.14	64439.65	0.10	0.71
	Baycol 0.3mg®	69	0.04	18881.45	0.03	0.75
	Baycol 0.4mg®	95	0.05	24072.40	0.04	0.80
Jan 2002 to April 2002 (P3)	Baycol 0.2mg®	10	0.00	2585.08	0.00	1.00
	Baycol 0.4mg®	2	0.00	514.62	0.00	1.00

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs for the corresponding period (calculated from table 5.22) multiplied by hundred
%# Is the total cost of individual hypolipidemic drugs divided by the total cost of all hypolipidemic drugs for the corresponding period (calculated from table 5.22) multiplied by hundred.

On average, the maximum cost per item of Baycol 0.2mg® was relatively higher than the maximum cost per item of other medicine items containing cerivastatin as an active ingredient during the first study year. The maximum cost per item of Baycol 0.2mg® was on average 1.97 times the average cost per medicine item of Baycol 0.2mg® during the study year.

Table 5.73 Cost analysis of individual medicine items containing cerivastatin as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Months	Cerivastatin	Number of patients	Average cost/ item (R)	Standard deviation	Maximum cost/ item (R)	Total cost (R)
May 2001 to Aug 2001 (P1)	Baycol 0.1mg®	571	245.39	32.97	266.10	140118.82
	Baycol 0.2mg®	5229	248.00	40.88	933.50	1296790.26
	Baycol 0.3mg®	2178	268.55	15.07	316.49	584905.40
	Baycol 0.4mg®	1938	267.03	28.37	553.76	517495.37
Sep 2001 to Dec 2001 (P2)	Baycol 0.1mg®	39	254.62	9.90	265.77	9930.07
	Baycol 0.2mg®	265	243.17	57.61	267.05	64439.65
	Baycol 0.3mg®	69	273.64	8.36	278.10	18881.45
	Baycol 0.4mg®	95	253.39	37.02	279.24	24072.40
Jan 2002 to April 2002 (P3)	Baycol 0.2mg®	10	258.51	9.31	265.74	2585.08
	Baycol 0.4mg®	2	257.31	0	257.31	514.62

5.8.2.2.2 The prescribed daily dose of medicine items containing cerivastatin as an active ingredient

The defined daily dose of medicine items containing cerivastatin as an active ingredient is 0.2mg orally (WHO, 2002: 61). Baycol® was available in doses of 0.1mg, 0.2mg, 0.3mg and 0.4mg. As seen in table 5.74, most of the prescriptions are for once daily doses (i.e. one tablet one times a day for a month supply). Based on that, none of the prescriptions of Baycol 0.1mg® conformed to the defined daily dose. It is apparent from table 5.73 that more than 50% (n= 5504) of the prescriptions for Baycol 0.2mg® conformed to the defined daily dose. By virtue of the strength of Baycol 0.4mg® the prescriptions for Baycol 0.4mg® could only conform to the defined daily dose when 30 tablets were taken for 15 day (refer to appendix E table E.21).

Table 5.74 The prescribed daily dose of individual medicine items containing cerivastatin as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Cerivastatin		May to Aug 2001 (P1)		Sept to Dec 2001 (P2)		Jan to April 2002 (P3)	
		P	%*	P	%*	P	%*
Baycol 0.1mg®	<0.1mg	303	53.06	22	56.41		
	=0.1mg	268	46.94	17	43.59		
	=0.2mg	0	0	0	0		
Baycol 0.2mg®	<0.2mg	2334	44.64	118	44.53	4	40
	=0.2mg	2872	54.92	147	55.47	6	60
	>0.2mg	23	0.44	0	0	0	0
Baycol 0.3mg®	<0.2mg	8	0.37	0	0		
	=0.2mg	0	0	0	0		
	<0.3mg	928	42.61	14	20.29		
	=0.3mg	1242	57.02	55	79.71		
Baycol 0.4mg®	<0.2mg	14	0.72	3	3.16	0	0
	=0.2mg	4	0.21	5	5.26	0	0
	<0.4mg	1052	54.28	62	65.26	2	100
	=0.4mg	855	44.12	25	26.32	0	0
	>0.4mg	13	0.67	0	0	0	0

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table
%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table (per study period e.g. P1) divided by the total number of prescriptions of the individual medicine item whose PDD is calculated multiplied by hundred.

5.8.2.3 Fluvastatin

Under this section, the utilization patterns and cost of medicine items containing fluvastatin as an active ingredient will be discussed

5.8.2.3.1 Prevalence and cost of individual medicine items containing fluvastatin as an active ingredient

The total number of individual medicine items containing fluvastatin as an active ingredient augmented from 28814 to 41180. This accounted for 5.10% (n=564161) and 5.63% (n=731222) of the total number of statins and 4.89% (n=589036) and 5.82% (n=759675) of the total number of all hypolipidemic drugs claimed during the first and second study years respectively. Lescol 20mg® and Lescol 40mg® accounted for 55.00% and 45.00% of the total number of fluvastatin drugs (n = 28814) prescribed during the first study year (refer to table 5.75).

The introduction of Lescol XL 80mg® during the second study year changed the prescribing patterns of individual medicine items containing fluvastatin as an active ingredient. As witnessed in table 5.76 below, the prevalence percentage of Lescol 20mg® and Lescol 40mg® declined. The two individual drugs constituted 42.25% (n = 41180) and 36.50% (n = 41180) of the total

number of individual medicine items containing fluvastatin as an active ingredient whereas on the other hand, Lescol XL 80mg® accounted for 21.24% during the second study year (n =41180).

The total cost of Lescol 20mg® and Lescol 40mg® accounted for 54.99% (n = R7 856 442.06) and 45.01% (n = R7 856 442.06) of the total costs of individual medicine items containing fluvastatin as an active ingredient during the first study year. During the second study year, the cost of Lescol 20mg® declined from P4 to P6, that of Lescol 40mg® had an indistinguishable trend. However, the cost of Lescol XL 80mg® increased from P4 to P6. Lescol 20mg® and Lescol 40mg® and Lescol XL 80mg accounted for 40.47%, 36.75% and 22.77% of the total expenditure (n = R 12 352 560.38) of all medicine items containing fluvastatin as an active ingredient during the second study year (refer to table 5.75 and table 5.76).

Table 5.75 Prevalence and cost of individual medicine items containing fluvastatin as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Months	Fluvastatin	Prevalence	Prevalence percentage %*	Cost (R)	Cost percentage %#	Cost prevalence index
May 2001 to Aug 2001 (P1)	Lescol 20mg®	3862	2.74	1022578.10	2.22	0.81
	Lescol 40mg®	3115	2.21	824231.43	1.79	0.81
Sep 2001 to Dec 2001 (P2)	Lescol 20mg®	5262	2.77	1394127.34	2.22	0.80
	Lescol 40mg®	4246	2.24	1127350.92	1.80	0.80
Jan 2002 to April 2002 (P3)	Lescol 20mg®	6725	2.60	1903703.66	2.18	0.84
	Lescol 40mg®	5604	2.17	1584450.61	1.81	0.83

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs for the corresponding period (calculated from table 5.22) multiplied by hundred
%# Is the total cost of individual hypolipidemic drugs divided by the total cost of all hypolipidemic drugs for the corresponding period (calculated from table 5.22) multiplied by hundred.

Table 5.76 Prevalence and cost of individual medicine items containing fluvastatin as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Months	Fluvastatin	Prevalence	Prevalence percentage %*	Cost	Cost percentage %#	Cost prevalence index
May 2002 to Aug 2002 (P4)	Lescol 20mg®	6509	2.48	1847135.35	2.08	0.84
	Lescol 40mg®	5517	2.10	1638054.08	1.84	0.88
Sep 2002 to Dec 2002 (P5)	Lescol 20mg®	5721	2.38	1610401.19	2.00	0.84
	Lescol 40mg®	4851	2.01	1442032.59	1.79	0.89
	Lescol XL 80mg®	2238	0.93	698813.08	0.87	0.94
Jan 2003 to April 2003 (P6)	Lescol 20mg®	5170	2.02	1542075.81	1.85	0.92
	Lescol 40mg®	4667	1.82	1460073.34	1.75	0.96
	Lescol XL 80mg®	6507	2.54	2113974.94	2.54	1.00

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs for the corresponding period (calculated from table 5.23) multiplied by hundred
%# Is the total cost of individual hypolipidemic drugs divided by the total cost of all hypolipidemic drugs for the corresponding period (calculated from table 5.23) multiplied by hundred.

The cost-prevalence index of all individual medicine items containing fluvastatin as an active ingredient was less than one during the first study year. It should be noted that the cost-prevalence indeces of both Lescol 20mg® and Lescol 40mg® were similar during each study period (refer to table 5.77) of the first study year. It is apparent from table 5.78 that the cost-prevalence index of both Lescol 20mg® and Lescol 40mg® increased from P4 to P6. The introduction of Lescol XL 80mg® decreased the prevalence of both Lescol 20mg® and Lescol 40mg®. The cost prevalence index of Lescol XL 80mg® increased from P5 (the period it was introduced to the market) to P6 reaching a maximum of one during P6. Based on the above discussion, it can be concluded that Lescol XL 80mg® was relatively expensive compared to other medicine items containing fluvastatin as an active ingredient.

5.8.2.3.2 Cost analysis of individual medicine items containing fluvastatin as an active ingredient

It can be seen from table 5.77 that the average cost of Lescol 20mg® was stable from P1 to P2 and it increased during P3. On the other hand, the average cost of Lescol 40mg® increased throughout the first study year from P1 to P3. There was an insignificant deviation in average cost of both Lescol 20mg® and Lescol 40mg® between different periods of the first study year (refer to table 5.77). The second study year revealed an increase in both the average cost of Lescol 40mg® and Lescol XL 80mg®. On the other hand, the average cost of Lescol 20mg® had no definite trend (refer to table 5.78). As shown in table 5.77 the maximum cost per item of Lescol 20mg® was relatively higher than the maximum cost per item of Lescol 40mg® during the first study year. However, during the second study year, the maximum cost of Lescol XL 80mg® was on average relatively higher than the maximum cost of other medicine items containing fluvastatin as an active ingredient (see table 5.78).

Table 5.77 Cost analysis of individual medicine items containing fluvastatin as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Months	Fluvastatin	Number of items	Average cost/ item (R)	Standard deviation	Maximum cost/ item (R)	Total cost (R)
May 2001 to Aug 2001 (P1)	Lescol 20mg®	3862	264.78	26.94	542.24	1022578.10
	Lescol 40mg®	3115	264.60	35.59	542.19	824231.43
Sep 2001 to Dec 2001 (P2)	Lescol 20mg®	5262	264.94	30.45	1504.03	1394127.34
	Lescol 40mg®	4246	265.51	34.50	542.19	1127350.92
Jan 2002 to April 2002 (P3)	Lescol 20mg®	6725	283.08	24.65	580.03	1903703.66
	Lescol 40mg®	5604	282.74	37.29	579.98	1584450.61

Table 5.78 Cost analysis of individual medicine items containing fluvastatin as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Months	Fluvastatin	Number [illegible]	Average [illegible] (R)	[illegible]	[illegible] item	Total cost (R)
May 2002 to Aug 2002 (P4)	Lescol 20mg®	6509	283.78	23.97	580.03	1847135.35
	Lescol 40mg®	5517	296.91	33.06	608.90	1638054.08
Sep 2002 to Dec 2002 (P5)	Lescol 20mg®	5721	281.49	34.23	580.03	1610401.19
	Lescol 40mg®	4851	297.27	34.51	608.89	1442032.59
	Lescol XL 80mg®	2238	312.25	44.80	925.38	698813.08
Jan 2003 to April 2003 (P6)	Lescol 20mg®	5170	298.27	29.76	614.68	1542075.81
	Lescol 40mg®	4667	312.85	37.95	645.29	1460073.34
	Lescol XL 80mg®	6507	324.88	27.18	684.38	2113974.94

There was a noticeable difference during the first and second study years between the average cost and the cost-prevalence index of both Lescol 20mg® and Lescol 40mg®. The d-value of the average cost of Lescol 40mg® between the different periods of the first and second study years was large and of a practical significance (refer to table 5.80). On the other hand, the d-value of the average cost of Lescol 20mg® between the different periods of the first and second study years was medium with an effect that is perceived and may be significant (refer to table 5.79).

Table 5.79 The d-value analysis of the average cost of Lescol 20mg® for the different time periods

[illegible]	May 2002 to [illegible] 2001 (P1)	Sep 2002 to Dec 2002 (P5)	Jan 2003 to Apr 2003 (P6)
May 2002 to Aug 2002 (P4)	0.70		
Sep 2002 to Dec 2002 (P5)		0.48	
Jan 2003 to Apr 2003 (P6)			0.51

Table 5.80 The d-value analysis of the average cost of Lescol 40mg® for the different time periods

	[illegible]	[illegible]	[illegible]
May 2002 to Aug 2002 (P4)	0.91		
Sep 2002 to Dec 2002 (P5)		0.92	
Jan 2003 to Apr 2003 (P6)			0.80

5.8.2.3.3 The prescribed daily dose of medicine items containing fluvastatin as an active ingredient

The World Health Organization assigned a defined daily dose of 40mg per day to fluvastatin (WHO, 2002: 60). According to MIMS Desk Reference (MDR) (2002: 1138), the dosage of fluvastatin is 20mg to 40mg daily and it may be increased to 80mg per day. In this study, the prescribed daily dose of fluvastatin as calculated from the prescriptions claimed (refer to appendix E, table E.22 to table E.26) is compared to the defined daily dose and the dosages as described in the MIMS desk reference. It is clear from table 5.81 that the number of prescriptions that conformed to the defined daily dose is lower than the number of prescriptions that were prescribed according to the manufacturer's recommendations as indicated in the MDR.

It is evident from Table 5.80 that only 26.75% (n=28814) of all the prescriptions with fluvastatin as an active ingredient conformed to the defined daily dose during the first study year. It can further be seen that 66.27% (n=15849) of the prescriptions for Lescol 20mg® were in line with the manufacturer's recommendations compared to fewer than 1% (n=15849) of those, which conformed, to the defined daily dose. On the other hand, because of its strength, 59.17% (n=12965) of the prescriptions for Lescol 40mg® conformed to the defined daily dose during the first study year.

During the second study year, the number of prescriptions that were actually in line with the defined daily was less than that of the first study year; only 22.29% (n=41180) of all the prescriptions containing fluvastatin conformed to the defined daily dose. It can be seen that more than 50% (n=32435) of all prescriptions for both Lescol 20mg® and Lescol 40mg® were prescribed as one tablet once daily for 30 days.

Unlike both Lescol 20mg® and Lescol 40mg®, most of the prescriptions (65.77% (n=8745) for Lescol XL 80mg® were prescribed for 28 days rather than 30 days. It can be concluded from this study, that most of the prescriptions that contained fluvastatin as an active ingredient did not conform to the defined daily dose because most prescriptions for Lescol® were prescribed according to the MIMS™ (2003: 158) i.e. 1 tablet (of Lescol 20mg®, Lescol 40mg® and Lescol XL 80mg®) once daily.

Table 5.81 The prescribed daily dose of individual medicine items containing fluvastatin as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Fluvastatin	PDD (mg)	May [illegible] (P1)		[illegible] (P2)		Jan [illegible] Apr 2002 (P3)	
		P	%*	P	%*	P	%*
Lescol 20mg®	<20	1169	30.27	1856	35.27	2266	33.70
	=20	2678	69.34	3392	64.46	4433	65.92
	>20<40	9	0.23	0	0	8	0.12
	=40	6	0.16	13	0.25	18	0.27
	>40	0	0	1	0.02	0	0
Lescol 40mg®	<20	5	0.16	14	0.33	15	0.27
	=20	31	1.00	28	0.66	31	0.55
	>20<40	1208	38.84	1699	40.01	2126	37.94
	=40	1837	58.91	2457	57.87	3378	60.28
	>40	34	1.09	48	1.13	54	0.96

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table
%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table (per study period e.g. P1) divided by the total number of prescriptions of the individual medicine item whose PDD is calculated multiplied by hundred.

Table 5.82 The prescribed daily dose of individual medicine items containing fluvastatin as an active ingredient from May 2002 to April 2003 (period P4 to P6)

[redacted]	PDD [redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Lescol 20mg®	<20	2128	32.69	2014	35.20	2058	39.81
	=20	4354	66.89	3689	64.48	3089	59.75
	>20<40	8	0.12	0	0	3	0.06
	=40mg	19	0.29	18	0.31	20	0.39
	>40mg	0	0	0	0	0	0
Lescol 40mg®	<20	11	0.20	15	0.31	29	0.62
	=20	43	0.78	42	0.87	48	1.03
	>20<40	2043	37.03	1776	36.61	1823	39.06
	=40	3374	61.16	2976	61.35	2729	58.47
	>40	46	0.83	42	0.87	38	0.81
Lescol XL 80mg®	<40			23	1.03	48	0.74
	=40			4	0.18	38	0.58
	>40<80			1607	71.81	4145	63.70
	=80			599	26.76	2271	34.90
	>80			5	0.22	5	0.08

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table
%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table (per study period e.g. P4) divided by the total number of prescriptions of the individual medicine item whose PDD is calculated multiplied by hundred.

5.8.2.4 Pravastatin

Under this section, the utilisation patterns and cost of medicine items containing pravastatin as an active ingredient will be discussed

5.8.2.4.1 Prevalence and cost of individual medicine items containing pravastatin as an active ingredient

The total number of individual items containing pravastatin as an active ingredient augmented from 37839 to 54411 during the first and second study years respectively. Prava 10mg®, Prava 20mg® and Prava 40mg® constituted 37.18%, 39.81% and 23.01% of the total number (n = 37839) of individual medicine items containing pravastatin as an active ingredient during the first study year (refer to table 5.83). During the second study year, the prevalence percentage of Prava 10mg® decreased whereas that of Prava 20mg® and Prava 40mg® increased. The prevalence percentage of Prava 10mg®, Prava 20mg® and Prava 40mg® was 32.34%, 41.22% and 26.45% of the total number (n = 54411) of individual medicine items containing pravastatin as an active ingredient for the second study year

The total number of medicine items containing pravastatin as an active ingredient accounted for 6.71% (n=564161) and 7.44% (n=731222) of the total number of statins and 6.42% (n=589036) and 7.16% (n=759675) of the total number of hypolipidemic drugs claimed during the first and second study years respectively. The above statement substantiates the conclusion that the rate of increase in utilisation of pravastatin contributed to the rate of increase in utilization of all hypolipidemic drugs during the second study year (refer to table 5.83 and table 5.84)

The total cost of all individual medicine items containing pravastatin as an active ingredient accounted for 5.49% (n=R188 790 239.30) and 6.23% (n=R244 246 815.30) of the total cost of all statins claimed and 5.29% (n=R196 076 050) and 6.01% (n=R 252 919 285) of the total cost of all hypolipidemic drugs claimed during the first and second study years respectively. From the above-mentioned discussion, it is clear that there is little deviation between the prevalence percentage and cost percentage of both the hypolipidemic drugs and statins. This is an indication that the statins are the prevalence and cost drivers of the hypolipidemic drugs claimed through this medical scheme administrator.

Table 5.83 Prevalence and cost of individual medicine items containing pravastatin as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Months	Pravastatin	Prevalence	Prevalence percentage	Cost (R)	Cost percentage	Cost prevalence index
May 2001 to Aug 2001 (P1)	Prava 10mg®	3207	2.28	765806.94	1.67	0.73
	Prava 20mg®	3053	2.17	909033.19	1.98	0.91
	Prava 40mg®	1581	1.12	488210.03	1.06	0.95
Sep 2001 to Dec 2001 (P2)	Prava 10mg®	4603	2.43	1098626.14	1.75	0.72
	Prava 20mg®	4916	2.59	1463377.18	2.33	0.90
	Prava 40mg®	2736	1.44	792254.41	1.26	0.88
Jan 2002 to April 2002 (P3)	Prava 10mg®	6260	2.42	1497521.07	1.71	0.71
	Prava 20mg®	7094	2.75	2096286.62	2.40	0.87
	Prava 40mg®	4389	1.70	1254405.65	1.44	0.85

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs for the corresponding period (calculated from table 5.22) multiplied by hundred
%# Is the total cost of individual hypolipidemic drugs divided by the total cost of all hypolipidemic drugs for the corresponding period (calculated from table 5.22) multiplied by hundred.

The cost-prevalence index of all medicine items containing pravastatin as an active ingredient was less than one for all study periods during both study years. This indicates that therapy with individual medicine items containing pravastatin as an active ingredient was relatively inexpensive (refer to table 5.83).

Table 5.84 Prevalence and cost of individual medicine items containing pravastatin as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Months	Pravastatin	Prevalence	Prevalence per hundred %	Cost (Rs)	Cost per hundred %	Cost-prevalence index
May 2002 to Aug 2002 (P4)	Prava 10mg®	6349	2.42	1518080.73	1.71	0.71
	Prava 20mg®	7757	2.96	2293320.22	2.58	0.87
	Prava 40mg®	4872	1.86	1372314.60	1.54	0.83
Sep 2002 to Dec 2002 (P5)	Prava 10mg®	5677	2.36	1359517.67	1.68	0.71
	Prava 20mg®	7347	3.05	2197197.04	2.72	0.89
	Prava 40mg®	4599	1.91	1304924.91	1.62	0.85
Jan 2003 to April 2003 (P6)	Prava 10mg®	5568	2.17	1403113.13	1.69	0.78
	Prava 20mg®	7323	2.86	2286244.37	2.75	0.96
	Prava 40mg®	4919	1.92	1472532.07	1.77	0.92

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs for the corresponding period (calculated from table 5.23) multiplied by hundred
%# Is the total cost of individual hypolipidemic drugs divided by the total cost of all hypolipidemic drugs for the corresponding period (calculated from table 5.23) multiplied by hundred.

5.8.2.4.2 Cost analysis of individual medicine items containing pravastatin as an active ingredient

It is apparent from table 5.85 that the average cost of Prava 40mg® increased from P1 to P3 whereas the average cost of Prava 20mg® decreased from P1 to P3. The average cost of Prava 10mg® was stable between P1 and P2 and it increased during P3. During the second study year, the average cost of all individual drugs containing pravastatin as an active ingredient increased from P4 to P6. It should be noted that the average cost increased with a decrease in prevalence especially for Prava 10mg® and Prava 20mg®. As indicated in table 5.85 the maximum cost per item of Prava 20mg® was on average relatively higher than the maximum cost per item of other medicine items containing pravastatin as an active ingredient during the first study year. The

maximum cost per item of Prava 10mg®, Prava 20mg® and Prava 40mg® was 1.71, 2.36, and 2.05 times the average cost per medicine item of the individual medicine items containing pravastatin as an active ingredient respectively. During the second study year, the maximum cost per medicine item of Prava 20mg® continued to be relatively higher than the maximum cost of other medicine items containing pravastatin as an active ingredient (see table 5.86).

Table 5.85 Cost analysis of individual medicine items containing pravastatin as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Month	Pravastatin	Number of units	Average cost per unit (R)	Variance of unit cost	Maximum cost per item (R)	Total cost (R)
May 2001 to Aug 2001 (P1)	Prava 10mg®	3207	238.79	14.96	372.24	765806.94
	Prava 20mg®	3053	297.75	33.76	599.37	909033.19
	Prava 40mg®	1581	308.80	79.27	716.73	488210.03
Sep 2001 to Dec 2001 (P2)	Prava 10mg®	4603	238.68	15.38	372.24	1098626.14
	Prava 20mg®	4916	297.68	38.57	897.97	1463377.18
	Prava 40mg®	2736	289.57	81.06	385.54	792254.41
Jan 2002 to April 2002 (P3)	Prava 10mg®	6260	239.22	20.01	479.72	1497521.07
	Prava 20mg®	7094	295.50	38.90	599.60	2096286.62
	Prava 40mg®	4389	285.81	86.74	716.73	1254405.65

Table 5.86 Cost analysis of individual medicine items containing pravastatin as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Month	Prava strength	[illegible]	[illegible]	[illegible]	[illegible]	Total cost (R)
May 2002 to Aug 2002 (P4)	Prava 10mg®	6349	239.11	13.43	372.24	1518080.73
	Prava 20mg®	7757	295.65	37.50	599.64	2293320.22
	Prava 40mg®	4872	281.67	83.79	398.46	1372314.60
Sep 2002 to Dec 2002 (P5)	Prava 10mg®	5677	239.48	17.64	480.34	1359517.67
	Prava 20mg®	7347	299.06	37.30	634.68	2197197.04
	Prava 40mg®	4599	283.74	84.51	379.60	1304924.91
Jan 2003 to April 2003 (P6)	Prava 10mg®	5568	252.00	18.14	508.10	1403113.13
	Prava 20mg®	7323	312.20	37.37	634.64	2286244.37
	Prava 40mg®	4919	299.36	87.79	757.80	1472532.07

As shown in table 5.87 to table 5.89, the d-value between different consecutive periods of the two study years were insignificant for all individual medicine items containing pravastatin as an active ingredient with the exception of the d-value of the average cost of Prava 10mg® between P3 and P6. The d-value of the average cost of Prava 10mg® between P3 and P6 was 0.64 and it has a medium effect that may be significant.

Table 5.87 The d-value analysis of the average cost of Prava 10mg® for the different time periods

Periods	[illegible]	[illegible]	[illegible]
May 2002 to Aug 2002 (P4)	0.02		
Sep 2002 to Dec 2002 (P5)		0.05	
Jan 2003 to Apr 2003 (P6)			0.64

Table 5.88 The d-value analysis of the average cost of Prava 20mg® for the different time periods

Periods	[illegible]	[illegible]	[illegible]
May 2002 to Aug 2002 (P4)	0.06		
Sep 2002 to Dec 2002 (P5)		0.03	
Jan 2003 to Apr 2003 (P6)			0.43

Table 5.89 The d-value analysis of the average cost of Prava 40mg® for the different time periods

Periods	[illegible]	[illegible]	[illegible]
May 2002 to Aug 2002 (P4)	0.32		
Sep 2002 to Dec 2002 (P5)		0.07	
Jan 2003 to Apr 2003 (P6)			0.15

5.8.2.4.3 The prescribed daily dose of individual medicine items containing pravastatin as an active ingredient

The dose of pravastatin is 10mg to 20mg once daily and can be increased to 40mg/day (MIMS, 2003: 158). The defined daily dose of pravastatin according to the World Health Organization is 20mg/day (WHO, 2002: 60). In South Africa, pravastatin is available in three strengths (i.e. 10mg, 20mg and 40mg). Prava 10mg® will give a defined daily dose of 20mg when taken twice daily. On the basis of its strength, Prava 20mg® once daily will conform to the defined daily dose whereas Prava 40mg® can conform to the defined daily dose when taken for 15 days for a month supply (with a provision that a month has 30 days).

It is evident from table 5.90 that an insignificant 0.09% (n=14070) of the total number of prescriptions for Prava 10mg® conformed to the defined daily dose as opposed to an alarming 97.37% (n=14070) that were prescribed according to the MIMS™ (one 10mg tablet once daily) during the first study year. It can be seen that 94.93% (n=15063) of the prescriptions for Prava 20mg® conformed to the defined daily dose during the first study year. On the other hand, 39.67% (n=8706) of the prescriptions for Prava 40mg® conformed to the defined daily dose as opposed to 57.70% (n=8706) that were issued in accordance with the MIMS™ during the first study year. It is generally evident that 46.95% (n= 37839) of the number of prescriptions of all

medicine items containing pravastatin as an active ingredient conformed to the defined daily dose during the first study year.

Table 5.90 The prescribed daily dose of individual medicine items containing pravastatin as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Pravastatin	PDD (mg)	May 01 to Apr 02 (P1)		May 02 to Apr 03 (P2)		May 03 to Apr 04 (P3)	
		P	%*	P	%*	P	%*
Prava 10mg®	<10	65	2.03	129	2.80	133	2.12
	=10	3138	97.85	4465	97.00	6098	97.41
	>10<20	4	0.12	9	0.20	16	0.26
	=20	0	0	0	0.00	13	0.21
Prava 20mg®	<10	6	0.20	15	0.31	29	0.41
	=10	80	2.62	166	3.38	315	4.44
	>10<20	14	0.46	24	0.49	17	0.24
	=20	2935	96.13	4675	95.10	6689	94.29
	>20<40	8	0.26	0	0	2	0.03
	=40	10	0.33	35	0.71	42	0.59
	>40	0	0	1	0.02	0	0
Prava 40mg®	<20	3	0.19	55	2.01	114	2.60
	=20	488	30.87	1102	40.28	1864	42.47
	>20<40	1	0.06	19	0.69	15	0.34
	=40	1085	68.63	1558	56.94	2380	54.23
	>40	4	0.25	2	0.07	16	0.36

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table
%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table per study period e.g. P1 divided by the total number of prescriptions of the individual medicine item whose PDD is calculated multiplied by hundred.

As depicted in table 5.91, 97.94% (n=17594) of the prescription for Prava 10mg® was prescribed according to the MIMS™ as opposed to an insignificant 0.08% of the prescriptions that were in line with the defined daily dose during the second study year (refer to table 5.91). It can be observed from the table below that 94.97% (n=22427) and 43.38% (n=14390) of the prescriptions for Prava 20mg® and Prava 40mg® respectively conformed to the defined daily dose during the second study year. On the other hand, 53.68% of the prescriptions for Prava 40mg were issued according to the MIMS™. Of the total number of all prescription issued during the second study year, 50.65% (n=54411) conformed to the defined daily dose. It is clear from the above-mentioned discussion that there was an increase in percentages of prescriptions from the first to the second study years that conformed to the defined daily dose of pravastatin.

Table 5.91 The prescribed daily dose of individual medicine items containing pravastatin as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Pravastatin		May '02-Jul '02 (P4)		Aug '02-Oct '02 (P5)		Nov '02-Apr '03 (P6)	
		P	%*	P	%*	P	%*
Prava 10mg®	<10	102	1.61	110	1.94	129	2.32
	=10	6239	98.27	5557	97.89	5435	97.61
	>10<20	8	0.13	0	0.00	0	0.00
	=20	0	0	10	0.18	4	0.07
Prava 20mg®	<10	19	0.24	21	0.29	13	0.18
	=10	334	4.31	213	2.90	265	3.62
	>10<20	17	0.22	33	0.45	60	0.82
	=20	7340	94.62	7014	95.47	6946	94.85
	>20<40	4	0.05	8	0.11	22	0.30
	=40	43	0.55	58	0.79	17	0.23
	>40	0	0.00	0	0.00	0	0.00
Prava 40mg®	<20	129	2.65	104	2.26	107	2.18
	=20	2132	43.76	1970	42.84	2141	43.53
	>20<40	16	0.33	24	0.52	39	0.79
	=40	2595	53.26	2501	54.38	2629	53.45
	>40	0	0.00	0	0.00	3	0.06

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table
%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table (per study period e.g. P4) divided by the total number of prescriptions of the individual medicine item whose PDD was calculated multiplied by hundred.

5.8.2.5 Simvastatin

Under this section, the utilisation patterns and cost of medicine items containing simvastatin as an active ingredient will be discussed.

5.8.2.5.1 Prevalence and cost of individual medicine items containing simvastatin as an active ingredient

The total number of individual medicine items containing simvastatin as an active ingredient increased from 93727 to 111592 during the first and second study years respectively. This class of drugs accounted for 16.61% (n=564161) and 15.26% (n=731222) of the total number of all statins as well as 15.91% (n=589036) and 14.69% (n=759675) of the total number of all hypolipidemic dugs claimed during the first and second study years respectively (refer to table 5.92 and table 5.93). Although there was an increase in number of individual medicine items containing simvastatin as an active ingredient from the first to the second study years, there was a decrease in prevalence percentages towards other statins and hypolipidemic drugs.

Table 5.92 revealed that the prevalence of all individual medicine items (Zocor 10mg®, Zocor 20mg® and Zocor 40mg®) containing simvastatin as an active ingredient increased from P1 to

P3. It indicated 52309, 33597 and 7821 for Zocor 10mg®, Zocor 20mg® and Zocor 40mg® respectively during the first study year.

During the second study year, Adco-simvastatin 10mg®, Adco-simvastatin 20mg® and Adco-simvastatin 40mg® were introduced into the market and their prevalence increased by more than 100% from P5 to P6. As a result, the prevalence of Zocor 10mg®, Zocor 20mg® and Zocor 40mg® declined from P4 to P6. Zocor 10mg®, Zocor 20mg®, Zocor 40mg®, Adco-simvastatin 10mg®, Adco-simvastatin 20mg® and Adco-simvastatin 40mg® each accounted for 41.50%, 26.59%, 7.99%, 10.53%, 10.05% and 3.34% of the total number of medicine items containing simvastatin (n =111592) as an active ingredient during the second study year. Although the prevalence of Zocor 40mg declined, the prevalence percentage increased from the first study year to the second study year (refer to table 5.93).

It is clear that the total cost of individual drugs containing simvastatin as an active ingredient declined from R31 227 067.66 to R30 115 435.22. This decrease in cost could have been brought about by the introduction of generic simvastatin on the market. It should be borne in mind that generally generic medicine items are relatively inexpensive compared to innovator medicine items. Zocor 10mg®, Zocor 20mg® and Zocor 40mg® accounted for 47.69%, 43.44% and 8.87% of the total cost of all medicine items containing simvastatin (n = R 31 227 067 .66) as an active ingredient during the first study year. During the second study year, Zocor 10mg®, Zocor 20mg®, Zocor 40mg®, Adco-simvastatin 10mg®, Adco-simvastatin 20mg® and Adco-simvastatin 40mg® accounted for 40.30%, 35.25%, 9.13%, 6.38%, 6.46% and 2.48% of the total expenditure of all medicine items containing simvastatin (n = R 30 115 435 .22) as an active ingredient during the second study year. Unlike the other innovator simvastatin, the cost percentage of Zocor 40mg® increased during the second study year.

Zocor 10mg was the only medicine item containing simvastatin as an active ingredient that had a cost-prevalence index of less than one for all three periods of the first year. The cost-prevalence index of Zocor 20mg® and Zocor 40mg® was above one for all periods of the first study year. During the second study year, the cost-prevalence index of Zocor 10mg®, Zocor 20mg® and Zocor 40mg® decreased. However, only Zocor 20mg® had a cost-prevalence index of more than one for the first two study periods. This indicates that Zocor 20mg® was relatively expensive compared to the other innovator simvastatin medicine items. It should, however, be taken into consideration that the dosage of "10mg" should be relatively cheaper due to the fact that it contains less of the active ingredient. The cost-prevalence index of all generic simvastatin

decreased from P5 to P6. Based on the above mentioned information, it can be concluded that the introduction of generic simvastatin items could probably have led to the decreased cost and cost-prevalence index of individual innovator medicine items containing simvastatin as an active ingredient and the general cost of all medicine items containing simvastatin as an active ingredient.

Table 5.92 Prevalence and cost of individual medicine items containing simvastatin as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Months	Simvastatin	Prescription	Prevalence percentage*	Cost	Cost percentage#	Cost-prevalence index
May 2001 to Aug 2001 (P1)	Zocor 10mg®	12524	8.88	3558067.21	7.74	0.87
	Zocor 20mg®	7987	5.67	3252684.29	7.07	1.25
	Zocor 40mg®	1586	1.13	585538.40	1.27	1.12
Sep 2001 to Dec 2001 (P2)	Zocor 10mg®	17624	9.29	5000870.79	7.97	0.86
	Zocor 20mg®	11012	5.81	4440780.94	7.08	1.22
	Zocor 40mg®	2524	1.33	904020.22	1.44	1.08
Jan 2002 to April 2002 (P3)	Zocor 10mg®	22161	8.58	6333407.45	7.25	0.84
	Zocor 20mg®	14598	5.65	5872351.41	6.72	1.19
	Zocor 40mg®	3711	1.44	1279346.95	1.46	1.01

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs for the corresponding period (calculated from table 5.22) multiplied by hundred
%# Is the total cost of individual hypolipidemic drugs divided by the total cost of all hypolipidemic drugs for the corresponding period (calculated from table 5.22) multiplied by hundred.

Table 5.93 Prevalence and cost of individual medicine items containing simvastatin as an active ingredient from May 2002 to April 2003 (period P4 to P6)

[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
May 2002 to Aug 2002 (P4)	Zocor 10mg®	20953	7.98	5978900.78	6.72	0.84
	Zocor 20mg®	13720	5.23	5503227.79	6.19	1.18
	Zocor 40mg®	3802	1.45	1275380.78	1.43	0.99
Sep 2002 to Dec 2002 (P5)	Adco simvastatin 10mg®	1551	0.64	294037.34	0.36	0.56
	Adco simvastatin 20mg®	1324	0.55	275510.03	0.34	0.62
	Adco simvastatin 40mg®	415	0.17	89015.07	0.11	0.65
	Zocor 10mg®	15795	6.56	4348635.05	5.39	0.82
	Zocor 20mg®	10179	4.23	3903911.40	4.84	1.14
	Zocor 40mg®	3029	1.26	980956.56	1.22	0.97
Jan 2003 to April 2003 (P6)	Adco simvastatin 10mg®	10191	3.97	1626255.36	1.95	0.49
	Adco simvastatin 20mg®	9892	3.86	1670023.07	2.01	0.52
	Adco simvastatin 40mg®	3317	1.29	659041.88	0.79	0.61
	Zocor 10mg®	9565	3.73	1807718.46	2.17	0.58
	Zocor 20mg®	5776	2.25	1209469.42	1.45	0.64
	Zocor 40mg®	2083	0.81	493352.23	0.59	0.73

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs for the corresponding period (calculated from table 5.23) multiplied by hundred
%# Is the total cost of individual hypolipidemic drugs divided by the total cost of all hypolipidemic drugs for the corresponding period (calculated from table 5.23) multiplied by hundred.

5.8.2.5.2 Cost analysis of individual medicine items containing simvastatin as an active ingredient

It is evident from table 5.94 that the average cost of Zocor 20mg® and Zocor 40mg® declined from P1 to P3. On the other hand, the average cost of Zocor 10mg® declined from P1 to P2 and then picked up during P3. During the second study year, the average cost of all individual medicine items containing simvastatin as an active ingredient decreased from P4 to P6 (refer to table 5.95).

The above discussion on simvastatin certainly indicates that the increase in utilisation of generic medicine items led to a decrease in overall cost of resources. As a result, the total disbursement on health care products decreases. The relative low cost of generic medicine items may force the cost of innovator medicine items' decline to make up for cost competition. As indicated in table 5.94 the maximum cost per item of Zocor 10mg® was on average relatively higher than the maximum cost per item of other medicine items containing simvastatin as an active ingredient during the first study year.

Table 5.94 Cost analysis of individual medicine items containing simvastatin as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Months	Simvastatin	Number of items	Average cost per item (R)	Standard deviation (R)	Maximum cost per item (R)	Total cost (R)
May 2001 to Aug 2001 (P1)	Zocor 10mg®	12524	284.10	35.99	590.69	3558067.21
	Zocor 20mg®	7987	407.25	43.15	833.79	3252684.29
	Zocor 40mg®	1586	369.19	87.87	830.09	585538.40
Sep 2001 to Dec 2001 (P2)	Zocor 10mg®	17624	283.75	33.63	1638.94	5000870.79
	Zocor 20mg®	11012	403.28	46.39	833.79	4440780.94
	Zocor 40mg®	2524	358.17	93.46	827.76	904020.22
Jan 2002 to April 2002 (P3)	Zocor 10mg®	22161	285.79	42.95	3276.40	6333407.45
	Zocor 20mg®	14598	402.27	50.96	1249.63	5872351.41
	Zocor 40mg®	3711	344.74	93.35	642.34	1279346.95

Table 5.95 Cost analysis of individual medicine items containing simvastatin as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Months	Simvastatin medicine items	Number of medicine items	Average cost per medicine item (R)	Standard deviation (R)	Maximum cost per medicine item (R)	Total cost (R)
May 2002 to Aug 2002 (P4)	Zocor 10mg®	20953	285.35	31.06	590.74	5978900.78
	Zocor 20mg®	13720	401.11	51.45	833.74	5503227.79
	Zocor 40mg®	3802	335.45	97.36	828.22	1275380.78
Sep 2002 to Dec 2002(P5)	Adco simvastatin 10mg®	1551	189.58	15.50	198.13	294037.34
	Adco simvastatin 20mg®	1324	208.09	33.33	430.37	275510.03
	Adco simvastatin 40mg®	415	214.49	81.98	580.34	89015.07
	Zocor 10mg®	15795	275.32	42.51	885.08	4348635.05
	Zocor 20mg®	10179	383.53	68.49	833.74	3903911.40
	Zocor 40mg®	3029	323.85	100.79	828.26	980956.56
Jan 2003 to April 2003 (P6)	Adco simvastatin 10mg®	10191	159.58	22.27	552.16	1626255.36
	Adco simvastatin 20mg®	9892	168.83	37.57	430.37	1670023.07
	Adco simvastatin 40mg®	3317	198.69	67.06	580.38	659041.88
	Zocor 10mg®	9565	188.99	48.08	2321.43	1807718.46
	Zocor 20mg®	5776	209.40	30.70	419.91	1209469.42
	Zocor 40mg®	2083	236.85	80.00	581.98	493352.23

During the second study year, the maximum cost per medicine item of Prava 10mg® continued to be relatively higher than the maximum cost of other medicine items containing simvastatin as an active ingredient (see table 5.86). The maximum cost per medicine item of both Prava 20mg® and Prava 40mg® was stable from P4 to P5 and it then decreased during P6. The maximum cost per medicine item of generic simvastatin was relatively lower than that of innovator simvastatin

during P5. During P6 there was little variation between maximum cost per medicine item of both generic and innovator simvastatin medicine items.

As seen in table 5.96 the d-value of Zocor 10mg®, Zocor 20mg® and Zocor 40mg® between P1 and P4, P2 and P5 was small and of no practical significance. However, the d-value between P3 and P6 was large and of practical significance for Zocor 10mg®, Zocor 20mg® and Zocor 40mg®. This large d-value might have been brought about by a noticeable difference in average cost of all three drugs during P3 and P6.

Table 5.96 The d-value analysis of the average cost of Zocor 10mg® for the different time periods

Periods			
May 2002 to Aug 2002 (P4)	0.03		
Sep 2002 to Dec 2002 (P5)		0.20	
Jan 2003 to Apr 2003 (P6)			2.0

Table 5.97 The d-value analysis of the average cost of Zocor 20mg® for the different time periods

Periods			
May 2002 to Aug 2002 (P4)	0.12		
Sep 2002 to Dec 2002 (P5)		0.29	
Jan 2003 to Apr 2003 (P6)			3.81

Table 5.98 The d-value analysis of the average cost of Zocor 40mg® for the different time periods

Periods			
May 2002 to Aug 2002 (P4)	0.35		
Sep 2002 to Dec 2002 (P5)		0.34	
Jan 2003 to Apr 2003 (P6)			1.16

5.8.2.5.3 The prescribed daily dose of individual medicine items containing simvastatin as an active ingredient

The World Health Organization assigned a defined daily dose of 15mg orally to simvastatin (WHO, 2002: 60). Simvastatin is available in South Africa in three strengths (10mg, 20mg and 40mg). None of the strengths will produce a prescribed daily dose of 15mg when issued once daily. As depicted in table 5.99 and table 5.100, generally the number of prescriptions that has a defined daily dose of 15mg constitutes less than 1% of the total number of prescriptions (n = 205319) prescribed for all individual drugs containing simvastatin as an active ingredient during both study years.

It can be seen in table 5.99 that during the first study year, 66.84 % (n=52309) of all the prescriptions for Zocor 10mg® were prescribed according to MIMS™, (2003: 158). Of the total number of prescriptions for Zocor 20mg® and Zocor 40mg® during the second study year, 66.01% (n=33597) and 66.16% (n=7821) were prescribed according to the MIMS™.

During the second study year, 65.39% (n=46313), 62.95% (n=29675) and 55.77% (n=9814) of Zocor 10mg®, Zocor 20mg® and Zocor 40mg® were prescribed according to the MIMS™ as apposed to 0.22% and 0.01% of the prescriptions of Zocor 10mg® and Zocor 20mg® which conformed to the defined daily dose. None of the prescriptions of Adco-simvastatin 10mg® and Adco-simvastatin 40mg® conformed to the defined daily dose. As indicated in table 5.100, only 2 prescriptions of Adco-simvastatin 20mg® conformed to the defined daily dose of simvastatin.

In South Africa, according to the medicine list in MIMS™ no simvastatin with strength of either 15mg or 30mg are available. It is for this reason that almost all of the prescriptions for simvastatin in this study did not conform to the defined daily dose. The reason for the non-availability of 15mg or 30mg dosage strengths in the Republic of South Africa was not further investigated as this falls outside the scope of this research study.

Table 5.99 The prescribed daily dose of individual medicine items containing simvastatin as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Simvastatin	PDD	P1	%*	P2	%*	P3	%*
Zocor 10mg®	<10	3586	28.63	6377	36.19	7214	32.55
	=10	8910	71.14	11198	63.54	14856	67.04
	>10<15	4	0.03	24	0.14	26	0.12
	=15	14	0.11	14	0.08	40	0.18
	>15	10	0.08	11	0.06	25	0.11
Zocor 20mg®	<15	184	2.30	347	3.15	614	4.21
	=15	1	0.01	1	0.01	6	0.04
	>15<20	2127	26.63	3601	32.70	4312	29.54
	=20	5622	70.39	6983	63.41	9571	65.56
	>20	53	0.66	80	0.73	95	0.65
Zocor 40mg®	<20	12	0.76	46	1.82	74	1.99
	=20	385	24.27	721	28.57	1310	35.30
	>20<40	19	1.20	9	0.36	42	1.13
	=40	1163	73.33	1738	68.86	2273	61.25
	>40	7	0.44	10	0.40	12	0.32

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table
%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table (per study period e.g. P1) divided by the total number of prescriptions of the individual medicine item whose PDD was calculated multiplied by hundred.

Table 5.100 The prescribed daily dose of individual medicine items containing simvastatin as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Simvastatin	PDD (mg)	May to Aug 2002 (P4)		Sept to Dec 2002 (P5)		Jan to Apr 2003 (P6)	
		P	%	P	%	P	%
Zocor 10mg®	<10	6571	31.36	5323	33.70	3908	40.86
	=10	14302	68.26	10396	65.82	5587	58.41
	>10<15	24	0.11	33	0.21	0	0.00
	=15	32	0.15	21	0.13	49	0.51
	>15	24	0.11	22	0.14	21	0.22
Zocor 20mg®	<15	626	4.56	474	4.66	267	4.62
	=15	1	0.01	0	0.00	3	0.05
	>15<20	4064	29.62	3130	30.75	2327	40.29
	=20	8954	65.26	6556	64.41	3170	54.88
	>20	75	0.55	19	0.19	9	0.16
Zocor 40mg®	<20	88	2.31	63	2.08	39	1.87
	=20	1533	40.32	1257	41.50	841	40.37
	>20<40	19	0.50	19	0.63	12	0.58
	=40	2141	56.31	1676	55.33	1154	55.40
	>40	21	0.55	14	0.46	37	1.78
Adco-simvastatin 10mg®	<10			243	15.67	1068	10.48
	=10			1308	84.33	9113	89.42
	>10<15			0	0	0	0.00
	=15			0	0	0	0.00
	>15			0	0	10	0.10
Adco-simvastatin 20mg®	<15			120	9.06	1524	15.41
	=15			0	0.00	2	0.02
	>15<20			166	12.54	720	7.28
	=20			1030	77.79	7587	76.70
	>20			8	0.60	59	0.60
Adco-simvastatin 40mg®	<20			2	0.48	42	1.27
	=20			227	54.70	1835	55.32
	>20<40			6	1.45	22	0.66
	=40			177	42.65	1403	42.30
	>40			3	0.72	15	0.45

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table
%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table (per study period e.g. P4) divided by the total number of prescriptions of the individual medicine item whose PDD was calculated multiplied by hundred.

5.8.2.3.4 MPL analysis of simvastatins

Individual medicine items that contained simvastatin as an active ingredient first appeared on the MPL from September 2002. This happened after generic simvastatin had been available on the market. It is evident from table 5.101, that the total cost of all packaging sizes of Zocor 10mg® claimed was higher than the calculated cost during P5. The total cost that was paid to the provider for Zocor 10mg® was R4 348 035.05. The cost difference (total cost minus the calculated cost) was R1 429 417.49. The cost difference is the expected cost that is paid to the

provider in excess of what the medical scheme administrator or medical scheme is prepared to pay.

It is apparent from table 5.101 that the total cost of both Zocor 20mg® and Zocor 40mg® was higher than the calculated cost for both drugs. The total cost of Zocor 20mg® was R3 903 911.4 and the calculated cost was R2 095 389.48; on the other hand, the total cost of Zocor 40mg® was R980 956.6 and the calculated cost was R686 096.17. The cost differences were R1 808 521.92 and R294 860.39 for Zocor 20mg® and Zocor 40mg® respectively. The patient expected co-payment accounted for 46.33% (n = R3 903 911.4) and 30.06% (n = R980 956.6) of the total cost of both Zocor 20mg® and Zocor 40mg® respectively.

It is apparent from table 5.103, that the total cost of Adco-simvastatin 10mg®, Adco-simvastatin 20mg® and Adco-simvastatin 40mg® was higher than the calculated cost during September. Though it was higher, the cost difference was minimal for all three drugs. The patient expected co-payment accounted for 1.23% (n=R294 037.34), 1.65% (n=R275 510.03) and 1.50% (n=R89 015.07) of the total cost of Adco-simvastatin 10mg®, Adco-simvastatin 20mg® and Adco-simvastatin 40mg® that was paid to the pharmacist or dispensing doctor respectively.

It is clear from table 5.104 and table 5.105 that the cost difference declined for the three innovator simvastatin drugs. The total cost of Zocor 10mg®, Zocor 20mg® and Zocor 40mg® was larger than the calculated cost throughout P6 except for Zocor 10mg® with a packaging size of 60 tablets and Zocor 40mg with a packaging size of 30 tablets. In the above cases, the calculated cost was higher than the total cost. If the calculated cost is higher than the total cost, then there will be no patient expected co-payment. This means that the medicine claims company paid the expected cost that the provider was asking for and that the patient did not pay anything to the provider. The cost difference of R34 880.06, R30 434.62 and R11 670.19 was evident for Zocor 10mg®, Zocor 20mg® and Zocor 40mg® respectively. The patient expected co-payment accounted for 1.93% (n=R18 077 158.46), 2.52% (n=1 209 469.42) and 2.37% (n=493 352.23) of the total cost of Zocor 10mg®, Zocor 20mg® and Zocor 40mg® respectively during P6 (January 2003 to April 2003).

As seen in table 5.106, generally the calculated cost was greater than the total cost for most packaging sizes of generic simvastatin. As a result, there was no patient expected co-payment with the use of generic simvastatin. The cost-difference was (-) R284 970.24, (-) R295 281.1 and (-) R32 585.53 for Adco-simvastatin 10mg®, Adco-simvastatin 20mg® and Adco-simvastatin

40mg®. (The negative sign shows that the calculated cost was greater than the total cost). This discussion confirms beyond doubt that generic prescribing minimises patient expected co-payment. It can then be concluded that the more frequently generic drugs are prescribed, the smaller the health care bill will become to the patients.

Table 5.101 MPL analysis of Zocor 10mg from September 2002 to December 2002 (P5)

Product name	Quantity	Number of scripts	Number of tablets	Average cost per item (R)	Total cost (R)	Medscheme price list®				
						Cost per unit (R)	Calculated cost (R)	Effect	Cost difference	Cost saving %
Zocor 10mg®	4	2	8	30.04±0	60.08	6.40	51.20	+	8.88	14.78
	7	3	21	76.99±0	230.97	6.40	134.40	+	96.57	41.81
	8	6	48	87.77±0	526.59	6.40	307.20	+	219.39	41.66
	10	11	110	99.16±77.20	1090.76	6.40	704.00	+	386.76	35.46
	14	142	1988	147.04±15.46	20879.53	6.40	12723.20	+	8156.33	39.06
	15	438	6570	156.48±19.67	68537.81	6.40	42048.00	+	26489.81	38.65
	16	6	96	173.50±0.01	1041.00	6.40	614.40	+	426.6	40.98
	19	1	19	205.66±0	205.66	6.40	121.60	+	84.06	40.87
	20	14	280	213.71±6.84	2991.92	6.40	1792.00	+	1199.92	40.11
	22	19	418	220.79±33.91	4194.94	6.40	2675.20	+	1519.74	36.23
	25	1	25	269.99±0	269.99	6.40	160.00	+	109.99	40.74
	28	4680	131040	265.65±25.21	1243244.60	6.40	838656.00	+	404588.6	32.54
	30	10396	311880	285.88±32.63	2971967.86	6.40	1996032.00	+	975935.9	32.84
	31	6	186	254.04±58.06	1524.21	6.40	1190.40	+	333.81	21.90
	32	7	224	317.75±0.03	2224.26	6.40	1433.60	+	790.66	35.55
	40	2	80	403.56±0	807.12	6.40	512.00	+	295.12	36.56
	42	18	756	424.95±0	7649.10	6.40	4838.40	+	2810.7	36.75
	45	21	945	412.00±73.11	8652.07	6.40	6048.00	+	2604.07	30.10
	56	10	560	547.34±0	5473.40	6.40	3584.00	+	1889.4	34.52
	60	10	600	529.30±98.90	5293.02	6.40	3840.00	+	1453.02	27.45
	90	2	180	885.08±0	1170.16	6.40	1152.00	+	18.16	1.55

Calculated cost is the cost that the medical administrator or medical scheme is prepared to pay; the total cost is the total cost claimed by the provider; Cost difference is the cost in excess of what the medical administrator or medical scheme is prepared to pay, it is the expected cost to be paid by the patient to the provider. This patient co-payment results when the calculated cost is less than the total cost. Cost saving % is the expected percentage co-paid by the patient. Effect (+) = the total cost is more than the cost that the medical administrator or medical scheme is prepared to pay. Effect (-) = the calculated cost is more than the total cost; this indicated the savings incurred by the medical administrator or medical scheme or patient.

Table 5.102 MPL analysis of Zocor 20mg and Zocor 40mg from September 2002 to December 2002 (P5)

Prescribed item	Quantity	Number of scripts	Number of tablets	Average cost/ item (R)	Total cost (R)	Med... price per unit (R)	Calculated cost (R)	Med... price list® Effect +/-	Med... price list® difference	Med... price list® saving %
Zocor 20mg®	2	3	6	32.27±0	96.81	7.17	43.02	+	53.79	55.56
	3	1	3	47.39±0	47.39	7.17	21.51	+	25.88	54.61
	4	2	8	62.58±0	125.16	7.17	57.36	+	67.8	54.17
	5	2	10	77.73±0	155.46	7.17	71.70	+	83.76	53.88
	7	7	49	108.03±0.01	756.21	7.17	351.33	+	404.88	53.54
	10	9	90	134.10±30.81	1206.90	7.17	645.30	+	561.6	46.53
	12	2	24	182.24±0	364.48	7.17	172.08	+	192.4	52.79
	14	85	1190	212.64±11.30	18074.22	7.17	8532.30	+	9541.92	52.79
	15	337	5055	217.50±33.74	73298.11	7.17	36244.35	+	37053.76	50.55
	16	3	48	244.38±0	733.14	7.17	344.16	+	388.98	53.06
	20	23	460	304.73±0.43	7008.79	7.17	3298.20	+	3710.59	52.94
	24	5	120	365.54±0	1827.70	7.17	860.40	+	967.3	52.92
	25	6	150	380.65±0	2283.90	7.17	1075.50	+	1208.4	52.91
	26	2	52	387.07±0	774.14	7.17	372.84	+	401.3	51.84
	28	3117	87276	370.15±50.23	1153747.55	7.17	625768.92	+	527978.6	45.76
	30	6556	196680	401.07±55.62	2629426.81	7.17	1410195.60	+	1219231	46.37
	45	7	315	645.00±0.19	4515.00	7.17	2258.55	+	2256.45	49.98
	56	3	168	655.40±203.53	1966.20	7.17	1204.56	+	761.64	38.74
	60	9	540	833.71±0.02	7503.43	7.17	3871.80	+	3631.63	48.40
Zocor 40mg®	2	2	4	32.21±0	64.42	9.67	38.68	+	25.74	39.96
	7	2	14	107.96±0	215.92	9.67	135.38	+	80.54	37.30
	8	44	352	118.23±12.52	5201.91	9.67	3403.84	+	1798.07	34.57
	10	4	40	153.44±0	613.76	9.67	386.80	+	226.96	36.98
	14	11	154	208.26±19.16	2290.88	9.67	1489.18	+	801.7	35.00
	15	1257	18855	223.07±19.48	280400.10	9.67	182327.85	+	98072.25	34.98
	28	19	532	414.62±0	7877.72	9.67	5144.44	+	2733.28	34.70
	30	1676	50280	402.26±37.21	674183.61	9.67	486207.60	+	187976	27.88

	45	8	360	642.34±0.05	5138.68	9.67	3481.20	+	1657.48	32.25
	60	6	360	828.26±0	4969.56	9.67	3481.20	+	1488.36	29.95

Calculated cost is the cost that the medical administrator or medical scheme is prepared to pay; the total cost is the total cost claimed by the provider; Cost difference is the cost in excess of what the medical administrator or medical scheme is prepared to pay, it is the expected cost to be paid by the patient to the provider. This patient co-payment results when the calculated cost is less than the total cost. Cost saving % is the expected percentage co-paid by the patient. Effect (+) = the total cost is more than the cost that the medical administrator or medical scheme is prepared to pay. Effect (-) = the calculated cost is more than the total cost; this indicated the savings incurred by the medical administrator or medical scheme or patient.

Table 5.103 MPL analysis of Adco-simvastatin 10mg®, Adco-simvastatin 20mg® & Adco-simvastatin 40mg®from September 2002 to December 2002 (P5)

Product name	Quantity	Number of scripts	Number of tablets	Average cost per item (R)	Total cost (R)	Cost per tablet (R)	Medical scheme Calculated cost (R)	Effect	Cost difference	Cost saving
Adco-simvastatin 10mg®	14	5	70	100.06±0.04	500.31	6.40	448.00	+	52.31	10.46
	15	46	690	107.06±0.04	4924.80	6.40	4416.00	+	508.8	10.33
	28	192	5376	192.77±1.12	37011.37	6.40	34406.40	+	2604.97	7.04
	30	1308	39240	192.36±2.25	251600.86	6.40	251136.0	+	464.86	0.18
Adco-simvastatin 20mg®	5	3	15	41.19±0	123.57	7.17	107.55	+	16.02	12.96
	14	6	84	111.92±0.03	671.49	7.17	602.28	+	69.21	10.31
	15	111	1665	119.77±0.02	13294.94	7.17	11938.05	+	1356.89	10.21
	28	166	4648	215.97±1.27	35851.44	7.17	33326.16	+	2525.28	7.04
	30	1030	30900	215.66±0.19	222126.37	7.17	221553.0	+	573.37	0.26
	60	8	480	430.28±0.17	3442.22	7.17	3441.60	+	0.62	0.02
Adco-simvastatin 40mg®	14	2	28	150.48±0	300.96	9.67	270.76	+	30.2	10.03
	15	227	3405	149.82±40.90	34008.66	9.67	32926.35	+	1082.31	3.18
	20	3	60	214.04±0	642.12	9.67	580.20	+	61.92	9.64
	28	3	84	290.68±0	872.04	9.67	812.28	+	59.76	6.85
	30	177	5310	290.68±0	51450.27	9.67	51347.70	+	102.57	0.20
	60	3	180	580.34±0	1741.02	9.67	1740.60	+	0.42	0.02

Calculated cost is the cost that the medical administrator or medical scheme is prepared to pay; the total cost is the total cost claimed by the provider; Cost difference is the cost in excess of what the medical administrator or medical scheme is prepared to pay, it is the expected cost to be paid by the patient to the provider. This patient co-payment results when the calculated cost is less than the total cost. Cost saving % is the expected percentage co-paid by the patient. Effect (+) = the total cost is more than the cost that the medical administrator or medical scheme is prepared to pay. Effect (-) = the calculated cost is more than the total cost; this indicated the savings incurred by the medical administrator or medical scheme or patient.

Table 5.104 MPL analysis of Zocor 10mg® from January 2003 to April 2003 (P6)

[illegible]	Quantity	Number of scripts	Number of tablets	Average cost/ script (R)	Total cost (R)	Medicine price list				
						Unit price (R)	Calculated cost (R)	Effect	Cost difference	Cost saving %
Zocor 10mg®	5	2	10	37.08±0	74.16	6.40	64.00	+	10.16	13.70
	6	3	18	44.19±0	132.57	6.40	115.20	+	17.37	13.10
	7	5	35	51.25±0.02	256.28	6.40	224.00	+	32.28	12.60
	10	9	90	72.37±0.02	651.34	6.40	576.00	+	75.34	11.57
	12	3	36	86.46±0	259.38	6.40	230.40	+	28.98	11.17
	14	87	1218	102.21±9.48	8892.18	6.40	7795.20	+	1096.98	12.34
	15	220	3300	107.51±0.17	23652.80	6.40	21120.00	+	2532.8	10.71
	16	6	96	114.62±0	687.72	6.40	614.40	+	73.32	10.66
	20	9	180	142.78±0	1285.02	6.40	1152.00	+	133.02	10.35
	22	8	176	156.83±0	1254.64	6.40	1126.40	+	128.24	10.22
	28	3556	99568	183.20±11.40	651461.41	6.40	637235.20	+	14226.21	2.18
	30	5587	167610	194.90±15.00	1088913.28	6.40	1072704.0	+	16209.28	1.49
	45	49	2205	300.10±10	14705.08	6.40	14112.00	+	593.08	4.03
	56	14	784	359.97±0.18	5039.60	6.40	5017.60	+	22	0.44
	60	1	60	3.85±0	3.85	6.40	384.00	-	-380.15	-9874.03
	180	3	540	1161.62±0	3484.86	6.40	3456.00	+	28.86	0.83
	360	3	1080	2321.43±0	6964.29	6.40	6912.00	+	52.29	0.75

The information for Zocor 10mg® with a packaging size of 60 tablets is copied directly from the database. The cost saving was calculated according to the information on the database Calculated cost is the cost that the medical administrator or medical scheme is prepared to pay; the total cost is the total cost claimed by the provider; Cost difference is the cost in excess of what the medical administrator or medical scheme is prepared to pay, it is the expected cost to be paid by the patient to the provider. This patient co-payment results when the calculated cost is less than the total cost. Cost saving % is the expected percentage co-paid by the patient. Effect (+) = the total cost is more than the cost that the medical administrator or medical scheme is prepared to pay. Effect (-) = the calculated cost is more than the total cost; this indicated the savings incurred by the medical administrator or medical scheme or patient.

Table 5.105 MPL analysis of Zocor 20mg® and Zocor 40mg® from January to April 2003 (P6)

Prescription name	Quantity	Number of claims	Number of tablets	Calculated cost per item (R)	Total cost (R)	Cost per tablet (R)	Medicine price (R) Estimated cost (R)	Effect	Cost difference	Cost saving %
Zocor 20mg®	6	2	12	49.24±0	98.48	7.17	86.04	+	12.44	12.63
	8	12	96	65.08±0	780.96	7.17	688.32	+	92.64	11.86
	10	1	10	80.81±0	80.81	7.17	71.70	+	9.11	11.27
	14	56	784	111.35±3.20	6235.78	7.17	5621.28	+	614.5	9.85
	15	194	2910	120.13±0.17	23305.00	7.17	20864.70	+	2440.3	10.47
	20	2	40	159.63±0	319.26	7.17	286.80	+	32.46	10.17
	23	3	69	183.33±0	549.99	7.17	494.73	+	55.26	10.05
	24	4	96	190.93±0	763.72	7.17	688.32	+	75.4	9.87
	28	2323	65044	205.49±18.23	477346.42	7.17	466365.48	+	10980.94	2.30
	30	3170	95100	220.17±24.19	697952.39	7.17	681867.00	+	16085.39	2.30
	31	9	279	226.29±0	2036.61	7.17	2000.43	+	36.18	1.78
Zocor 40mg®	2	3	6	23.23±0	69.69	9.67	58.02	+	11.67	16.75
	3	2	6	33.84±0	67.68	9.67	58.02	+	9.66	14.27
	8	26	208	87.02±0.07	2262.42	9.67	2011.36	+	251.06	11.10
	14	8	112	150.58±0.18	1204.66	9.67	1083.04	+	121.62	10.10
	15	841	12615	160.87±15.04	135292.09	9.67	121987.05	+	13305.04	9.83
	21	3	63	225.28±0	675.84	9.67	609.21	+	66.63	9.86
	28	9	252	283.72±22.22	2553.46	9.67	2436.84	+	116.62	4.57
	30	1154	34620	287.89±34.77	332228.58	9.67	334775.40	-	-2546.82	-0.77
	40	1	40	398.29±0	398.29	9.67	386.80	+	11.49	2.88
	45	18	810	451.35±0.39	8124.24	9.67	7832.70	+	291.54	3.59
	60	18	1080	581.96±0.02	10475.28	9.67	10443.60	+	31.68	0.30

Calculated cost is the cost that the medical administrator or medical scheme is prepared to pay; the total cost is the total cost claimed by the provider; Cost difference is the cost in excess of what the medical administrator or medical scheme is prepared to pay, it is the expected cost to be paid by the patient to the provider. This patient co-payment results when the calculated cost is less than the total cost. Cost saving % is the expected percentage co-paid by the patient. Effect (+) = the total cost is more than the cost that the medical administrator or medical scheme is prepared to pay. Effect (-) = the calculated cost is more than the total cost; this indicated the savings incurred by the medical administrator or medical scheme or patient.

Table 5.106 MPL analysis of Adco-simvastatin 10mg®, Adco-simvastatin 20mg® & Adco-simvastatin 40mg® from January to April 2003 (P6)

Medicine	Quantity	Number of scripts	Number of tablets	Average cost/item (R)	Total cost (R)	Cost per unit (R)	Medscheme Calculated cost (R)	Claim	Cost difference	Cost saving %
Adco-simvastatin 10mg®	7	2	14	41.08±0	82.16	6.40	89.60	-	-7.44	-9.06
	10	9	90	57.83±0.03	520.45	6.40	576.00	-	-55.55	-10.67
	14	26	364	87.83±9.87	2283.56	6.40	2329.60	-	-46.04	-2.02
	15	362	5430	89.56±8.16	32421.33	6.40	34752.00	-	-2330.67	-7.19
	23	3	69	130.43±0	391.29	6.40	441.60	-	-50.31	-12.86
	28	666	18648	166.77±17.75	111070.03	6.40	119347.20	-	-8277.17	-7.45
	30	9113	273390	161.96±15.86	1476020.94	6.40	1749696.0	-	-273675	-18.54
	60	9	540	323.72±33.93	2913.44	6.40	3456.00	-	-542.56	-18.62
	84	1	84	552.16±0	552.16	6.40	537.60	+	14.56	2.64
Adco-simvastatin 20mg®	7	3	21	56.98±0	170.94	7.17	150.57	+	20.37	11.92
	10	7	70	69.09±7.79	483.63	7.17	501.90	-	-18.27	-3.78
	14	60	840	97.00±10.65	5820.07	7.17	6022.80	-	-202.73	-3.48
	15	1448	21720	99.22±8.44	143673.28	7.17	155732.40	-	-12059.1	-8.39
	20	2	40	159.08±0	318.16	7.17	286.80	+	31.36	9.86
	21	4	84	133.33±0	533.32	7.17	602.28	-	-68.96	-12.93
	23	2	46	182.63±0	365.26	7.17	329.82	+	35.44	9.70
	28	720	20160	185.96±19.66	133893.61	7.17	144547.20	-	-10653.6	-7.96
	30	7587	227610	179.74±19.42	1363678.05	7.17	1631963.7	-	-268286	-19.67
	45	2	90	333.94±0	667.88	7.17	645.30	+	22.58	3.38
	60	57	3420	358.23±33.50	20418.87	7.17	24521.40	-	-4102.53	-20.09
Adco-simvastatin 40mg®	5	2	10	49.73±0	99.46	9.67	96.70	+	2.76	2.77
	8	25	200	79.69±3.18	1992.25	9.67	1934.00	+	58.25	2.92
	10	4	40	97.43±0	389.72	9.67	386.80	+	2.92	0.75
	11	2	22	106.93±0	213.86	9.67	212.74	+	1.12	0.52
	14	9	126	135.59±0	1220.31	9.67	1218.42	+	1.89	0.15
	15	1835	27525	145.22±18.42	266486.66	9.67	266166.75	+	319.91	0.12
	25	2	50	240.58±0	481.16	9.67	483.50	-	-2.34	-0.49

	28	20	560	266.10±10.59	5322.07	9.67	5415.20	-	-93.13	-1.75
	30	1403	42090	267.16±11.43	374824.77	9.67	407010.30	-	-32185.5	-8.59
	60	15	900	534.11±23.95	8011.62	9.67	8703.00	-	-691.38	-8.63

Calculated cost is the cost that the medical administrator or medical scheme is prepared to pay; the total cost is the total cost claimed by the provider; Cost difference is the cost in excess of what the medical administrator or medical scheme is willing to pay, it is the expected cost to be paid by the patient to the provider. This patient co-payment results when the calculated cost is less than the total cost. Cost saving % is the expected percentage co-paid by the patient. Effect (+) = the total cost is more than the cost that the medical administrator or medical scheme is prepared to pay. Effect (-) = the calculated cost is more than the total cost; this indicated the savings incurred by the medical administrator or medical scheme or patient.

5.8.3 "Others" active ingredients

Under this section, the utilisation patterns and cost of medicine items containing "others" as an active ingredient will be discussed.

5.8.3.1 Prevalence and cost of individual medicine items containing "others" as an active ingredient

The miscellaneous active ingredients that will be discussed under this section are the following: acipimox, cholestyramine, essential phospholipids, nicotinic acid and olbetam. The individual medicine items containing these active ingredients were the least prescribed of the hypolipidemic drugs. As seen on table 5.107 and table 5.108, the total number of individual medicine items containing other active ingredients declined from 7524 to 7272 during the first and second study years respectively. This class of drugs accounted for 1.28% (n =589036) and 0.96% (n =759675) of the total number of hypolipidemic drugs claimed during the first and second study years respectively.

Questran lite® was the most frequently prescribed drug of the seven individual hypolipidemic drugs claimed; on the other hand, Nicotinic acid 30mg® was the least claimed drug during the two study years. It can be seen from table 5.107 and table 5.108 during the first study year that the prevalence of most of the drugs containing other active ingredients increased from P1 to P2 then decreased during P3. Lurselle® was an exception. Its prevalence increased from P1 to P3. As discussed above, the total prevalence of all drugs of the pharmacological group statins and fibrates increased from the first to the second study year. The increase in utilisation of statins and fibrates could have led to the decreased utilisation of medicine items containing other active ingredients (through therapeutic substitution or change).

The total cost of individual drugs containing other active ingredients decreased from R1 526 095.89 to R1 242 296.87 during the first and second study years respectively. It is apparent from table 5.107 and table 5.108 that Lurselle® was relatively expensive compared to the other individual medicine items. The cost-prevalence index of Lurselle® was above one during the first study year and it decreased to one during P5 and P6. Nicotinic acid BT® was the least expensive of the six medicine items containing "others" as an active ingredient for both study years. The cost-prevalence index of Lipostabil 5ml® was one for all study years. This is an indication that there was a balance between the cost and the prevalence of Lipostabil 5ml® for the two study years.

Table 5.108 Prevalence and cost of individual medicine items containing "others" as an active ingredient from May 2002 to April 2003 (period P4 to P6)

[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
May 2002 to Aug 2002 (P4)	Olbetam 250mg®	134	0.05	36724.05	0.04	0.8
	Questran lite®	2140	0.82	366668.49	0.41	0.5
	Lipostabil cap®	24	0.01	8669.60	0.01	1.00
	Lipostabil 5ml®	33	0.01	11460.46	0.01	1.00
	Nicotinic acid BT®	180	0.07	4660.51	0.01	0.14
	Nicotinic acid 30mg®	21	0.01	63.99	0.00	0.00
	Lurselle®	117	0.04	56706.61	0.06	1.50
Sep 2002 to Dec 2002 (P5)	Olbetam 250mg®	122	0.05	34727.51	0.04	0.80
	Questran lite®	1609	0.67	295946.30	0.37	0.55
	Lipostabil cap®	13	0.01	4350.39	0.01	1.00
	Lipostabil 5ml®	45	0.02	14521.09	0.02	1.00
	Nicotinic acid BT®	188	0.08	6352.96	0.01	0.13
	Nicotinic acid 30mg®	10	0.00	93.83	0.00	1.00
	Lurselle®	14	0.01	4396.06	0.01	1.00
Jan 2003 to April 2003 (P6)	Olbetam 250mg®	96	0.04	29264.99	0.04	1.00
	Questran lite®	2294	0.89	356904.04	0.43	0.48
	Lipostabil cap®	4	0.00	382.64	0.00	1.00
	Lipostabil 5ml®	7	0.00	2368.14	0.00	1.00
	Nicotinic acid BT®	204	0.08	5540.38	0.01	0.13
	Nicotinic acid 30mg®	10	0.00	63.28	0.00	1.00
	Lurselle®	7	0.00	2431.55	0.00	1.00

%* Is the prevalence of individual hypolipidemic drugs divided by the prevalence of the total number of all hypolipidemic drugs (calculated from table 5.23) multiplied by hundred
%# Is the total cost of individual hypolipidemic drugs divided by the total cost of all hypolipidemic drugs (calculated from table 5.23) multiplied by hundred.

5.8.3.2 Cost analysis of individual medicine items containing "others" as an active ingredient

The average cost of individual medicine items containing "others" as an active ingredient had an erratic trend during the first study year with the exception of Lipostabil cap® and Lipostabil 5ml®. Both drugs had an increased average cost from P1 to P3. During the second study year, the average cost of Olbetam 250mg® increased from P4 to P6 whereas the average cost of Lipostabil capsules® declined from P4 to P6. It can be seen that the average cost of the remaining individual drugs containing "others" as an active ingredient was unstable during the second study year. It is apparent that during P3 and P6, the trend of the average cost of most individual drugs containing "others" as an active ingredient altered (e.g. the average cost of Olbetam® 250mg increased from P1 to P2, it then decreased during P3) (refer to table 5.109)

Table 5.109 Cost analysis of individual medicine items containing "others" as an active ingredient from May 2001 to April 2002 (period P1 to P3)

[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
May 2001 to Aug 2001 (P1)	Olbetam 250mg®	105	245.17	44.79	399.73	25742.44
	Questran lite®	1433	166.02	163.69	1518.65	237913.02
	Lipostabil cap®	27	262.60	92.40	337.19	7090.07
	Lipostabil 5ml®	14	271.02	107.15	460.31	3794.27
	Nicotinic acid BT®	227	16.76	21.47	91.15	3803.47
	Nicotinic acid 30mg®	2	18.32	22.02	33.89	36.64
	Lurselle®	236	475.48	202.98	692.18	112212.33
Sep 2001 to Dec 2001 (P2)	Olbetam 250mg®	115	251.22	46.73	399.73	28890.49
	Questran lite®	1366	185.16	156.59	625.36	252934.63
	Lipostabil cap®	43	289.69	80.16	411.54	12456.50
	Lipostabil 5ml®	9	306.86	115.07	460.29	2761.73
	Nicotinic acid BT®	228	25.06	26.20	91.59	5713.75
	Nicotinic acid 30mg®	7	3.27	0.76	4.09	22.91
	Lurselle®	343	422.99	186.19	726.62	145084.53
Jan 2002 to April 2002 (P3)	Olbetam 250mg®	102	204.16	116.80	439.53	20824.39
	Questran lite®	2602	168.01	158.53	687.54	437154.51
	Lipostabil cap®	38	333.88	186.47	812.68	12687.34
	Lipostabil 5ml®	42	335.38	106.80	556.28	14085.81
	Nicotinic acid BT®	182	23.51	26.95	96.08	4279.34
	Nicotinic acid 30mg®	3	21.19	0	21.19	63.57
	Lurselle®	400	496.36	226.22	842.62	198544.15

Table 5.110 Cost analysis of individual medicine items containing "others" as an active ingredient from May 2002 to April 2003 (period P4 to P6)

Month	Medication	Total no. of items	Average cost per item (RM)	Standard deviation (RM)	Maximum cost (RM)	Total cost (RM)
May 2002 to Aug 2002 (P4)	Olbetam 250mg®	134	274.06	65.86	461.43	36724.05
	Questran lite®	2140	171.34	159.80	687.46	366668.49
	Lipostabil cap®	24	361.23	94.56	406.85	8669.60
	Lipostabil 5ml®	33	347.29	49.53	381.78	11460.46
	Nicotinic acid BT®	180	25.89	28.60	114.22	4660.51
	Nicotinic acid 30mg®	21	3.05	0.58	4.13	63.99
	Lurselle®	117	484.67	210.24	842.62	56706.61
Sep 2002 to Dec 2002 (P5)	Olbetam 250mg®	122	284.65	55.97	461.43	34727.51
	Questran lite®	1609	183.93	162.70	712.53	295946.30
	Lipostabil cap®	13	334.65	120.63	443.43	4350.39
	Lipostabil 5ml®	45	322.69	84.32	483.68	14521.09
	Nicotinic acid BT®	188	33.79	30.25	114.23	6352.96
	Nicotinic acid 30mg®	10	9.38	4.84	18.01	93.83
	Lurselle®	14	314.00	96.90	421.82	4396.06
Jan 2003 to April 2003 (P6)	Olbetam 250mg®	96	304.84	84.10	507.43	29264.99
	Questran lite®	2294	155.58	166.48	1378.37	356904.04
	Lipostabil cap®	4	95.66	5.17	100.14	382.64
	Lipostabil 5ml®	7	338.31	40.67	381.78	2368.14
	Nicotinic acid BT®	204	27.16	22.67	114.23	5540.38
	Nicotinic acid 30mg®	10	6.33	2.53	9.11	63.28
	Lurselle®	7	347.36	142.41	499.61	2431.55

As indicated in table 5.111, the d-value of Olbetam 250mg®, Nicotinic acid 30mg® and Lurselle® increased from P1 to P6 throughout the different periods. On the other hand, the d-value of Lipostabil 5ml® and Nicotinic acid BT® decreased. It is evident from table 5.111 that most of the d-values of the average cost were of practical significance between P3 and P6.

Table 5.111 d-value analysis of individual medicine items containing "others" as an active ingredient from May 2001 to May 2002

Periods	Olbetam 250mg®	Questran	Lipostabil	Lipostabil	Nicotinic	Nicotinic	Lurselle®
P1 and P4	0.44	0.03	1.04	0.71	0.32	0.69	0.04
P2 and P5	0.60	0.01	0.38	0.14	0.29	1.26	0.59
P3 and P6	0.86	0.07	1.28	0.03	0.14	2.32	0.66

5.8.3.3 The prescribed daily dose of individual medicine items containing "others" as an active ingredient

According to the World Health Organization (2002: 61), the defined daily dose of Olbetam 250mg® is 0.5g/d orally. On the other hand, the dosage according to the MIMS™ (2003: 159) is 500mg to 750mg/day in divided doses. For the available strength of acipimox to conform to the defined daily dose, the patients must take two tablets of Olbetam 250mg® twice daily. It is evident from table 5.112 that 58.07% (n=322) of the number of prescriptions for Olbetam 250mg® conformed to the defined daily dose during the first study year as opposed to 51.99% (n=352) of the number of prescriptions that conformed to the defined daily dose during the second study year. The total number of prescription whose prescribed daily dose was more than the defined daily dose accounted for 40.99% (n= 322) and 42.05% (n= 352) of the total number of prescriptions prescribed for Olbetam 250mg®claimed during the first and second study years respectively.

Questran lite® contains 4g of cholestyramine. The usual dosage of Questran lite® in adults according to the MIMS™ (2003: 160) is 4g taken twice daily. The dosage can be increased to a maximum of 24g/day. The World Heath Organisation (2002: 61) assigned the defined daily dose of 14g/day to Questran lite®. As indicated on both table 5.112 and table 5.113, none of the prescriptions of Questran lite® conformed to the defined daily dose for both study years. It is evident that 99.93% (n=5397) and 99.95% (n=6034) of the prescriptions of Questran lite® were less than the value assigned for the defined daily dose for the first and second study year respectively. It should be noted that the defined daily dose of probucol and essential phospholipids have not yet been assigned. As a result it will not be discussed in this study.

The defined daily dose of nicotinic acid is 2g/d orally (WHO, 2002: 60). It is clear that none of the prescriptions for nicotinic acid 30mg® conformed to the defined daily dose during both study years and 100% of the prescriptions were below the defined daily dose during P1 and P2 and during all the periods of the second study year. However, during P3, 100% of the prescriptions were above the defined daily dose. Of all the prescriptions of nicotinic acid BT tablets® during the first study year, 0.68% (n=657) conformed to the defined daily dosage compared to 5.07% (n=572) during the second study years.

Table 5.112 The prescribed daily dose of individual medicine items containing "others" as an active ingredient from May 2001 to April 2002 (period P1 to P3)

Other active ingredient	PDD	P	%*	P	%*	P	%*
Olbetam 250mg®	<0.5g	1	0.95	2	1.74	0	0.00
	=0.5g	64	60.95	60	52.17	63	61.76
	>0.5g	40	38.10	53	46.09	39	38.24
Questran lite®	<14g	1429	99.72	1366	100	2602	100
	=14g	0	0.00	0	0	0	0
	>14g	4	0.28	0	0	0	0
Nicotinic acid BT tablets®	<2g	210	92.51	218	87.90	163	89.56
	=2g	0	0.00	4	1.61	0	0.00
	>2g	17	7.49	26	10.48	19	10.44
Nicotinic acid 30mg®	<2g	2	100	7	100	0	0
	=2g	0	0	0	0	0	0
	>2g	0	0	0	0	3	100

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table
%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table (per study period e.g. P1) divided by the total number of prescriptions of the individual medicine item whose PDD was calculated multiplied by hundred.

Table 5.113 The prescribed daily dose of individual medicine items containing "others" as an active ingredient from May 2002 to April 2003 (period P4 to P6)

[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Olbetam 250mg®	<0.5g	8	5.97	3	2.46	10	10.42
	=0.5g	80	59.70	67	54.92	36	37.50
	>0.5g	46	34.33	52	42.62	50	52.08
Questran lite®	<14g	2140	100	1609	100	2285	99.61
	=14g	0	0	0	0	0	0.00
	>14g	0	0	0	0	9	0.39
Nicotinic acid BT tablets®	<2g	157	87.22	166	88.30	187	91.67
	=2g	6	3.33	8	4.26	15	7.35
	>2g	17	9.44	14	7.45	2	0.98
Nicotinic acid 30mg®	<2g	21	100	10	100	10	100
	=2g	0	0	0	0	0	0
	>2g	0	0	0	0	0	0

P is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table
%* Is the number of prescriptions that correspond to the prescribed daily doses as displayed on the table (per study period e.g. P4) divided by the total number of prescriptions of the individual medicine item whose PDD was calculated multiplied by hundred.

5.9 CHAPTER SUMMARY

In this chapter, the results of the empirical investigation were outlined. The prevalence and medicine treatment cost of hypolipidemic drugs and all medicine items claimed from the database were established a year before and a year after the implementation of the Medscheme® Price list. A comparison was made between the prescribed daily dosages of the individual sub-pharmacological groups of the hypolipidemic drugs to the defined daily dosages. The MPL of drugs appearing on the reference price list was analysed and the results were discussed. Conclusions and recommendation will be outlined in chapter 6.

CHAPTER 6: CONCLUSIONS AND RECOMMENDATIONS

6.1 INTRODUCTION

In this chapter, conclusions and recommendations regarding the management of dyslipidemia will be outlined.

6.2 CONCLUSIONS

The following conclusions can be formulated with regard to the specific research objectives.

The **first research objective** was to describe from literature the epidemiology of dyslipidemia. As described in paragraph 2.2, it was found that despite severe consequences of raised blood cholesterol, over 4.8 million South African adults suffer from raised cholesterol levels. Only 58% of urban South Africans have ever heard of cholesterol. Only 14% of urban South Africans have had their cholesterol tested and not even 4 % know what their cholesterol level are (Anon., 2002: 1).

The **second research objective** was to differentiate between different lipoproteins. It was found that there are only two types of lipids in blood namely cholesterol and triglycerides (Baron, 2002: 1251). Both of these lipids join with proteins to produce lipoproteins (AAFP, 1998: 1). Five different lipoproteins (chylomicrons, very low-density lipoproteins, low-density lipoproteins, high-density lipoproteins and intermediate-density lipoproteins) have been differentiated on the basis of their density (Siguel, 2000: 2). Chylomicrons are the less dense lipoproteins (Baron, 2002: 1251). They contain high triglyceride and low cholesterol content (Anaizi, 1997: 4). Very low-density lipoprotein cholesterol are produced in the liver (Scheig, 1995: 305), transporting triglycerides to extrahepatic sides and are hydrolysed to low-density lipoproteins (LDL) and intermediate-density lipoprotein (IDL). IDL is taken by the liver or reduced to triglycerides (Malloy & Kane, 1998: 564). LDL is sometimes being referred to as "bad" cholesterol; it contains more than 60% of cholesterol and as a result, has a high atherogenic potential. HDL, on the other hand, is referred to as "good" cholesterol. HDL appears to be responsible for reverse cholesterol transport because it brings cholesterol from cells in the periphery to be excreted (refer to paragraph 2.3).

The **third research objective** was to determine the pathophysiology of dyslipidemia. As indicated above, LDL has high cholesterol content. It was found that upon its oxidation, LDL becomes toxic contributing to the development of atherosclerosis and when in excess it is deposited outside the cell thereby causing the formation of atherogenic plagues in vascular endothelium (Thornton & Holt, 2000: 413) (refer to paragraph 2.5 for a detailed discussion of the pathophysiology of dyslipidemia).

The **fourth research objective** was to define and differentiate between different types of dyslipidemia. Dyslipidemia is defined according to Ahmed *et al.* (1998: 1) as "*disorders of lipoprotein metabolism, including lipoprotein overproduction or deficiency*". These disorders may be manifested by increased levels of total cholesterol, LDL or triglycerides concentration (Malloy & Kane, 1998: 563) (refer to paragraph 2.6.1). Dyslipidemia may be classified as either primary or secondary in terms of causation (Berger & Marais, 2000: 168). As described in paragraph 2.6.2.1, primary dyslipidemia results mainly due to genetic inheritances (table 2.2 outlines the different types of primary dyslipidemias). On the other hand, secondary dyslipidemia is characterised by normal or minor gene defects (refer to paragraph 2.6.2.2). Secondary dyslipidemia may be brought about by the environment, underlying incidental diseases, and several factors including drugs (e.g. thiazides diuretics). Some causes of secondary dyslipidemia are summarised in table 2.3.

The **fifth research objective** was to identify possible risk factors of dyslipidemia. Risk factors for high cholesterol can be divided into controllable and uncontrollable (see paragraph 2.7). Controllable risk factors are factors that may reduce the incidence and severity of the disease if taken cognisance of (Siguel, 2000: 3). These factors include disease conditions such as diabetes mellitus and hepatic diseases, which are primarily associated with bad diet, lack of exercise and overweight. Uncontrollable risk factors are genetically inherited disorders, which result in high cholesterol levels in blood (Schneider, 2002: 2). Age and gender are also regarded as uncontrollable risk factors (Siguel, 2000: 3).

The **sixth research objective** was to describe the diagnosis and test procedures for diagnosis of dyslipidemia. As described in paragraph 2.11, the essential part of the diagnostic procedure of dyslipidemia for patients with total cholesterol levels of less than 5.0 mmol/l but established coronary heart disease and patients with total cholesterol levels of greater than 5.0 mmol/l, is the determination of the lipoprotein profile (Berger & Marais, 2000: 170). A specimen for a lipoprotein profile requires 12 hours overnight fast in adults and older children. The blood

sample should be taken between 08h00 and 10h00. The patient should be sitting and undue venestasis should be avoided. Blood should be collected in tubes without anticoagulant and allowed to clot or into tubes containing heparin or ethylene diamine tetra acetic acid (EDTA) and mixed carefully by inversion. The tubes should be filled to the top to avoid dilution errors if EDTA is used. Plasma or serum should ideally be separated from the cells within two hours of sampling and definitely within six hours. Blood cholesterol measurements should be conducted in people over 20 years of age with a lipogram (AAFP, 1998: 2). It was recommended that blood cholesterol measurement be performed at least once in the life of each adult (Berger & Marais, 2000: 166). When deemed necessary, the decision must be to initiate treatment with lipid modifying drugs on at least two or three fasting low-density lipoprotein measurements obtained 1 week or more using the same laboratory to minimise variability (Ahmed *et al.*, 1998: 2).

The **seventh research objective** was to describe the signs and symptoms, candidates for screening as well as the complications of dyslipidemia. Generally, dyslipidemia is asymptomatic (see paragraph 2.13). Patients may usually complain of symptoms related to complications of dyslipidemia (Bhatnagar, 1998: 213). Extremely high levels of chylomicrons and very low-density lipoproteins result in the formation of eruptive xanthomas (red-yellow papules) especially on the buttocks (Baron, 2002: 1255). In some patients, the first symptom of dyslipidemia is usually a heart attack or stroke (Schneider, 2002: 2). Berger and Marais, (2000:166) recommended that the following people be routinely screened to obtain a fasting lipoprotein profile (refer to paragraph 2.12):

- Men over the age of forty.
- Women over the age of fifty.
- Patients with clinical evidence of coronary artery disease, peripheral vascular disease, carotid atherosclerosis, diabetes mellitus, xanthoma or other stigma of dyslipidemia.
- Patients with a family history of dyslipidemia or coronary artery disease.

The complications for dyslipidemia include the following conditions: transient ischaemic attack (TIA), angina pectoris or abdominal pain (Bhatnagar, 1998: 213), however, dyslipidemia manifests to atherosclerosis (Schneider, 2002:2) refer to paragraph 2.14.

The **eighth research objective** was to describe the treatment protocols and the drugs that are used in the management of dyslipidemia. As described in paragraph 2.16.2, the main purpose of treating people with dyslipidemia is to reduce the risk of coronary artery disease, peripheral vascular disease and acute pancreatitis (Bhatnagar, 1998: 213). That can be achieved through lifestyle modification (advantageous in all patients) and the use of appropriate lipid-lowering

drugs (particularly in patients at high risk for cardiovascular diseases). The main targets of life style modification are a healthy diet, regular aerobic exercise, loss of weight and quitting smoking (Berger & Marais, 2000: 171). This usually lasts up to 3 to 6 months (Anaizi, 1997: 6). At initiation of therapeutic lifestyle changes, the patient is instructed to reduce saturated fat and dietary cholesterol (Griffith, 2001: 2). Pharmacological therapy may be initiated in patients with severe coronary heart disease due to severe dyslipidemia that is not likely to be corrected by diet and other lifestyle modification (Anaizi, 1997: 6) (refer to paragraph 2.16.5). The decision to use such therapy must be based on the specific metabolic defects and their potential for causing atherosclerosis or pancreatitis (Malloy & Kane, 1998: 570). Drug treatment agents that are available for dyslipidemia in South Africa according to the MIMS™ are fibrates, e.g. bezafibrates (e.g. Bezalip retard 400mg®), fenofibrate (Lipsin 300mg®), gemfibrozil (Lopid 600mg®); HMG-CoA reductase inhibitors, e.g. fluvastatin (e.g. Lescol 20mg®), atorvastatin (e.g. Lipitor 10mg®), pravastatin (e.g. Prava 10mg®) and simvastatin (e.g. Zocor 10mg®); other hypolipidemic drugs, e.g. acipimox (Olbetam®), probucol (Lurselle®), cholestyramine (Questran lite®), essential phospholipids (Lipostabil 5ml®) and nicotinic acid.

The **ninth research objective** was to determine the relationship between dyslipidemia and other diseases such as hypertension, cardiovascular heart disease and diabetes.

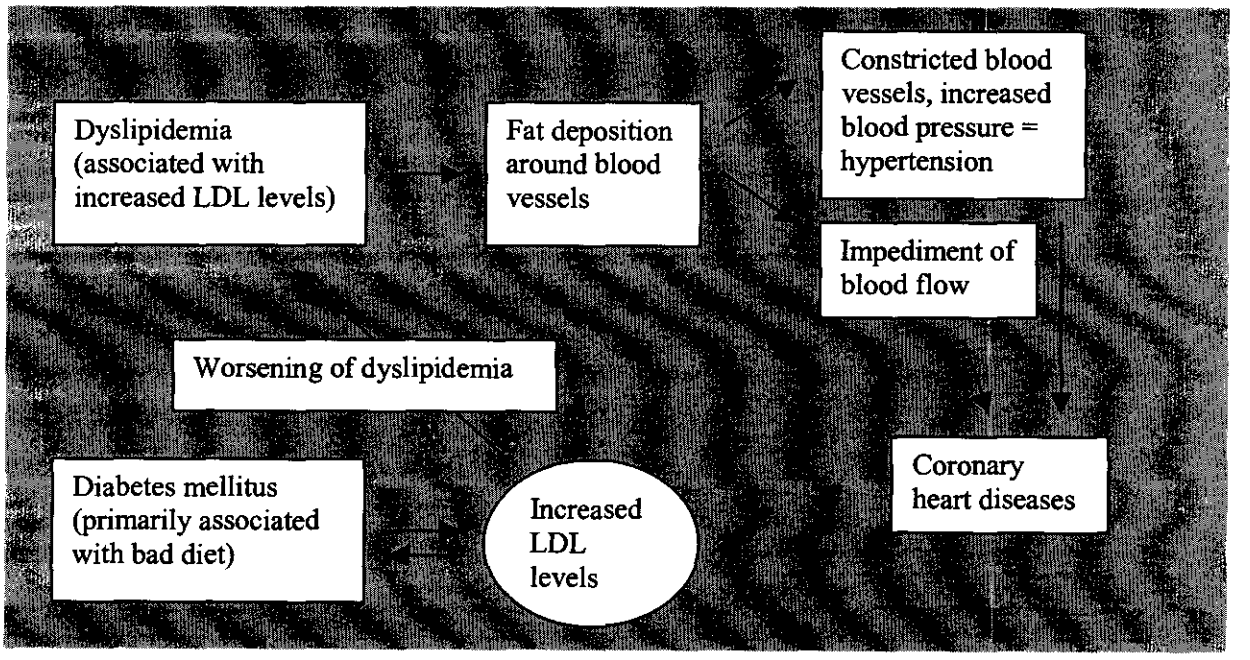


Figure 6.1 Relationships between dyslipidemia and other diseases such as hypertension, cardiovascular heart disease and diabetes

As depicted in figure 6.1 and described in paragraph 2.9.2, dyslipidemia, hypertension and diabetes are risk factors for coronary artery disease. These diseases need to be controlled in order to reduce coronary heart disease mortality and morbidity.

The **tenth research objective** was to describe the concept of managed pharmaceutical care. To have a clear understanding of the concept of managed pharmaceutical care, the concept of pharmaceutical care must first be explained. Mortality and morbidity due to drug consumption gradually increased in the United States (Bootman, 1995: 2). Pharmaceutical care evolved as a process, which had the ability to identify, resolve and prevent potential and actual drug-related problems (Hepler & Strand, 1990: 539), by establishing a philosophy of practice (pharmaceutical care, refer to paragraph 3.4) and an organisational structure to support this philosophy (pharmaceutical care system, see paragraph 3.4.6) (Plumridge & Wojnar-Horton, 1998: 177). A pharmaceutical care system is the system that ensures that pharmacists take responsibility for monitoring the unwanted drug effects and take initiatives in resolving drug-related problems before they manifest to become drug-related morbidities (Segal, 1996: 195). Pharmaceutical care means different things to different people, and there are several definitions internationally (Mason, 2000: 854). Depending on the time and the country of origin, different definitions of pharmaceutical care are being used (Van Mil *et al.*, 1999: 202). Mikael *et al.*, (1975: 567) were the first to describe pharmaceutical care as "*the care that a given patient requires and receives which assures safe and rational drug usage*". Pharmaceutical care was later defined as "*the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve patient's quality of life*" (Hepler & Strand, 1990: 539). Pharmaceutical care as an important element of health care should be intertwined with other elements such as managed care and disease management (Van Mil *et al.*, 1999: 203), hence managed pharmaceutical care evolved. Managed pharmaceutical care is described according to MacKeigan and Larson, (1988: 49) as the aspects of managed care that can be undertaken in the pharmacy to improve the patient's quality of care and to control health care resource utilisation that has not been extensively addressed before. Managed pharmaceutical care is aimed at identifying, preventing and resolving medicine-related problems in a cost-effective manner (Serfontein, 1998:1).

The **eleventh research objective** was to investigate the application of managed pharmaceutical care principles in the management of dyslipidemia. Paragraph 3.4.7 describes pharmaceutical care practice. Pharmaceutical care practice is defined by Cipolle *et al.* (1998: 28) as the practice in which the practitioner takes responsibility for the patient's drug-related needs and is held accountable for this commitment. Pharmaceutical care practice is defined by its foundation philosophy, dedicated to a patient care process with its responsibilities, and holding all practitioner interventions through its practice management system. The patient care process is the rational, organised, comprehensive, problem solving process that allows thorough and consistent provision of quality care to the patient (Cipolle *et al.*, 1998: 121-123). As part of the

patient care process, the pharmacist plays an important role in cholesterol management (Irons *et al.*, 2002: 1622) because management of dyslipidemia is a critical component of care for patients with existing cardiovascular diseases (Patel & Perez, 2001:12s). The pharmacist contributes to patient care by developing treatment algorithms that target cost-effective therapy and extend the benefit of lipid-lowering drugs to greater percentage of appropriate patients (patients requiring therapy) (Lopez, 2002:1177). In addition to the above roles, the pharmacist's role in the management of dyslipidemia includes assessment for drug interactions and suitable drug regimens, provision of education to patient and practitioner, screening for dyslipidemia as well as pharmacological management with lipid lowering drugs (Irons *et al.*, 2002: 1622). Pharmaceutical care starts with the assessment of the patient's drug-related needs. As described in paragraph 3.4.8.1, for patients with dyslipidemia, the practitioner assesses the physical activity as well as diet of the patients (Dambro, 1999: 513). Given the asymptomatic nature of dyslipidemia, the health care team initiates early screening of predisposed or high-risk patients to prevent complications (Irons *et al.*, 2002: 1622). Once therapy begins, the pharmacists communicate regularly with the patient's physician to provide early intervention (Irons *et al.*, 2002: 1622) and then assess problems that may arise due to the administration of hypolipidemic drugs (Dambro, 1999: 513). In addition to the above, intervention may include treatment algorithms (physicians are provided with specific guidelines to determine the best treatment algorithm for patients with mild, moderate and severe dyslipidemia). The last plan of the patient care process is the follow-up evaluation to determine the patient's actual outcomes. For dyslipidemic patients, patient monitoring is performed while the patient is on medication. Cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides and liver enzymes are monitored every 6 weeks until the goal low-density lipoprotein cholesterol level has been reached, then every 6 months for patients on statins and niacin. If the cholesterol level is below 200 mg/dl, (5.2 mmol/l) follow-up is repeated in 5 years (Dambro, 1999: 513).

The **twelfth research objective** was to investigate the application of pharmaco-economic principles in the management of dyslipidemia. As described in paragraph 3.8.1, pharmacological therapy becomes a successful and cost-effective practice when medicines are rationally prescribed and appropriately utilised. However, when these fundamentals are not met, patients are denied the full benefits of therapy and that will result in an increase in cost of an overburdened health care system (Munroe *et al.*, 1997: 114). The treatment of coronary heart diseases places a substantial financial burden on health care resources (McMurray, 1999: 2). This is because the cost of coronary heart disease is the sum of three components (Larson, 1996: 46):

- The medical resources used to treat the illness.
- The nonmedical resources associated with it.
- Lost productivity due to illness

As a result, pharmaco-economic analysis of the management as well as impediment strategies for coronary heart diseases is a valuable tool for comparing the cost-effectiveness of new medical interventions allowing health care decision makers to contain cost by choosing those interventions that are most efficient (McMurray, 1999: 2). This is imperative especially because intervention by means of drugs in the case of lowering cholesterol levels involves a large population of patients and potentially high costs (Johannesson *et al.,* 1997: 332). The following pharmaco-economic study has been applied in patients with dyslipidemia. A cost minimisation study that estimated the benefits of lowering cholesterol using data from the 4S study (Scandinavian Simvastatin Survival Study*) was conducted, and it was found that simvastatin therapy produced a 10% decrease in length of hospital stay, a 26% reduction in number of hospitalisation, a 31% reduction in hospital costs and a 34% reduction in total hospital days. As a result of these savings, though not in South Africa, the cost of simvastatin was reduced (Pedersen *et al.,* 1996: 1796). Hilleman *et al.,* (1999: 536-562) conducted a study called "*A population - based treat - to - target pharmacoeconomic analysis of HMG-CoA reductase inhibitors in hypercholesterolaemia*". It was found that the most cost-effective treatment approach was to individualise the selection of statins based on coronary risk and it was further stated that atorvastatin and fluvastatin be available in the national formulary (refer to paragraph 3.8.7). Ballesteros *et al.* (2001: 516) investigated the economic cost generated in one year in primary care because of inadequate (unnecessary) prescriptions of hypolipidemic agents. It was found that the cost of inadequate prescription for hypolipidemic drugs reached 1166480.60 US dollars (1997 values) for quality level one (patients whose age, risk factors, total cholesterol level and low-density lipoprotein cholesterol level were known before pharmacological intervention) and 37893.37 US dollars for level two (patients whose low-density lipoprotein levels and diet were unknown before pharmacological intervention). It was also found that 12.3% of the health professionals ordered all their prescriptions inadequately. Of the total inadequate prescriptions expenditure, 20.4% represented treatment initiated by family physicians and 35.3% by specialists. Statins made up 78.2% of the total cost; the inadequate expenditure for this therapeutic group reached 88797 US dollars. Of the prescriptions for fibrates, 88% were inadequate (Ballesteros *et al.*, 2001:513).

* Refer to glossary

The **thirteenth research objective** was to investigate the application of pharmaco-epidemiological principles in the management of dyslipidemia. Epidemiology was described in paragraph 3.7.1 as the study of the occurrence and transmission of diseases in human population (Waning & Montagne, 2001:1&2). Due to growing concern on the frequency and preventability of drug-induced illnesses, pharmaco-epidemiology has emerged (Anon, 2003 (c): 1). Pharmaco-epidemiology is defined according to Chauvin *et al.* (2002: 455) as "*the application of epidemiological reasoning, methods and knowledge to the study of the uses and effects (beneficial and adverse) of drugs within a large consumer population*". Some pharmaco-epidemiological studies have been used in patients with dyslipidemia. Eaton *et al,* (2002: 1389) quantified the effect of statins on 1-year mortality, hospitalisations and decline in physical functions among patients with cardiovascular diseases aged 65 and older in nursing homes. It was found in that retrospective cohort study that the prevalence of statins was 2.6%. Statin use was varied according to gender, age, comorbid condition, medication use, and cognitive and physical function. It was concluded that statin therapy improved clinical outcomes; including reduction in 1-year all cause mortality. Statin therapy also decreased death and hospitalisation in the older population with cardiovascular diseases. Thus pharmaco-epidemiological studies evolved as an imperative tool to determine the utilisation of drugs amongst people of varied age groups. Pharmoco-epidemiological studies can also be used to determine the prescribing practices of hypolipidemic drugs.

The **fourteenth research objective** was to investigate the application of drug utilisation principles in the management of dyslipidemia. Drug utilisation review has emerged in response to the needs to control both cost and the quality of medication usage (Chriscilles *et al.,* 1996: 172). The principal aim of drug utilisation research is to facilitate the rational use of drugs in populations (WHO, 2003: 9) and at the same time reducing needless expenditure and improving the quality of care (Chriscilles *et al.,* 1996: 172). That is achieved through the detection of drug interactions, contraindications, overdoses, over-utilisation and under-utilisation (Monane, *et al.,* 1998: 2). One of the drug utilisation studies was conducted by Savoie and Kazanjian (2001: 95-100). Savoie and Kazanjian (2001: 95- 100) applied pharmaco-epidemiological principles to study the utilisation of lipid-lowering agents in men and women. The results of this study indicated that, 74.7% of individuals on statins had no reported history of coronary heart disease. Women without coronary heart disease formed 23.1% of statins recipients and were aged 70 and over.

The **fifteenth research objective** was to investigate the differences in the utilisation patterns of drugs in general before and after implementation of the Medscheme® price list. It was found that the total number of all medicine items claimed a year before implementation of the Medscheme® price list amounted to 21820911 as compared to 27277825 which was claimed a year after the implementation of the Medscheme® price list. This resulted in a 25.01% increase in the total number of medicine items claimed. On the other hand, the total number of prescriptions increased from 11060996 during the first study year to 14347442 during the second study year. Although there was an increase in the total number of medicine items claimed between the first and the second years, there were no practically significant differences between the average numbers of medicine items claimed per prescription between the different four-month periods ($d < 0.8$). The results further revealed that there was no difference of practical significance between the average costs of medicine items claimed per prescription for the different four-month periods ($d < 0.8$). A similar trend was observed for the average cost per medicine item (refer to paragraph 5.5.1). The results further revealed that there was a decrease in utilisation of innovator medicine items from the first study year to the second study year. Innovator medicine items accounted for 73.4 % (n=21820911) and 68.92% (n=27277825) of the total number of all medicine items claimed during the first and second study years respectively. Generic prescribing on the other hand increased from 26.60% (n=21820911) to 31.08% (n=27277825) of the total number of all medicine items claimed during the first and second study years respectively (refer to paragraph 5.5.2).

The **sixteenth research objective** was to investigate the differences in the utilisation patterns of hypolipidemic drugs before and after implementation of the Medscheme® price list. It was found that hypolipidemic drugs constituted 2.70% (n = 21820911) and 2.78% (n =27277825) of the total number of all medicine items claimed during the first study year and the second study year respectively. This shows that there was a 0.08% difference in utilisation patterns of hypolipidemic drugs according to prevalence for the two study years. The average number of all hypolipidemic drugs claimed per prescription stayed the same for all study periods and as a result, the d-value of 0.00 was obtained between the different study periods. Statins were the hypolipidemic drugs most frequently utilised and accounted for 95.77% (n=589036) to 96.26% (n=759675) of the total number of hypolipidemic drugs prescribed in the first and second study years respectively. In the pharmacological group: hypolipidemic drugs, fibrates were rated the second–highest prescribed drugs and accounted for 2.93% (n=589036) and 2.78% (n=759675) of the total number of hypolipidemic drugs prescribed during the first and second study years respectively. On the other hand, "others" accounted for 1.28% (n=589036) and 0.95%

(n=759675) of the total number of hypolipidemic drugs claimed during the first and second study years respectively. The medicine items containing atorvastatin as an active ingredient had the highest rate of prescriptions of the hypolipidemic drugs according to both prevalence and cost. They accounted for 66.78% (n=589036) and 69.00% (n=759675) of the total number of all hypolipidemic drugs and 1.80% (n=21820911) and 1.92% (n=27277825) of the total number of all medicine items claimed during the first and second study years respectively. Lipitor 10mg® was the top prescribed drug of the hypolipidemic drugs (according to both prevalence and cost) and of the total number of all medicine items (according to prevalence) claimed during the first and second study years (refer to paragraph 5.8.2.1.1).

The **seventeenth research objective** was to determine the effect of the Medscheme® Price List (MPL) on the cost of hypolipidemic drugs. As discussed in chapter 5, it was found that the cost percentage of hypolipidemic drugs slightly decreased from the year before the implementation of MPL to the year after the implementation of the MPL. The total cost of all hypolipidemic drugs claimed during the first study year constituted 6.33% (n= R3 097 604 602) of the total cost of all medicine items claimed whereas during the second study year the total cost of hypolipidemic drugs accounted for 6.23 % (n= R 4 053 280 295) of the total cost of all medicine items claimed. The average cost per hypolipidemic drug increased from P1 to P3 during the first study year and during the second study year it decreased from P4 to P6 (refer to paragraph 5.6.2). There was a 0.1% difference in cost percentage of hypolipidemic drugs for the two study years. In actual terms, the cost difference could have been brought about by many factors (e.g. the introduction of new generic hypolipidemic drugs on the market during the second study year) and it can therefore not be safely concluded that the MPL had a positive effect (cost reduction) on the total cost of hypolipidemic drugs. More than 95% of the total cost of hypolipidemic drugs ((n =R 196 076 050 (first study year) and (n=R 252 919 285 (second study year)) was allocated to statins during both study years. As shown in tables 5.28 and 5.29, there was a slight increase in cost percentage of statins from the first (96.28%) to the second (96.57) study year. The total cost of fibrates accounted for 2.94% and 2.94% while, the total cost of "others" accounted for 0.78% and 0.49% of the total cost of all hypolipidemic drugs claimed during the first (n =R 196 076 050) and the second (n=R 252 919 285) study years respectively (refer to paragraph 5.7). Lipitor 10mg® was the top prescribed drug of the hypolipidemic drugs according to cost for the two study years. It accounted for 47.87% (n=R 196 076 050) and 51.67% (n=R 252 919 285) of the total cost of hypolipidemic drugs claimed during the first and second study years respectively.

The **eighteenth research objective** was to determine and compare the difference in prevalence of innovator products vs. generic products that were claimed before and after implementation of the Medscheme® Price List for drugs in general and hypolipidemic drugs specifically. For the general data it was found that the total number of innovator products claimed during the first study year was 73.47% (n=21820911) compared to 68.92% (n=27277825) claimed during the second study year. Generic prescribing on the other hand increased from 26.53% (n=21820911) to 31.08% (n=27277825) during the first study year to the second study year correspondingly. From these figures it can be concluded that the implementation of MPL might have a positive effect (increment) on utilisation of all medicine items according to generic medicine items. For the hypolipidemic drugs, it was found that the prevalence of generic drugs accounted for 0.89% (n=589036) during the first study year compared to 4.88% (n=759675) during the second study year. Innovator drugs on the other hand constituted 99.11% (n=589036) and 95.11% (n=759675) of the total number of hypolipidemic drugs for the first and second study years respectively. It should be noted that generic bezafibrate was the only generic hypolipedimic drug available in the Republic of South Africa during the first study year. During the second study year, generic fibrates (Rolab-bezafibrate 400mg®) accounted for 1.37% whereas generic simvastatin (Adco-simvastatin, 10mg®, Adco-simvastatin 20mg® and Adco-simvastatin 40mg®), accounted for 3.51% of the total number of hypolipidemic drugs claimed. In this case it cannot be assumed that the implementation of MPL was accompanied by an increased utilisation of generic drugs as the introduction of new generic hypolipidemic drugs (Adco-simvastatin 10mg®, Adco-simvastatin 20mg® and Adco-simvastatin 40mg®) was witnessed in the market during the second study year.

The **nineteenth research objective** was to determine the difference in cost between the innovator and the generic drugs for both the general data and hypolipidemic drugs. For the general data it was found that the total cost of generic drugs accounted for 13.26% (n=R 3 097 064 602) of the total cost of all medicine items claimed during the first study year and 15.86% (n=R 4 053 280 295) of the total cost of all medicine items claimed during the second study year. On the other hand, the total cost of innovator drugs accounted for 86.74% (n=R 3 097 064 602) of the total cost of all medicine items claimed during the first study year to 84.14% (n=R 4 053 280 295) of the total cost of all medicine items claimed during the second study year. For hypolipidemic drugs, it was found that the total cost of generic drugs accounted for 0.60% and 2.94%, and the total cost of innovator drugs accounted for 99.40% and 97.06% of the total cost of hypolipidemic drugs claimed during the first (n=R 196 076 050) and second (n=R 252 919 285) study years respectively. It should be noted that generic bezafibrate was the only generic

hypolipidemic drug available in the Republic of South Africa during the first study year. During the second study year, generic fibrates (Rolab-bezafibrate 400mg®) accounted for 1.11% whereas generic simvastatin (Adco-simvastatin, 10mg®, Adco-simvastatin 20mg® and Adco-simvastatin 40mg®), accounted for 1.94% of the total cost of hypolipidemic drugs claimed. The average cost of innovator drugs was 2.3 times higher than the average cost of generic drugs during the two study years for the general data. Although there was a decrease in cost percentages of innovator drugs, it can still be concluded that the cost of innovator drugs was higher than the cost of generic drugs for all study years for both the general data and the hypolipidemic drugs.

The **twentieth research objective** was to determine the cost savings that could have been incurred if hypolipidemic drugs had been sold at MPL prices. The following table shows the summary of the cost differences (total cost subtract the MPL calculated cost as discussed in chapter 5) between medicine items that were on the MPL.

Table 6.1 Summary of the cost differences between medicine items that were on the MPL

Innovator bezafibrate (Bezalip retard 400mg®)	119 341.3
Generic bezafibrate (Rolab-bezafibrate 400mg®)	(-) 23 694.5
Innovator simvastatin (All Zocors)	3 609 784.67
Generic simvastatin (All Adco-simvastatins)	(-) 603 277.36

(-) Cost savings

As described in chapter 5, the utilisation of generic medicines resulted in little or no patient co-payment. The above table shows that R23 694.5 and R603 277.36 could have been saved for generic bezafibrate and generic simvastatin respectively if they had been sold at MPL prices. There was no probability of cost savings due to utilisation of innovator drugs (refer to paragraph 5.8.1.1.4). If therapeutic substitution were an option, then some of the atorvastain could have been therapeutically subsbstituted with generic simvastatin. This could have brought further cost reduction of hypolipidemic drugs. However, as described in paragraph 5.8.2.1.1, Raal (2004: 120) found that there was a worsening trend in total cholesterol in patients switched from atorvastatin to simvastatin, and based on that, therapeutic substitution is not an option.

The **twenty-first research objective** was to determine the cost savings that could have been incurred if generic medicine items were prescribed instead of innovator products (provided that the patent time on the original drug has expired). For example, if 50% of all medicine items claimed were sold at generic prices R465 664 331.5 (0.5*total number of all medicine items per study year = (answer a), answer a – (total number of generic medicine items per study year = answer b), answer b*cost per unit of generic medicine items per study year) and R391304176.8 could have been saved for the first and second study years for general data (refer to paragraph 5.5.2 for the total number of all medicine items claimed as well as the total number of innovator medicine items and total number of generic medicine items claimed during the first and second study years). For hypolipidemic drugs, R64 910 165.5 and R68 623 507.91 could have been saved for the first and second study years respectively if 50% of innovator hypolipidemic drugs had been substituted with generic hypolipidemic drugs (refer to paragraph 5.6.3 for the total number of all hypolipidemic drugs claimed as well as the total number of innovator hypolipidemic drugs and total number of generic hypolipidemic drugs claimed during the first and second study years).

The **twenty-second research objective** was to compare the prescribed daily dose with the defined daily dose of individual hypolipidemic drugs. As discussed in chapter 5 it was found that most of the prescriptions for individual hypolipidemic drugs did not conform to the defined daily dose. It was, however, found that most prescription whose prescribed daily dose was for one tablet once daily and whose strength was similar to the defined daily dose conformed to the defined daily dose. In South Africa most prescriptions were prescribed according to the monthly index of the medical specialty rather than the defined daily dose (DDD) set by the World Health Organization. Below is the summary of the average prescribed daily doses (PDD) of individual hypolipidemic drugs.

Table 6.2 Summary of the average prescribed daily doses of individual hypolipidemic drugs during both study years.

Active ingredient	Trade name	Average PDD [illegible]	Average PDD [illegible]	Prescribed DD [illegible]
Cerivastatin	Baycol 0.1mg®	0.07mg		0.2mg
	Baycol 0.2mg®	0.18mg		
	Baycol 0.3mg®	0.22mg		
	Baycol 0.4mg®	0.36mg		
Bezafibrate	Bezalip 200mg®	0.35g	0.31g	0.6g
	Bezalip retard 400mg®	0.37g	0.31g	
	Rolab bezafibrate 400mg®	0.37g	0.38	
Fluvastatin	Lescol 20mg®	18.34mg	16.77mg	40mg
	Lescol 40mg®	36.43mg	32.29mg	
	Lescol XL 80mg®		61.78mg	
Atorvastatin	Lipitor 10mg®	9.03mg	11.01mg	10mg
	Lipitor 20mg®	23.22mg	17.76mg	
	Lipitor 40mg®	38.12mg	32.56mg	
Fenofibrate	Lipsin 300mg®	0.38g	0.30g	0.2g
Gemfibrozil	Lopid 600mg®	0.83g	0.80g	1.2g
Nicotinic acid	Nicotinic acid 30mg®	0.33g	0.11g	2g
	Nicotinic acid BT®	0.81g	1.01g	
Acipimox	Olbetam 250mg®	0.65g	0.56g	0.5g
Pravastatin	Prava 10mg®	8.00mg	7.69mg	20mg
	Prava 20mg®	15.96mg	15.10mg	
	Prava 40mg®	26.31mg	22.40mg	
Cholestyramine	Questran lite®	3.72g	3.77g	14g
Simvastatin	Adco-simvastatin 10mg®		9.18mg	15mg
	Adco-simvastatin 20mg®		16.67mg	
	Adco-simvastatin 40mg®		31.08mg	
	Zocor 10mg®	10.65mg	11.23mg	
	Zocor 20mg®	17.68mg	13.81mg	
	Zocor 40mg®	26.93mg	31.77mg	

6.3 LIMITATIONS AND SHORTCOMINGS OF THIS STUDY

The following limitations and shortcomings should be borne in mind when the results and conclusions of this study are evaluated:

- All data entered on the database after data refinement were considered precise and correct.
- All medicine items and prices on the database were considered to be correctly submitted.
- The database did not contain information on the diagnosis of patients, patients' history, their low-density lipoprotein cholesterol, total cholesterol and high-density lipoprotein levels a year before and a year after the implementation of the MPL. The conclusion

drawn from the seventeenth research objective indicated that there was a slight decrease in cost of hypolipidemic drugs but due to a lack of patient information, the relationship between cost reduction and improved or maintained quality of life cannot be drawn.

- The cost-prevalence index is only limited to cost and does not provide information on the patient's clinical outcomes.

6.4 RECOMMENDATIONS

The following recommendations can be made after analysis of the database with the aim of improving the management of dyslipidemia in a private health care setting:

- Cholesterol-related diseases are a leading cause of death worldwide (refer to paragraph 1.1). Due to the fact that most South Africans are unaware of their high cholesterol levels (refer to paragraph 2.2), it is recommended that a national cholesterol education programme be developed to promote public health awareness of cholesterol-related diseases.
- As discussed in paragraph 5.6.1.1 hypolipidemic drugs are relatively expensive compared to some of the drugs of the cardiovascular system. Due to that, it is recommended that capitation payment method (refer to paragraph 3.4.12) be used to control and manage dyslipidemia.
- Atorvastatin is the hypolipidemic drug that reduces LDL levels to a greater extent than any other hypolipidemic drug (refer to Table 2.11) and it is well tolerated (refer to paragraph 2.16.5.4.2). It is recommended that newly diagnosed patients be given atorvastatin as a starting drug of choice (provided that diet therapy did not achieve target LDL levels).

The following recommendation can be made for further research on issues not investigated in this study:

- The database had no clinical data; it is recommended that further studies be conducted on the cost-effectiveness of individual hypolipidemic drugs. Those studies must be able to indicate the best therapy per rand spent.
- Further studies must be conducted to determine on the impact of MPL on drug prices. Such studies must be conducted for at least a period of ten years (five years before the implementation of the MPL and five years after the implementation of the MPL) to enhance the reliability and validity of the results.

- LDL reduction is a necessity for achieving cholesterol target levels. Further studies should be conducted to answer the question of how low the cholesterol level should be. Those studies might give information on whether too much reduction of LDL could result in the formation of "hypolipidemia".

6.5 CHAPTER SUMMARY

It was in this chapter that the conclusions of this research were drawn. The limitations and shortcomings of this study as well as the recommendations for the management of dyslipdemia were discussed in this chapter.

Hereby the research questions have been answered and their research objectives reached.

GLOSSARY

CHOLESTEROL is a substance in animal tissue that is an essential component of cell membranes and nerve fiber insulation. Cholesterol is important for the metabolism and transport of fatty acids and in the production of hormones and Vitamin D. Cholesterol is manufactured by the liver, and is also present in certain foods (e.g., eggs, shellfish).

CONSUMER PRICE INDEX (CPI) is a series of figures (numbers) showing how the average price level of goods and services bought by a typical consumer or household changes over time (Statistics South Africa, 2002: 1). It measures how the price level of consumer goods and services changes between two periods of time. This index is used to calculate the official rate of inflation and consists of price increase for all goods and services in the main metropolitan areas of the country (South Africa, 2002: 58)

COST SAVING PERCENTAGE as calculated in this study is the percentage of expenditure that could have been saved if a certain percentage of innovator products are substituted with generic products of equal therapeutic effectiveness.

DEFINED DAILY DOSE is the assumed average maintenance dose per day for a drug used for its main indication in adults.

DESIGNATED SERVICE PROVIDER is a health care provider or group of providers selected by the medical scheme concerned as the preferred provider or providers to provide its members diagnosis, treatment and car in respect of one or more prescribed minimum benefit condition

DYSLIPIDEMIA is defined as the clinically significant modification in the circulating lipids and lipoprotein predisposing to coronary heart disease and related disorders.

GROSS DOMESTIC PRODUCT (GDP) is the measure of the value of total goods and services produced nationally over a given period of time.

HMG-CoA in this study means 3-hydroxy-3-methylglutaryl-coenzyme A

INDIVIDUAL CLINICAL EXPERTISE means the proficiency and judgement that individual clinician acquire through clinical experience and clinical practice

INFLATION RATE is the annual percentage change in the CPI (Statistics South Africa, 2002: 1).

MANAGED HEALTH CARE means clinical and financial risk assessment and management of health care, with a view to facilitating appropriateness and cost-effectiveness of relevant health services within the constraints of what is affordable, through the use of rules based and clinical management-based program

MANAGED HEALTH CARE ORGANIZATION means a person who has made contract with the medical scheme to provide managed health care services

MEDSHEME® PRICE LIST (MPL) is a reference pricing system that allocates a ceiling price to a group of drugs, which are similar in terms of efficacy, safety and quality. Most of the drugs will be generic equivalents (for example the same active ingredient but different formulation. The objective of MPL is to ensure that at least one product in each MPL group will be fully reimbursed based on the recommended retail price. This will avoid patient co-payment for at least one drug.

MIMS refers to monthly index of medical specialities

PRESCRIBED MINIMUM BENEFIT means the scope of level of benefits that are available to beneficiaries as prescribed by the Medical schemes Act (131/1998).

PRESCRIBED DAILY DOSE is the average daily amount of a drug that is actually prescribed

SCANDINAVIAN SIMVASTATIN SURVIVAL STUDY (4S) is a randomized trial of cholesterol lowering in 4444 patients with coronary heart disease (CHD). The trial was designed to evaluate the effect of cholesterol lowering with simvastatin on morbidity and mortality in patients with CHD. It was found that there were 189 coronary deaths in the placebo group and 111 in the simvastatin group. The benefit of treatment included 37% reduction in the risk of undergoing myocardial revascularization. It was then concluded that long-term treatment with simvastatin is safe and improves survival in CHD patients.

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APPENDIX A

Table A.1 Total number of all medicine items claimed per month from May 2001 to April 2002

Month		Innovator medicine items	Generic medicine items	Medicine items
May 2001	P	1137441	386855	1524296
	%*	74.62	25.38	100
Jun 2001	P	913491	317263	1230754
	%*	74.22	25.78	100
Jul 2001	P	935998	330103	1266101
	%*	73.93	26.07	100
Aug 2001	P	1487472	527526	2014998
	%*	73.82	26.18	100
Sep 2001	P	1277418	74.18	1722109
	%*	444691	25.82	100
Oct 2001	P	1264403	443765	1708168
	%*	74.02	25.98	100
Nov 2001	P	1033791	366662	1400453
	%*	73.82	26.18	100
Dec 2001	P	1182315	414466	1596781
	%*	74.04	25.96	100
Jan 2002	P	1684564	627315	2311879
	%*	72.87	27.13	100
Feb 2002	P	1630700	607076	2237776
	%*	72.87	27.13	100
Mar 2002	P	1712506	647767	2360273
	%*	72.56	27.44	100
Apr 2002	P	1770895	676428	2447323
	%*	72.36	27.64	100

*% Innovator is the total number of innovator medicine items claimed for the specific month divided by the total number of all medicine items claimed for that month.

*% Generic is the total number of generic medicine items claimed for the specific month divided by the total number of all medicine items claimed for that month.

P is the prevalence of either the generic or innovator medicine items claimed for the specific month

Table A.2 Total number of all medicine items claimed per month from May 2002 to April 2003

Month		Innovator medicine items	Generic medicine items	Medicine items
May 2002	P	870266	359115	1229381
	%*	70.79	29.21	100
Jun 2002	P	1679268	706172	2385440
	%*	70.40	29.60	100
Jul 2002	P	1707375	732673	2440048
	%*	69.97	30.03	100
Aug 2002	P	1682257	744987	2427244
	%*	69.31	30.69	100
Sep 2002	P	1450748	648065	2098813
	%*	69.12	30.88	100
Oct 2002	P	1481572	668316	214988
	%*	68.91	31.09	100
Nov 2002	P	1373390	610075	1986435
	%*	69.24	30.76	100
Dec 2002	P	1306602	575191	1881793
	%*	69.43	30.57	100
Jan 2003	P	1646785	78770	2434555
	%*	67.64	32.36	100
Feb 2003	P	1501304	727495	2228799
	%*	67.36	32.64	100
Mar 2003	P	1632647	781547	2414194
	%*	67.63	32.37	100
Apr 2003	P	1558530	751486	2310016
	%*	67.47	32.53	100

*% Innovator is the total number of innovator medicine items claimed for the specific month divided by the total number of all medicine items claimed for that month.

*% Generic is the total number of generic medicine items claimed for the specific month divided by the total number of all medicine items claimed for that month.

P is the prevalence of either the generic or innovator medicine items claimed for the specific month

Table A.3 Average number of medicine items claimed per prescription from May 2001 to April 2002

Months	Total no. of prescriptions	Average number	Standard deviation	Minimum	Maximum	Total no. of drugs
May 2001	740708.00	2.06	1.26	1.00	19.00	1524296
Jun 2001	595871	2.07	1.26	1.00	16.00	1230754
Jul 2001	616329	2.05	1.26	1.00	19.00	1266101
Aug 2001	998795	2.02	1.23	1.00	15.00	2014998
Sep 2001	872305	1.97	1.22	1.00	20.00	1722109
Oct 2001	885892	1.93	1.20	1.00	20.00	1708168
Nov 2001	724293	1.93	1.20	1.00	20.00	1400453
Dec 2001	812710	1.96	1.21	1.00	16.00	1596781
Jan 2002	1187338	1.95	1.21	1.00	15.00	2311879
Feb 2002	1148370	1.95	1.20	1.00	19.00	2237776
Mar 2002	1217185	1.94	1.20	1.00	15.00	2360273
Apr 2002	1261200	1.94	1.20	1.00	16.00	2447323

Table A.4 Average number of medicine items claimed per prescription from May 2002 to April 2003

Months	Total no.of prescriptions	Average number	Standard deviation	Minimum	Maximum	Total no. of drugs
May 2002	650519	1.89	1.15	1.00	15.00	1229381
Jun 2002	1211046	1.97	1.20	1.00	15.00	2385440
Jul 2002	1257723	1.94	1.18	1.00	15.00	2440048
Aug 2002	1260648	1.93	1.16	1.00	17.00	2427244
Sep 2002	1107865	1.89	1.15	1.00	17.00	2098813
Oct 2002	1146070	1.88	1.13	1.00	17.00	2149888
Nov 2002	1058583	1.87	1.13	1.00	16.00	1983465
Dec 2002	997993	1.89	1.14	1.00	20.00	1881793
Jan 2003	1304379	1.87	1.14	1.00	15.00	2434555
Feb 2003	1188840	1.87	1.13	1.00	16.00	2228799
Mar 2003	1289640	1.87	1.13	1.00	18.00	2414253
Apr 2003	1233177	1.87	1.12	1.00	16.00	2310016

Table A.5 Top ten medicine items claimed from May 2001 to October 2001

Drug description	May 2001		Jun 2001		Jul 2001		Aug 2001		Sep 2001		Oct 2001	
	P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
Alcophylex syrup®	10373(5)	0.68	8681(4)	0.71	9320(4)	0.74	13091(6)	0.65	8150(10)	0.47		
Amiloretic teblets®												
Augmaxil 375mg®	7370(10)	0.48	6322(10)	0.51	6585(10)	0.52						
Corenza C tablets®												
Coversyl tablets®									8794(9)	0.51	8875(9)	0.52
Dapamax 2.5mg®	7531(9)	0.49	6531(9)	0.53	7004(9)	0.55	10296(9)	0.51	10148(7)	0.59	10366(6)	0.61
Dispirin cv 100mg®												
Ecotrin 81mg®								0.48	9647(8)	0.56	9996(7)	0.59
Eltroxin® 0.1mg	13015(3)	0.85	10376(3)	0.84	11323(3)	0.89	18942(3)	0.94	18379(3)	1.07	18543(3)	1.09
Flixonase Aques®	9327(7)	0.61	7398(7)	0.60	7388(8)	0.58	11794(7)	0.59	11049(5)	0.64	10706(5)	0.63
Lipitor 10mg®	15718(2)	1.03	12951(2)	1.05	14112(2)	1.11	24407(2)	1.21	24896(1)	1.45	26127(1)	1.53
Mybulen tablets®							9910(10)	0.49				
Mypaid capsules®											8472(10)	0.50
Myprodol capsules®	23856(1)	1.57	18936(1)	1.54	20574(1)	1.62	30739(1)	1.53	23821(2)	1.38	21440(2)	1.26
Premarin	10427(4)	0.68	8388(5)	0.68	8796(5)	0.69	14680(4)	0.73	14258(4)	0.83	14282(4)	0.84

0.625mg®												
Solphylex®	8188[8]	0.54	6992[8]	0.57	7579[7]	0.60	10852[8]	0.54				
Stilpane®	10206[6]	0.67	7916[6]	0.64	8633[6]	0.68	14147[5]	0.70	10550[6]	0.61	9758[7]	0.57
Vioxx 25mg®												
Zyrtec 10mg®							8610[7]	0.43				
Total	116011	7.61	94482	7.68	101314	8.00	158858	7.88	139692	8.11	138565	8.11

%* Total number of medicine items for the specific drug divided by the total number of all items claimed multiplied by hundred. The superscript represents the position occupied by the specific medina item during the specified month.

Table A.6 Top ten medicine items claimed from November 2001 to April 2002

Drug description	Nov 2001		Dec 2001		Jan 2002		Feb 2002		Mar 2002		Apr 2002	
	P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
Alcophylex syrup®												
Amiloretic tablets®												
Augmaxil 375mg®												
Corenza C tablets®												
Coversyl tablets	7377(9)	0.53	8898(10)	0.56								
Dapamax 2.5mg®	8470(6)	0.60	10469(6)	0.66	13001(7)	0.56	12260(8)	0.55	13392(8)	0.57	13728(8)	0.56
Dispirin cv 100mg®												
Ecotrin 81mg®	8140(7)	0.58	9492(7)	0.59	12908(8)	0.56	12528(7)	0.56	13561(7)	0.57	14213(7)	0.58
Eltroxin 0.1mg®	15578(3)	1.11	18779(3)	1.18	23826(3)	1.03	22570(3)	1.01	24925(3)	1.06	25328(3)	1.03
Flixonase Aques®	8789(5)	0.63	11593(5)	0.73	14587(6)	0.63	13312(6)	0.59	13786(7)	0.58	14345(6)	0.59
Lipitor 10mg®	21809(1)	1.56	25927(1)	1.62	33006(2)	1.43	31752(2)	1.42	34559(1)	1.46	35975(1)	1.47
Mybulen tablets®							11664(10)	0.52	12168(10)	0.52	13082(10)	0.53
Mypaid capsules®												
Myprodol capsules®	16246(2)	1.16	19592(2)	1.23	33768(1)	1.46	31843(1)	1.42	33706(2)	1.43	34806(2)	1.42
Premarin	11992(4)	0.86	14566(4)	0.91	18469(4)	0.80	17473(4)	0.78	18744(4)	0.79	19243(4)	0.79

0.625mg®												
Solphylex syrup®												
Stilpane® tablets	7757(8)	0.55	9295(8)	0.58	18149(5)	0.79	16217(5)	0.72	17496(5)	0.74	18781(5)	0.77
Vioxx 25mg®					12407(9)	0.54	11807(9)	0.53	12366(9)	0.52	13170(9)	0.54
Zyrtec 10mg®	7015(10)	0.50	8971(9)	0.56	12295(10)	0.53						
Total	113173	8.08	137582	8.62	192416	8.32	181426	8.11	194703	8.25	202671	8.28

%* Total number of medicine items for the specific drug divided by the total number of all items claimed multiplied by hundred. The superscript represents the position occupied by the specific medina item during the specified month.

Table A.7 Top ten medicine items claimed from May 2002 to October 2002

Drug description	May 2002		Jun 2002		Jul 2002		Aug 2002		Sep 2002		Oct 2002	
	P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
Alcophylex syrup®	12032(3)	0.98	23180(4)	0.97	21626(4)	0.89	20610(4)	0.85	14435(6)	0.69		
Amiloretic tablets®												
Augmaxil 375mg®												
Corenza C tablets®	6448(10)	0.52										
Coversyl tablets®												
Dapamax 2.5mg®			13082(10)	0.55	13942(8)	0.57	13916(9)	0.57	12760(10)	0.61	13233(8)	0.62
Dispirin cv 100mg®												
Ecotrin 81mg®			13107(9)	0.55	13941(9)	0.57	14090(8)	0.58	12812(9)	0.61	13076(9)	0.61
Eltroxin 0.1mg®	11345(4)	0.92	23521(3)	0.99	24665(3)	1.01	24959(3)	1.03	22905(3)	1.09	23380(2)	1.09
Flixonase Aques®							13297(10)	0.55			13075(10)	0.61
Lipitor 10mg®	15988(1)	1.30	33749(1)	1.41	35550(1)	1.46	36415(1)	1.50	33098(1)	1.58	33801(1)	1.57
Mypaid capsules®	7028(8)	0.57										
Myprodol capsules®	10365(5)	0.84	16009(7)	0.67	16811(7)	0.69	15587(7)	0.64	13692(7)	0.65	19546(4)	0.91
Mybulen tablets®	12806(2)	1.04	28032(2)	1.18	32459(2)	1.33	30904(2)	1.27	24105(2)	1.15	19940(3)	0.93
Premarin	8479(7)	0.69	17190(6)	0.72	18050(6)	0.74	17949(6)	0.74	16383(5)	0.78	16916(6)	0.79

0.625mg®												
Solphylex syrup®	6819[9]	0.55	13639[8]	0.57	13668[10]	0.56						
Stilpane tablets®	9404[6]	0.76	18086[5]	0.76	19922[5]	0.82	19736[5]	0.81	16725[4]	0.80	17612[5]	0.82
Vioxx 25mg®												
Zyrtec 10mg®									13131[8]	0.63	14702[7]	0.68
Total	100714	8.19	199595	8.37	210634	8.63	207463	8.55	180046	8.58	185281	8.62

%* Total number of medicine items for the specific drug divided by the total number of all items claimed multiplied by hundred. The superscript represents the position occupied by the specific medina item during the specified month.

Table A.8 Top ten medicine items claimed from November 2002 to April 2003

Drug description	Nov 2002		Dec 2002		Jan 2003		Feb 2003		Mar 2003		Apr 2003	
	P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
Alcophylex syrup®							13856(8)	0.62	17348(6)	0.72	18563(5)	0.80
Amiloretic tablets®												
Augmaxil 375mg®												
Corenza C tablets®												
Coversyl tablets®												
Dapamax 2.5mg®	12957(8)	0.65	12691(7)	0.67	14029(10)	0.58	12620(10)	0.57	13234(10)	0.55	13005(9)	0.56
Dispirin cv 100mg®												
Ecotrin 81mg	12705(9)	0.64	12577(8)	0.67	15922(8)	0.65	13826(9)	0.62	14952(8)	0.62	14587(8)	0.63
Eltroxin 0.1mg®	22429(2)	1.13	22348(2)	1.19	25375(3)	1.04	21987(3)	0.99	23989(3)	0.99	23336(3)	1.01
Flixonase Aques®	12211(10)	0.62	11765(10)	0.63	14511(9)	0.60						
Lipitor 10mg®	32131(1)	1.62	32277(1)	1.72	35951(1)	1.48	30288(1)	1.36	32403(2)	1.34	30574(2)	1.32
Mybulen tablets®	15643(5)	0.79	13691(5)	0.73	20431(5)	0.84	18320(5)	0.82	18908(5)	0.78	17296(6)	0.75
Mypaid capsules®											12310(10)	0.53
Myprodol capsules®	19902(3)	1.00	20394(3)	1.08	31960(2)	1.31	29623(2)	1.33	32741(1)	1.36	31296(1)	1.35
Premarin	16035(4)	0.81	16132(4)	0.86	17271(6)	0.71	14938(6)	0.67	16004(7)	0.66	15685(7)	0.68

0.625mg®												
Solphylex syrup®												
Stilpane® tablets	14354[6]	0.72	12498[9]	0.66	21884[5]	0.90	19597[4]	0.88	19678[4]	0.82	18597[4]	0.81
Vioxx 25mg®												
Zyrtec 10mg®	13729[7]	0.69	13067[6]	0.69	16061[7]	0.66	13934[7]	0.63	13650[9]	0.57		
Total	172096	8.68	167440	8.90	213395	8.77	188989	8.48	202907	8.40	195249	8.45

%* Total number of medicine items for the specific drug divided by the total number of all items claimed multiplied by hundred. The superscript represents the position occupied by the specific medina item during the specified month.

Table A.9 Prevalence of the different main pharmacological groups claimed from May 2001 to April 2002

Months		Analgesics	Antimicrobials	Cardiovascular drugs	Drugs of the endocrine system	Drugs of the respiratory system	Others	Total
May 2001	P	132195	178315	173131	130277	253798	656580	1524296
	%*	8.67	11.70	11.36	8.55	16.65	43.07	100
Jun 2001	P	108361	147574	142074	106172	210133	516438	1230752*
	%*	8.80	11.54	11.54	8.63	17.07	41.96	100
Jul 2001	P	111071	152571	152742	110253	217882	521582	1266101
	%*	8.77	12.05	12.06	8.71	17.21	41.20	100
Aug 2001	P	172922	234847	248183	180639	326866	851541	2014998
	%*	8.58	11.66	12.32	8.96	16.22	42.26	100
Sep 2001	P	134788	180280	242216	170951	232607	761265	1722109
	%*	7.83	10.47	14.07	9.93	13.51	44.20	100
Oct 2001	P	134683	135278	247490	169444	217537	779826	1708168
	%*	7.88	7.92	14.49	9.92	12.74	45.66	100
Nov 2001	P	110057	132832	2036069	139693	180738	633527	1400453
	%*	7.86	9.48	14.54	9.97	12.91	45.24	100
Dec 2001	P	117876	156839	241949	168111	180026	731980	1596781
	%*	7.38	9.82	15.15	10.53	11.27	45.84	100
Jan 2002	P	197227	247258	312457	222110	227452	1105375	2311879
	%*	8.53	10.70	13.52	9.61	9.84	47.81	100
Feb 2002	P	193897	244509	296816	212429	268683	1021442	2237776

	%*	8.66	10.93	13.26	9.49	12.01	45.65	100
Mar	P	204401	256263	320327	229301	289468	1060513	2360273
2002	%*	8.66	10.86	13.57	9.72	12.26	44.93	100
Apr	P	210154	265958	329050	233999	319669	1088493	2447323
2002	%*	8.59	10.87	13.45	9.56	13.06	44.48	100
*Frequency missing = 2 #Frequency missing =10								

%* Frequency of the specific main pharmacological group divided by the frequency of the total number of all medicine items claimed multiplied by hundred. Others refer to other main pharmacological groups except the ones listed on this Table.

Table A.10 Prevalence of different main pharmacological groups claimed from May 2002 to April 2003

Months		Analgesics	Antimicrobials	Cardiovascular drugs	Drugs of the endocrine system	Drugs of the respiratory system	Others	Total
May 2002	P	111279	136304	144737	104944	222341	509776	1229381
	%*	9.05	11.09	11.77	8.54	18.09	41.47	100
Jun 2002	P	209282	281930	305292	217800	424407	946729	2385440
	%*	8.77	11.82	12.80	9.13	17.79	39.69	100
Jul 2002	P	211111	286442	321321	227518	393022	1000634	2440048
	%*	8.65	11.74	13.71	9.32	16.11	41.01	100
Aug 2002	P	210207	281818	325157	229943	385491	994628	2427244
	%*	8.66	11.61	13.40	9.47	15.88	40.98	100
Sep 2002	P	173985	231987	294197	206819	291147	900678	2098813
	%*	8.29	11.05	14.02	9.85	13.87	42.91	100
Oct 2002	P	179264	238091	301052	211599	268684	951198	2149888
	%*	8.34	11.07	14.00	9.84	12.50	44.24	100
Nov 2002	P	164384	215700	286713	199179	239086	878403	1983465
	%*	8.29	10.87	14.46	10.04	12.05	44.29	100
Dec 2002	P	153636	194461	286029	194604	205175	847888	1881793
	%*	8.16	10.33	15.20	10.34	10.90	45.06	100
Jan 2003	P	225859	277743	338349	229328	263771	1099505	2434555
	%*	9.28	11.41	13.90	9.42	10.83	45.16	100

Feb	P	209854	259302	291859	202498	267724	997562	2228799
2003	%*	9.09	11.63	13.09	9.09	12.01	44.76	100
Mar	P	224709	280359	314038	217087	323672	1054329	2414194
2003	%*	9.31	11.61	13.01	8.99	13.41	43.67	100
Apr	P	212195	269041	305149	207237	331844	984550	2310016
2003	%*	8.97	11.65	13.21	8.97	14.37	42.62	100

%* Frequency of the specific main pharmacological group divided by the frequency of the total number of all medicine items claimed multiplied by hundred. Others refer to other main pharmacological groups except the ones listed on this Table.

Table A.11 Prevalence of main pharmacological group according to generic or innovator medicine items claimed from May 2001 to April 2002

Months	Analgesics				Anti-microbial drugs				Cardiovascular drugs			
	Innovator		Generic		Innovator		Generic		Innovator		Generic	
	P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
May2001	82410	62.34	49785	37.66	93068	52.19	85247	47.81	139383	80.51	33748	19.49
Jun 2001	66623	61.48	41738	38.52	77115	52.26	70459	47.74	113519	79.90	28555	20.10
Jul 2001	67839	61.08	43232	38.92	79510	52.11	73061	47.89	121734	79.70	31008	20.30
Aug2001	104311	60.32	68611	39.68	121792	51.86	113055	48.14	196784	79.29	51399	20.71
Sep2001	81821	60.70	52967	39.30	91920	50.99	88360	49.01	191779	79.17	504967	20.83
Oct2001	80263	59.59	54420	40.40	80231	50.40	78957	49.60	195616	79.04	51874	20.96
Nov2001	65007	59.06	45050	40.93	66866	50.34	65966	49.66	160327	78.74	43279	21.26
Dec2001	71502	60.66	46374	39.34	77791	49.60	79048	50.40	190509	78.74	51440	21.26
Jan2002	120031	60.86	77196	39.14	122708	49.63	124550	50.37	244368	78.21	68089	21.79
Feb 2002	117611	60.66	76286	39.34	122243	49.99	122266	50.01	231956	78.15	64860	21.85
Mar2002	123250	60.30	81151	39.70	125131	48.83	131132	51.17	250476	78.19	69851	21.81
Apr2002	125206	59.58	84948	40.42	128856	48.45	137102	51.55	256917	78.08	72133	21.92

%* Quotient of either the innovator or generic drugs and the total number of drugs within the pharmacological group multiplied by hundred. For instance the percentage of the innovator of the analgesics will be calculated by dividing 82410 by 132195 X100, which amounts to 62.34. This figure shows that innovator drugs of the analgesics contributed 62.34 percentage of the total number of analgesics claimed for the month of May 2001.

Table A.12 Prevalence of main pharmacological group according to generic or innovator medicine items claimed from May 2001 to April 2002

Months	Endocrine system drugs				Respiratory drugs				Others[#]			
	Innovator		Generic		Innovator		Generic		Innovator		Generic	
	P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
May2001	112764	86.56	17516	13.44	201607	79.44	52191	20.56	508209	77.40	238484	22.60
*Jun2001	91493	86.17	14679	13.83	166129	79.06	44004	20.94	398610	77.18	117828	22.82
Jul2001	94855	86.03	15398	13.97	172046	78.96	45836	21.04	400014	76.69	121568	23.31
Aug2001	156212	86.48	24427	13.52	256581	78.50	70285	21.50	651792	76.54	199749	23.46
Sep2001	148519	86.88	22432	13.12	184127	79.16	48480	20.84	578950	76.08	182015	23.92
Oct2001	147786	87.22	21658	12.78	172394	79.25	45143	20.75	588113	75.42	191713	24.58
Nov2001	121546	87.01	18147	12.99	143355	79.32	37383	20.68	476690	75.24	156837	24.76
Dec2001	146392	87.08	21719	12.92	144220	80.11	35806	19.89	551901	75.39	180179	24.61
Jan2002	191865	86.38	30245	13.62	182121	80.07	45331	19.93	823471	74.50	281904	25.50
Feb2002	183942	86.59	28487	13.41	211612	78.76	57071	21.24	763336	74.73	258106	25.27
Mar2002	197989	86.34	31312	13.66	226373	78.20	63095	21.80	789287	74.43	271226	25.57
Apr2002	201505	86.11	32494	13.89	248916	77.87	70753	22.13	809495	74.37	278998	25.63

%* Quotient of either the innovator or generic drugs and the total number of drugs within the pharmacological group multiplied by hundred.
P for others = the total number of either generic medicine items subtracting the sum of the other five main pharmacological group.
%* for others[#] = the value for P above divided by the total number of others[#] as calculated in Table A.9. Others refer to other main pharmacological groups except the ones listed on this Table.

Table A.13 Prevalence of main pharmacological group according to generic or innovator medicine items from May 2001 to April 2002

Months	Analgesics				Anti-microbial drugs				Cardiovascular drugs			
	Innovator		Generic		Innovator		Generic		Innovator		Generic	
	P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
May2002	56480	50.76	54799	49.24	66867	49.06	69437	50.94	111261	76.87	33476	23.13
Jun2002	99898	47.73	109384	52.27	139633	49.53	142297	50.47	234753	76.89	70539	23.11
Jul2002	100444	47.58	110667	52.42	142378	49.71	144064	50.29	245885	76.52	75436	23.48
Aug2002	99462	47.32	110745	52.68	138447	49.13	143371	50.87	248609	76.46	76548	23.54
Sep2002	83252	47.85	90733	52.15	111243	47.95	120744	52.05	224835	76.42	69362	23.58
Oct2002	90238	50.34	89026	49.66	114533	48.10	123558	51.90	229715	76.30	71337	23.70
Nov2002	87278	53.09	77106	46.91	105147	48.75	110553	51.25	218861	76.33	67852	23.67
Dec2002	84207	54.81	69429	45.19	95641	49.18	98820	50.82	215353	75.29	70676	24.71
Jan2003	120953	53.55	104906	46.45	129404	46.59	148339	53.41	251879	74.44	86470	25.56
Feb2003	111833	53.29	98021	46.71	121729	46.94	137573	53.06	215991	74.01	75868	25.99
Mar2003	119687	53.26	105022	46.74	132743	47.35	147616	52.65	231267	73.64	82771	26.36
Apr2003	113375	53.43	98820	46.57	128183	47.64	140858	52.36	222977	73.07	82172	26.93

%* Quotient of either the innovator or generic drugs and the total number of drugs within the pharmacological group multiplied by hundred.

Table A.14 Prevalence of main pharmacological group according to generic or innovator medicine items from May 2002 to April 2003

Months	Endocrine system drugs				Respiratory drugs				Others			
	Innovator		Generic		Innovator		Generic		Innovator		Generic	
	P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
May2002	89005	84.81	15939	15.19	173808	78.17	48533	21.83	372845	73.14	136931	26.86
Jun2002	183368	84.19	34432	15.81	333398	78.56	91009	21.44	688218	72.69	258511	27.31
Jul2002	192053	83.52	37890	16.48	300654	78.00	84837	22.00	719742	71.93	280892	28.07
Aug2002	190292	83.64	37226	16.36	308634	78.53	84388	21.47	703032	70.68	291596	29.32
Sep2002	173010	83.65	33809	16.35	228463	78.47	62684	21.53	629945	69.94	270733	30.06
Oct2002	176097	83.22	35502	16.78	211355	78.66	57329	21.34	556716	65.63	291564	34.37
Nov2002	166204	83.44	32975	16.56	188635	79.66	50451	20.34	607265	69.13	271138	30.87
Dec2002	163366	83.95	31238	16.05	163998	79.93	41177	20.07	584037	66.67	291966	33.33
Jan2003	188990	82.41	40338	17.59	209385	79.38	54386	20.62	746174	67.86	353331	32.14
Feb2003	165427	81.69	37071	18.31	209787	78.39	57937	21.61	676537	67.82	321025	32.18
Mar2003	177766	81.89	39321	18.11	252914	78.14	70758	21.86	718329	68.13	336059	31.87
Apr2003	169823	81.95	37414	18.05	257973	77.74	73871	22.26	666199	65.43	352024	34.57

%* Quotient of either the innovator or generic drugs and the total number of drugs within the pharmacological group multiplied by hundred.
P for others = the total number of either generic medicine items subtracting the sum of the other five main pharmacological group.
%* for others# = the value for P above divided by the total number of others# as calculated in Table A.9. Others refer to other main pharmacological groups except the ones listed on this Table.

Table A.15 Average medicine cost of all medicine items claimed per prescription from May 2001 to April 2002

Months	Total no. Prescriptions	Average cost (R)	Standard deviation (R)	Minimum cost (R)	Maximum cost (R)	Median (R)	Total cost (R)
May2001	740708	269.174	313.57	0.01	38942.21	182.61	199379399
Jun2001	595871	271.60	318.87	0.01	24531.60	184.41	161836026
Jul2001	616329	271.57	306.53	0.01	20660.22	183.91	167376142
Aug2001	998795	267.40	293.15	0.01	24531.06	183.55	267079044
Sep2001	872305	276.03	305.28	0.01	24531.06	187.47	240778497
Oct2001	885892	270.14	307.83	0.01	11479.41	176.58	239312390
Nov2001	724293	272.78	312.27	0.01	10123.68	178.45	197569799
Dec2001	812710	287.64	314.04	0.01	24040.38	198.57	233770458
Jan2002	1187338	288.41	314.10	0.01	24067.38	198.56	342444664
Feb2002	1148370	287.98	314.63	0.06	23761.15	198.26	330702915
Mar2002	1217185	289.56	315.38	0.09	24552.01	198.07	352449547
Apr2002	1261200	288.90	313.93	0.03	24552.01	197.11	364365722

Table A.16 Average medicine cost of all medicine items claimed per prescription from May 2002 to May 2003

Months	Total no. Prescriptions	Average cost (R)	Standard deviation (R)	Minimum cost (R)	Maximum cost (R)	Median (R)	Total cost (R)
May2002	650519	256.32	295.20	0.01	24573.80	165.57	166740336
Jun2002	1211046	279.10	306.00	0.02	14547.35	187.07	337998335
Jul2002	1257723	281.87	307.57	0.05	20403.92	188.96	354516468
Aug2002	1260648	277.77	303.40	0.01	33084.05	186.40	350165125
Sep2002	1107865	282.04	346.96	0.05	96152.96	187.88	312465164
Oct2002	1146070	282.62	432.17	0.04	129490.32	188.03	323904056
Nov2002	1058583	287.83	386.98	0.03	129490.32	192.96	304691145
Dec2002	997993	297.34	454.13	0.06	129490.32	203.28	296742825
Jan2003	1304379	289.16	373.42	0.02	129490.32	191.28	377173643
Feb2003	1188840	283.25	310.03	0.03	33084.10	186.34	336741645
Mar2003	1289640	277.61	303.73	0.02	33084.10	181.77	358014042
Apr2003	1233177	276.02	305.31	0.05	29321.37	180.69	340379016

Table A.17 Average cost per medicine item claimed from May 2001 to April 2002

Months	Total no. of medicine items	Average cost (R)	Standard deviation (R)	Minimum cost (R)	Maximum cost (R)	Median (R)	Total cost (R)
May2001	1524296	130.80	164.23	0.01	38793.12	86.54	199379399
Jun2001	1230754	131.49	166.89	0.01	19248.28	86.54	161836026
Jul2001	1266101	132.20	159.13	0.01	12019.01	86.54	167376142
Aug2001	2014998	132.55	154.13	0.01	19248.28	87.18	267079044
Sep2001	1722109	139.82	161.05	0.01	19248.28	93.34	240778497
Oct2001	1708168	140.10	163.14	0.01	10787.14	93.20	239312390
Nov2001	1400453	141.08	165.24	0.01	10123.68	93.84	197569799
Dec2001	1596781	146.40	167.42	0.01	17736.21	100.26	233770458
Jan2002	2311879	148.12	167.29	0.01	21837.88	101.86	342444664
Feb2002	2237776	147.78	166.74	0.01	19474.36	100.87	330702915
Mar2002	2360273	149.33	167.51	0.01	21837.88	101.86	352449547
Apr2002	2447323	148.88	166.82	0.02	21837.88	100.44	364365722

Table A.18 Average cost per medicine item claimed from May 2002 to April 2003

Months	Total number of items	Average cost (R)	Standard deviation (R)	Minimum cost (R)	Maximum cost (R)	Median (R)	Total cost (R)
May2002	1229381	135.63	160.94	0.01	21837.88	82.70	166740336
Jun2002	2385440	141.69	163.88	0.01	11777.79	88.49	337998335
Jul2002	2440048	145.29	169.12	0.01	20403.92	95.45	354516468
Aug2002	2427244	144.26	168.02	0.01	33084.05	94.02	350165125
Sep2002	2098813	148.88	199.49	0.01	83769.48	98.78	312465164
Oct2002	2149888	150.66	235.62	0.01	73304.28	100.97	323904056
Nov2002	1983465	153.62	212.90	0.01	73304.28	102.20	304691145
Dec2002	1881793	157.69	246.49	0.01	73304.28	104.49	296742825
Jan2003	2434555	154.93	203.33	0.01	73304.28	100.98	377173643
Feb2003	2228799	151.09	172.40	0.01	33084.10	97.75	336741645
Mar2003	2414253	148.29	170.10	0.02	33084.10	94.62	358014042
Apr2003	2310016	147.35	172.94	0.01	29321.37	90.66	340379016

Table A.19 Average cost of medicine items according to different main pharmacological groups claimed from May 2001 to April 2002

Months	Analgesics			Anti-microbial drugs			Cardiovascular drugs		
	N	Mean ± Std dev R	Total cost R	N	Mean ± Std dev R	Total cost R	N	Mean ± Std dev R	Total cost R
May2001	132195	60.74 ±62.98	8029584.0	178315	168.01 ±237.72	29959243.0	173131	215.48 ±115.33	37305732.3
Jun2001	108361	59.25 ±61.62	6419893.5	147574	172.15 ±245.22	25405428.7	142074	216.32 ±114.32	30732941.5
Jul2001	111071	59.26 ±60.17	6581811.7	152571	172.39 ±243.91	26302288.7	152742	216.18 ±115.66	33020040.3
Aug2001	172922	59.55 ±61.28	10296920.1	234847	163.73 ±219.98	38451623.0	248183	216.96 ±115.77	53845759.6
Sep2001	134788	60.45 ±62.71	8147650.2	180280	172.99 ±246.36	31187833.9	242216	217.96 ±115.36	52792633.3
Oct2001	134683	59.84 ±69.89	8058840.95	159188	183.02 ±268.30	29134445	247490	218.24 ±113.85	54013147.7
Nov2001	110057	58.74 ±64.74	6464544.46	132832	189.80 ±276.78	25211156.5	203606	217.85 ±113.55	44355363.9
Dec2001	117876	62.14 ±68.50	7325338.34	156839	193.63 ±275.61	30368420.3	241949	219.64 ±112.10	53140613.2
Jan2002	197227	68.82 ±77.11	13572529.2	247258	180.24 ±224.14	44565171.9	312457	223.53 ±115.12	69844747.1
Feb2002	193897	68.94 ±80.46	13367254.9	244509	180.42 ±220.49	44115153.7	296816	225.90 ±115.88	67051191.4
Mar2002	204401	71.50 ±84.34	14615493.9	256263	182.09 ±223.69	46663758.2	320327	227.38 ±118.15	72837216.4
Apr2002	210154	70.70 ±82.59	14857499.4	265958	182.66 ±225.23	48579056.4	329050	228.82 ±117.95	75293961.9

Table A.20 Average cost of medicine items according to different main pharmacological claimed groups from May 2001 to April 2002

Months	Endocrine system drugs			Respiratory drugs			Others		
	N	Mean ± Std dev R	Total cost R	N	Mean ± Std dev R	Total cost R	N	Mean* ± Std dev R	Total cost R
May 2001	130277	142.13 ±169.14	18516722.4	253798	81.82 ±163.36	20766956.8	656580	205.215 ±248.20	84801160.73
Jun 2001	106172	143.23 ±174.41	15206552.1	210133	81.57 ±94.70	17141180.7	516438	219.36 ±277.10	66929974.94
Jul 2001	110253	142.36 ±166.03	15695874.6	217882	82.28 ±95.45	17928010.5	521582	469.57 ±1309.57	67827204.88
Aug 2001	180639	141.69 ±166.78	25595464.5	326866	84.58 ±100.02	27647302.1	851541	520.87 ±1471.76	111239925.6
Sep 2001	170951	144.34 ±171.80	24675164.8	232607	96.79 ±112.92	22514258.1	755427	457.60 ±1219.56	101460482.2
Oct 2001	169444	146.39 ±182.05	24804865.1	217537	99.54 ±116.75	21654049.3	779826	474.44 ±1344.26	101647040.5
Nov 2001	139693	145.91 ±178.49	20381977.4	180738	101.19 ±118.67	18288320.7	633527	595.21 ±1788.75	82868436.59
Dec 2001	168111	144.64 ±172.64	24315382.7	180026	113.34 ±126.99	20404032.8	730245	433.81 ±1103.89	98216670.26
Jan 2002	222110	155.03 ±190.48	34434214.2	227452	116.28 ±131.10	26448629.2	1093820	521.82 ±1439.01	153579371.9
Feb 2002	212429	160.69 ±204.90	34135809.4	268683	104.95 ±122.11	28197593.0	1018717	445.85 ±1061.97	143835912.4
Mar 2002	229301	159.86 ±193.05	36655758.3	289468	105.80 ±122.32	30625147.1	1059497	535.78 ±1436.12	151052173.4
Apr 2002	233999	159.36 ±199.86	37289933.1	319669	104.53 ±122.12	33316329.6	1089286	577.15 ±1081.03	155028941.2

Mean* is the weighted average of all the remaining main pharmacological groups. Refer to chapter 4 for an overview of weighted averages.
Others refer to other main pharmacological groups except the ones listed on this Table

Table A.21 Average cost of medicine items according to different main pharmacological groups from May 2002 to April 2003

Months	Analgesics			Anti-microbial drugs			Cardiovascular drugs		
	N	Mean ± Std dev R	Total cost R	N	Mean ± Std dev R	Total cost R	N	Mean ± Std dev R	Total cost R
May2002	111279	61.43 ±73.82	6835444.72	136304	170.43 ±205.51	23230047.5	144737	226.43 ±117.05	32773344.6
Jun2002	209282	61.11 ±74.99	12788947.9	281930	176.46 ±216.40	49747964.1	305292	227.29 ±116.26	69389970.2
Jul2002	211111	63.43 ±74.08	13390425.5	286442	185.62 ±224.40	53170653.4	321321	226.03 ±115.45	72627238.9
Aug2002	210207	62.17 ±76.83	13067913.7	281818	183.89 ±224.77	51823186.5	325157	225.06 ±113.97	73179786.8
Sep2002	173985	63.40 ±74.68	11030084.7	231987	195.30 ±393.54	45306687.9	294197	225.96 ±113.85	66476956.0
Oct2002	179264	64.45 ±77.24	11553039.6	238091	201.95 ±531.25	48082497.0	301052	225.85 ±113.84	67992791.8
Nov2002	173985	63.40 ±74.68	11030084.7	215700	209.62 ±432.78	45306687.9	286713	226.83 ±113.30	66476956.0
Dec2002	153636	67.89 ±74.22	10430325.6	194461	223.46 ±579.54	43454883.1	286029	227.40 ±114.48	65044231.5
Jan2003	225859	71.82 ±85.57	16221488.1	27890	203.12 ±391.81	56416137.4	338349	230.61 ±117.96	78025894.4
Feb2003	209854	67.69 ±83.23	14205947.8	259302	197.54 ±242.75	51222146.4	291859	229.68 ±118.05	67030558.6
Mar2003	224709	66.03 ±78.79	14836631.0	280359	196.21 ±240.53	55009791.5	314038	228.98 ±117.45	71909142.0
Apr2003	212195	66.25 ±82.47	14058404.8	269041	200.74 ±247.40	54007171.0	305149	227.21 ±117.08	69333965.5

Table A.22 Average cost of medicine items according to different main pharmacological groups from May 2002 to April 2003

Months	Endocrine system drugs			Respiratory drugs			Others		
	N	Mean ± Std dev R	Total cost R	N	Mean ± Std dev R	Total cost R	N	Mean* ± Std dev R	Total cost R
May2002	104944	155.31 ±197.75	16298831.8	222341	85.30 ±103.06	18965732.0	509776	442.82 ±1059.59	69114348.64
Jun2002	217800	155.60 ±188.55	33889453.5	424407	90.73 ±109.26	38507648.4	946729	594.32 1861.64±	133674351.0
Jul2002	227518	158.03 ±201.115	35954528.4	393022	94.99 ±113.70	37335045.7	1000634	708.69 ±2103.53	142037576.2
Aug2002	229943	155.83 ±191.63	35832235.3	385491	95.20 ±114.36	36697820.9	994628	549.14 ±1549.44	139564181.8
Sep2002	206819	157.20 ±197.09	32511598.9	291147	103.81 ±123.56	30222561.0	900678	314.66 ±411.54	126917275.7
Oct2002	211599	156.95 ±231.00	33209921.3	268684	110.40 ±130.33	29662730.0	951198	326.86 ±422.96	128717349.6
Nov2002	199179	156.45 ±223.61	32511598.9	239086	114.64 ±132.78	30222561.0	878403	242.15 ±283.07	125000597.1
Dec2002	194604	157.36 ±224.59	30623103.9	205175	125.81 ±142.55	25813797.7	847888	216.63 ±298.67	121376483.8
Jan2003	229328	163.02 ±213.16	37385136.6	263771	119.97 ±143.25	31646816.3	1099505	2233.56 ±9771.65	157478169.7
Feb2003	202498	163.89 ±213.50	33187933.3	267724	111.40 ±135.71	29823224.1	997562	240.40 ±375.58	140271834.2
Mar2003	217087	162.11 ±200.40	35192720.5	323672	104.42 ±128.47	33798105.8	1054329	253.74 ±291.02	147240256.1
Apr2003	207237	161.25 ±229.73	33416524.6	331844	101.91 ±124.34	33817206.6	984550	366.06 ±863.71	135745743.4

Mean* is the weighted average of all the remaining main pharmacological groups. Refer to chapter 4 for an overview of weighted averages. Others refer to other main pharmacological groups except the ones listed on this Table

Table A.23 Average cost of all medicine items according to generic and innovator medicine items claimed from May 2001 to April 2002

Month	I or G	Total no of items (R)	Average cost (R)	Standard deviation (R)	Minimum cost (R)	Maximum cost (R)	Median (R)	Total cost (R)
May 2001	I	1137441	153.16	181.26	0.01	38793.12	106.24	174211269.00
	G	386855	65.06	62.29	0.01	1649.07	42.98	25168130.32
Jun 2001	I	913491	154.34	184.71	0.01	19248.28	105.74	140992512.00
	G	317263	65.70	63.02	0.02	1298.39	44.06	20843513.83
Jul 2001	I	935998	155.62	175.42	0.01	12019.01	108.83	145663196.00
	G	330103	65.78	62.43	0.01	1336.94	44.98	21712945.57
Aug 2001	I	1487472	156.02	169.34	0.01	19248.28	110.48	232079205.00
	G	527526	66.35	62.80	0.01	1649.04	45.09	34999839.70
Sep 2001	I	1277418	164.46	176.40	0.01	19248.28	117.68	210085736.00
	G	444691	69.02	65.53	0.01	4733.59	47.46	30692761.34
Oct 2001	I	1264403	164.90	179.11	0.01	10787.14	117.63	208494741.00
	G	443765	69.45	65.59	0.01	1649.04	47.26	30817648.25
Nov 2001	I	1033791	166.28	181.58	0.01	10123.68	117.58	171899517.00
	G	366662	70.01	67.01	0.01	1402.09	67.01	25670281.98
Dec 2001	I	1182315	172.23	183.46	0.01	17736.21	126.32	203630342.00
	G	414466	72.72	68.17	0.01	1504.54	51.19	30140115.51
Jan 2002	I	1684564	176.02	183.62	0.01	21837.88	131.67	296510901.00
	G	627315	73.22	70.02	0.01	2742.61	50.28	45933762.55
Feb 2002	I	1630700	175.15	183.00	0.01	19474.36	129.66	285622567.00
	G	607076	74.26	71.44	0.04	1819.14	49.59	45080347.45
Mar 2002	I	1712506	177.26	183.89	0.02	21837.88	130.48	303563760.00
	G	647767	75.47	72.95	0.01	1897.18	51.24	48885787.04
Apr 2002	I	1770895	177.07	183.28	0.02	21837.88	129.73	313571245.00
	G	676428	75.09	72.21	0.02	1869.74	50.49	50794476.19

Table A.24 Average cost of all medicines items according to generic and innovator medicine items claimed from May 2002 to April 2003

Month	I or G	Total no of items (R)	Average cost (R)	Standard deviation (R)	Minimum cost (R)	Maximum cost (R)	Median (R)	Total cost (R)
May 2002	I	1779338	172.52	182.81	0.01	21837.88	122.95	306962819.00
	G	744173	71.93	68.83	0.03	1472.13	48.63	53526011.18
Jun 2002	I	1679268	171.20	182.32	0.01	11777.79	119.05	287496279.00
	G	706172	71.52	68.43	0.02	3417.20	48.07	50502055.84
Jul 2002	I	1707375	176.14	188.80	0.01	20403.92	127.85	300739196.00
	G	732673	73.40	69.25	0.03	2157.11	52.78	53777271.98
Aug 2002	I	1682257	175.68	188.24	0.01	33084.05	127.21	295530890.00
	G	744987	73.34	68.60	0.01	2987.23	52.42	54634234.71
Sep 2002	I	1450748	181.86	227.74	0.01	83769.48	131.65	263826547.00
	G	648065	75.05	69.91	0.01	2987.23	55.28	48638617.48
Oct 2002	I	1481572	184.53	273.16	0.01	73304.28	133.88	273401803
	G	668316	75.57	70.69	0.02	5304.06	55.44	50502253.04
Nov 2002	I	1373390	187.11	243.80	0.01	73304.28	135.88	256978009.00
	G	610075	78.21	73.09	0.03	2423.66	58.13	47713135.28
Dec 2002	I	1306602	191.52	285.16	0.01	73304.28	137.35	250245496.00
	G	575191	80.84	74.52	0.03	1781.78	60.48	46497329.12
Jan 2003	I	1646785	190.83	232.92	0.01	73304.28	137.13	314259541.00
	G	787770	79.86	77.64	0.02	5916.62	58.49	62914101.75
Feb 2003	I	1501304	186.65	193.74	0.01	33084.10	135.52	280221510.00
	G	727495	77.69	74.79	0.01	1846.51	55.63	56520134.29
Mar 2003	I	1632647	182.46	191.17	0.02	33084.10	128.88	297895360.00
	G	781547	76.89	73.70	0.02	2708.69	54.38	60091286.53
Apr 2003	I	1558530	181.54	195.56	0.01	29321.37	126.48	282935087.00
	G	751486	76.44	71.91	0.02	2053.48	54.81	57443928.64

APPENDIX B

Table B.1 Average number of hypolipidemic drugs claimed per prescription from May 2001 to April 2002

Months	Total no of prescriptions	Average no of hypolipidemic drugs	Standard deviation	Minimum	Maximum	Median	Total no hypolipidemic drugs
May 2001	33552	1.01	0.11	1.00	2.00	1.00	33930.00
Jun 2001	27502	1.01	0.10	1.00	3.00	1.00	27804.00
Jul 2001	29599	1.01	0.10	1.00	3.00	1.00	29882.00
Aug2001	48889	1.01	0.10	1.00	3.00	1.00	49346.00
Sep2001	48300	1.01	0.10	1.00	3.00	1.00	48784.00
Oct2001	49769	1.01	0.10	1.00	3.00	1.00	50250.00
Nov2001	40887	1.01	0.10	1.00	3.00	1.00	41257.00
Dec2001	48950	1.01	0.09	1.00	3.00	1.00	49361.00
Jan2002	62944	1.01	0.10	1.00	3.00	1.00	63519.00
Feb2002	60212	1.01	0.09	1.00	3.00	1.00	60763.00
Mar2002	65205	1.01	0.09	1.00	3.00	1.00	65771.00
Apr2002	67799	1.01	0.09	1.00	3.00	1.00	68369.00

Table B.2 Average number of hypolipidemic drugs claimed per prescription from May 2002 to April 2003

Months	Total no of prescriptions	Average no of hypolipidemic drugs	Standard deviation	Minimum	Maximum	Median	Total no hypolipidemic drugs
May 2002	66161	1.01	0.09	1.00	3.00	1.00	66692.00
Jun 2002	62610	1.01	0.09	1.00	3.00	1.00	63125.00
Jul 2002	65389	1.01	0.09	1.00	3.00	1.00	65870.00
Aug2002	66203	1.01	0.09	1.00	3.00	1.00	66718.00
Sep2002	59955	1.0	0.09	1.00	3.00	1.00	60418.00
Oct2002	61434	1.01	0.09	1.00	3.00	1.00	61905.00
Nov2002	58710	1.01	0.09	1.00	3.00	1.00	59129.00
Dec2002	58947	1.01	0.09	1.00	3.00	1.00	59374.00
Jan2003	69350	1.01	0.09	1.00	3.00	1.00	69881.00
Feb2003	59449	1.01	0.08	1.00	3.00	1.00	59827.00
Mar2003	64002	101	0.08	1.00	3.00	1.00	64415.00
Apr2003	61932	1.01	0.08	1.00	3.00	1.00	62321.00

Table B.3 Prevalence of the pharmacological groups in the main pharmacological group cardiovascular drugs claimed from May 2001 to April 2002

Months		Antianginal drugs	Antiarrythmic drugs	Antihypertensive drugs	Hypolipidemic drugs	Other vasodilators	Positive inotropic drugs	Vaso-constrictors	Total
May 2001	P	26960	1271	105583	33930	671	3533	1183	173131
	%*	15.57	0.73	60.98	19.60	0.39	2.04	0.68	100
Jun 2001	P	22224	1085	86843	27804	512	2743	863	142074*
	%*	15.64	0.76	61.13	19.57	0.36	1.93	0.61	100
Jul 2001	P	23807	1136	93354	29882	782	2971	810	152742*
	%*	15.59	0.74	61.12	19.56	0.51	1.95	0.53	100
Aug 2001	P	37994	2080	151690	49246	804	4817	1452	248183#
	%*	15.31	0.84	61.12	19.84	0.32	1.94	0.59	100
Sep 2001	P	36568	1881	148324	48784	548	4774	1335	242216
	%*	15.09	0.78	61.24	20.14	0.23	1.97	0.55	100
Oct 2001	P	37329	2040	150923	50250	600	4903	1445	247490
	%*	15.08	0.82	60.98	20.30	0.24	1.98	0.58	100
Nov 2001	P	30612	1591	124558	41257	403	4093	1092	203606
	%*	15.03	0.78	61.18	20.26	0.20	2.01	0.54	100
Dec 2001	P	35640	1802	148894	49361	408	4587	1257	241949
	%*	14.73	0.74	61.54	20.40	0.17	1.90	0.52	100
Jan 2002	P	47293	2788	189286	63519	945	6028	2598	312457

	%*	15.14	0.89	60.58	20.33	0.30	1.93	0.83	100
Feb	P	44681	2637	179903	60763	701	5655	2476	296816
2002	%*	15.05	0.89	60.61	20.47	0.24	1.91	0.83	100
Mar	P	47796	2858	194952	65771	754	5925	2271	320327
2002	%*	14.92	0.89	60.86	20.53	0.24	1.85	0.71	100
Apr	P	49011	2805	200043	68369	705	6179	1938	329050
2002	%*	14.89	0.85	60.79	20.77	0.21	1.88	0.59	100

%* Is the quotient of frequency of pharmacological group and total number of cardiovascular drugs claimed multiplied by hundred

Table B.4 Prevalence of the pharmacological groups in the main pharmacological group cardiovascular drugs claimed from May 2002 to April 2003

Months		Antianginal drugs	Antiarrythmic drugs	Antihypertensive drugs	Hypolipidemic drugs	Other vasodilators	Positive inotropic drugs	Vaso-constrictors	Total
May 2002	P	21701	1234	87997	30027	339	2621	818	144737
	%*	14.99	0.85	60.80	20.75	0.23	1.81	0.57	100
Jun 2002	P	44960	2572	186797	63125	830	5615	1393	305292
	%*	14.72	0.84	61.19	20.68	0.27	1.84	0.46	100
Jul 2002	P	47217	2582	197285	65870	970	5946	1451	321321
	%*	14.69	0.80	61.40	20.50	0.30	1.85	0.45	100
Aug 2002	P	47201	2525	200620	66718	661	5875	1557	325157
	%*	14.52	0.78	61.70	20.52	0.20	1.81	0.48	100
Sep 2002	P	42124	2253	182467	60418	560	4960	1415	294197
	%*	14.32	0.77	62.02	20.54	0.19	1.69	0.48	100
Oct 2002	P	42676	2180	186800	61905	557	5190	1744	301052
	%*	14.18	0.72	62.05	20.56	0.19	1.72	0.58	100
Nov 2002	P	40234	2113	178437	59129	488	4727	1585	286713
	%*	14.03	0.74	62.24	20.62	0.16	1.65	0.55	100
Dec 2002	P	39439	2070	178715	59374	372	4772	1287	286029
	%*	13.79	0.72	62.48	20.76	0.13	1.67	0.45	100
Jan 2003	P	47796	2788	209087	69881	656	5736	2406	338349

	%*	14.13	0.82	61.80	20.65	0.19	1.70	0.71	100
Feb	P	41710	2283	180429	59827	502	4768	2340	291859
2003	%*	14.29	0.78	61.82	20.50	0.17	1.63	0.80	100
Mar	P	44328	2490	195017	64415	525	5215	2048	314038
2003	%*	14.12	0.79	62.10	20.51	0.17	1.66	0.65	100
Apr	P	43513	2400	189735	62321	487	5023	1670	305149
2003	%*	14.26	0.79	62.18	20.42	0.16	1.65	0.55	100

%* Is the quotient of frequency of pharmacological group and the total number of medicine items claimed multiplied by hundred

Table B.5 Prevalence of the different sub-pharmacological groups of hypolipidemic drugs claimed from May 2001 to April 2002

Months		Fibrates	Statins	"Others"	Total
May 2001	P	995	32428	507	33930
	%*	2.93	95.57	1.49	100
Jun 2001	P	816	26558	430	27804
	%*	2.93	95.52	1.55	100
Jul 2001	P	856	28590	436	29882
	%*	2.86	95.68	1.46	100
Aug 2001	P	1440	47235	671	49346
	%*	2.92	95.72	1.36	100
Sep 2001	P	1514	46689	581	48784
	%*	3.10	95.70	1.19	100
Oct 2001	P	1444	48257	549	50250
	%*	2.87	96.03	1.09	100
Nov 2001	P	1207	39577	473	41257
	%*	2.93	95.93	1.15	100
Dec 2001	P	1398	47455	508	49361
	%*	2.83	96.14	1.03	100
Jan 2002	P	1827	60832	860	63519
	%*	2.88	95.77	1.35	100
Feb 2002	P	1839	58108	816	60763
	%*	3.03	95.63	1.34	100
Mar 2002	P	1993	62960	818	65771
	%*	3.03	95.73	1.24	100
Apr 2002	P	2021	65473	875	68369
	%*	2.96	95.76	1.28	100

%* is the quotient of frequency of sub-pharmacological group and total number of hypolipidemic drugs claimed multiplied by hundred. "Others" refer to other hypolipidemic drugs as listed on paragraph 5.4.

Table B.6 Prevalence of the sub-pharmacological group of hypolipidemic drugs claimed from May 2002 to April 2003

Months		Fibrates	Statins	"Others"	Total
May 2002	P	895	28758	374	30027
	%*	2.98	95.77	1.25	100
Jun 2002	P	1861	60592	672	63125
	%*	2.95	95.99	1.06	100
Jul 2002	P	1920	63339	611	65870
	%*	2.91	96.16	0.93	100
Aug 2002	P	1871	64276	571	66718
	%*	2.80	96.34	0.85	100
Sep 2002	P	1584	58331	503	60418
	%*	2.62	96.55	0.83	100
Oct 2002	P	1690	59715	500	61905
	%*	2.73	96.46	0.81	100
Nov 2002	P	1725	56881	523	59129
	%*	2.92	96.20	0.88	100
Dec 2002	P	1642	57257	475	59374
	%*	2.77	96.43	0.80	100
Jan 2003	P	2013	67119	749	69881
	%*	2.88	96.05	1.07	100
Feb 2003	P	1619	57626	582	59827
	%*	2.71	96.32	0.97	100
Mar 2003	P	1639	62145	631	64415
	%*	2.54	96.48	0.98	100
Apr 2003	P	1662	59999	660	62321
	%*	2.67	96.27	1.06	100

%* is the quotient of frequency of sub-pharmacological group and total number of medicine items claimed multiplied by hundred. "Others" refer to other hypolipidemic drugs as listed on paragraph 5.4.

Table B.7 Prevalence of individual hypolipidemic drugs claimed from May 2001 to October 2001

Active ingredient	Drugs		May 2001		Jun 2001		Jul 2001		Aug 2001		Sep 2001		Oct 2001	
			P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
Cerivastatin	Baycol 0.1mg®	I	188	0.55	134	0.48	139	0.47	110	0.22	33	0.07	3	0.01
	Baycol 0.2mg®	I	1466	4.32	1273	4.58	1326	4.44	1164	2.36	151	0.31	70	0.14
	Baycol 0.3mg®	I	615	1.81	500	1.80	585	1.96	478	0.97	41	0.08	17	0.03
	Baycol 0.4mg®	I	429	1.26	413	1.49	542	1.81	554	1.12	59	0.12	27	0.05
Bezafibrate	Bezalip 200mg®	I	76	0.22	59	0.21	70	0.23	111	0.22	84	0.17	101	0.20
	Bezalip 400mg®	I	254	0.75	184	0.66	201	0.67	281	0.57	308	0.63	247	0.49
	Rolab bezafibrate 400mg®	G	188	0.55	180	0.65	163	0.55	363	0.74	440	0.90	433	0.86
Fluvastatin	Lescol 20mg®	I	939	2.77	782	2.81	843	2.82	1298	2.63	1399	2.87	1346	2.68
	Lescol 40mg®	I	7.71	2.27	611	2.20	632	2.11	1101	2.23	1163	2.38	1098	2.19
	Lescol XL 80mg®	I	0	0	0	0	0	0	0	0	0	0	0	0
Atorvastatin	Lipitor 10mg®	I	15718	46.3	12951	46.58	14112	47.2	24447	49.5	24896	51.03	26127	51.99
	Lipitor 20mg®	I	4983	14.7	3969	14.27	4227	14.2	7318	14.8	7643	15.67	7688	15.30
	Lipitor 40mg®	I	3	0.01	31	0.11	56	0.19	205	0.42	235	0.48	286	0.57
Clofibrate	Lipaten caps®	I	0	0	0	0	0	0	0	0	0	0	0	0
Essential phospholip	Lipostabil caps®	I	5	0.01	3	0.01	6	0.02	13	0.03	12	0.02	9	0.02
	Lipostabil 5ml®	I	2	0.01	2	0.01	1	0.00	9	0.09	3	0.01	1	0.00

Fenofibrate	Lipsin 300mg®	I	340	1.00	277	1.00	306	1.02	513	1.04	468	0.96	481	0.96
Gemfibrozil	Lopid 600mg®	I	137	0.40	116	0.42	116	0.39	172	0.35	214	0.44	182	0.36
Probucol	Lurselle®	I	62	0.18	40	0.14	44	0.15	90	0.18	89	0.18	94	0.19
Nicotinic acid	Nicotinic acid 30mg®	I	0	0	0	0	1	0.00	1	0.00	1	0.00	5	0.01
	Nicotinic acid BT®		37	0.11	42	0.15	72	0.24	76	0.15	55	0.11	75	0.15
Acipimox	Olbetam®	I	25	0.77	29	0.10	19	0.06	32	0.06	28	0.06	34	0.07
Pravastatin	Prava 10mg®	I	790	2.33	619	2.23	640	2.14	1158	2.35	1152	2.36	1191	2.37
	Prava 20mg®	I	728	2.15	573	2.06	599	2.00	1153	2.34	1209	2.48	1298	2.58
	Prava 40mg®	I	346	1.02	349	1.26	311	1.04	575	1.17	710	1.46	721	1.43
Cholestyramine	Questran lite®	I	376	1.11	314	1.13	293	0.98	450	0.91	393	0.81	331	0.66
Simvastatin	Adco-simvastatin 10mg®	G	0	0	0	0	0	0	0	0	0	0	0	0
	Adco-simvastatin 20mg®	G	0	0	0	0	0	0	0	0	0	0	0	0
	Adco-simvastatin 40mg®	G	0	0	0	0	0	0	0	0	0	0	0	0
	Zocor 10mg®	I	3093	9.12	2468	8.88	2638	8.83	4325	8.76	4528	9.28	4696	9.35
	Zocor 20mg®	I	2001	5.90	1594	5.73	1621	5.42	2771	5.62	2844	5.83	3017	6.00
	Zocor 40mg®	I	358	1.06	291	1.05	319	1.07	618	1.25	626	1.28	672	1.34
Total			33930	100	27804	100	29882	100	49346	100	48784	100	50250	100

%* The quotient of the frequency of individual hypolipidemic drugs and the total number of all hypolipidemic drugs multiplied by hundred

Table B.8 The prevalence of individual hypolipidemic drugs claimed from November 2001 to April 2002

Active ingredient	Drugs		Nov2001		Dec2001		Jan2002		Feb2002		Mar2002		Apr2002	
			P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
Cerivastatin	Baycol 0.1mg®	I	3	0.01	0	0	0	0	0	0	0	0	0	0
	Baycol 0.2mg®	I	21	0.05	23	0.05	6	0.01	4	0.01	0	0	0	0
	Baycol 0.3mg®	I	6	0.01	5	0.01	0	0	0	0	0	0	0	0
	Baycol 0.4mg®	I	7	0.02	2	0.00	2	0.00	0	0	0	0	0	0
Bezafibrate	Bezalip 200mg®	I	71	0.17	108	0.22	113	0.18	117	0.19	132	0.20	136	0.20
	Bezalip 400mg®	I	214	0.52	254	0.51	292	0.46	263	0.43	326	0.50	304	0.44
	Rolab bezafibrate 400mg®	G	370	0.90	416	0.84	608	0.96	628	1.03	734	1.12	713	1.04
Fluvastatin	Lescol 20mg®	I	1181	2.86	1336	2.71	1664	2.62	1632	2.69	1697	2.58	1732	2.53
	Lescol 40mg®	I	898	2.18	1087	2.20	1348	2.12	1350	2.22	1421	2.16	1485	2.17
	Lescol XL 80mg®	I	0	0	0	0	0	0	0	0	0	0	0	0
Clofibrate	Lipaten capsules®	I	0	0	0	0	8	0.01	0	0	0	0	0	0
Atorvastatin	Lipitor 10mg®	I	21809	52.86	25927	52.53	33006	51.96	31752	52.26	34559	52.54	35975	52.62
	Lipitor 20mg®	I	6048	14.66	7399	14.99	9889	15.57	9152	15.06	9948	15.13	10194	14.91
	Lipitor 40mg®	I	237	0.57	292	0.59	515	0.81	525	0.86	606	0.92	698	1.02
Essential phospho lipids	Lipostabil®	I	14	0.03	8	0.02	13	0.02	11	0.02	3	0.00	11	0.02

	Lipostabil 5ml®	I	2	0.00	3	0.01	14	0.02	5	0.01	11	0.02	12	0.02
Fenofibrate	Lipsin 300mg®	I	367	0.89	429	0.87	529	0.83	559	0.92	562	0.85	566	0.83
Gemfibrozil	Lopid 600mg®	I	185	0.45	191	0.39	277	0.44	272	0.45	239	0.36	302	0.44
Probucol	Lurselle®	I	87	0.21	73	0.15	101	0.16	106	0.17	104	0.16	89	0.13
Nicotinic acid	Nicotinic acid 30mg®	I	0	0	1	0.00	3	0.00	0	0	0	0	0	0
	Nicotinic acid (BT) ®	I	51	0.12	47	0.10	40	0.06	43	0.07	53	0.08	46	0.07
Acipimox	Olbetam®	I	20	0.05	33	0.07	23	0.03	24	0.04	29	0.04	26	0.04
Pravastatin	Prava 10mg®	I	1045	2.53	1215	2.46	1572	2.47	1440	2.37	1537	2.34	1711	2.50
	Prava 20mg®	I	1081	2.62	1328	2.69	1639	2.58	1692	2.78	1852	2.82	1911	2.80
	Prava 40mg®	I	565	1.37	740	1.50	990	1.56	985	1.62	1176	1.79	1238	1.81
Cholestyramine	Questran lite®	I	299	0.72	343	0.69	666	1.05	627	1.03	618	0.94	691	1.01
Simvastatin	Adco-simvastatin 10mg®	G	0	0	0	0	0	0	0	0	0	0	0	0
	Adco-simvastatin 20mg®	G	0	0	0	0	0	0	0	0	0	0	0	0
	Adco-simvastatin 40mg®	G	0	0	0	0	0	0	0	0	0	0	0	0
	Zocor 10mg®	I	3778	9.16	4622	9.36	5666	8.92	5263	8.66	5496	8.36	5736	8.39
	Zocor 20mg®	I	2363	5.73	2788	5.65	3661	5.76	3428	5.64	3723	5.66	3786	5.54
	Zocor 40mg®	I	535	1.30	691	1.40	874	1.38	885	1.46	945	1.44	1007	1.47

Total	41257	100	49361	100	63519	100	60763	100	65771	100	68369	100

%* The quotient of the frequency of individual hypolipidemic drugs and the total number of all hypolipidemic drugs multiplied by hundred

Table B.9 The prevalence of individual hypolipidemic drugs claimed from May 2002 to October 2002

Active ingredient	Drugs		May2002		Jun2002		Jul2002		Aug2002		Sep2002		Oct2002	
			P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
Cerivastatin	Baycol 0.1mg®	I	0	0	0	0	0	0	0	0	0	0	0	0
	Baycol 0.2mg®	I	0	0	0	0	0	0	0	0	0	0	0	0
	Baycol 0.3mg®	I	0	0	0	0	0	0	0	0	0	0	0	0
	Baycol 0.4mg®	I	0	0	0	0	0	0	0	0	0	0	0	0
Bezafibrate	Bezalip 200mg®	I	137	0.21	124	0.20	127	0.19	132	0.20	114	0.19	94	0.15
	Bezalip 400mg®	I	176	0.26	152	0.24	134	0.20	109	0.16	90	0.15	95	0.15
	Rolab bezafibrate 400mg®	G	862	1.29	847	1.34	904	1.37	915	1.37	760	1.26	844	1.36
Fluvastatin	Lescol 20mg®	I	1674	2.51	1580	2.50	1632	2.48	1623	2.43	1493	2.47	1490	2.41
	Lescol 40mg®	I	1384	2.08	1356	2.15	1404	2.13	1372	2.06	1221	2.02	1304	2.11
	Lescol XL 80mg®	I	0	0	0	0	0	0	0	0	33	0.05	344	0.56
Clofibrate	Lipaten capsules®	I	0	0	0	0	0	0	0	0	0	0	0	0
Atorvastatin	Lipitor 10mg®	I	35589	53.89	33749	53.46	35550	53.97	36415	54.58	33098	54.78	33801	54.60
	Lipitor 20mg®	I	9883	14.82	9265	14.68	9499	14.42	9559	14.33	8858	14.66	9017	14.57
	Lipitor 40mg®	I	733	1.10	749	1.19	799	1.21	880	1.32	845	1.40	964	1.56
Essential phospho lipids	Lipostabil®	I	5	0.01	8	0.01	7	0.01	4	0.01	5	0.01	4	0.01
	Lipostabil® 5ml	I	7	0.01	5	0.01	11	0.02	10	0.01	21	0.03	8	0.01

Fenofibrate	Lipsin 300mg®	I	504	0.76	464	0.74	492	0.75	471	0.71	408	0.68	457	0.74
Gemfibrozil	Lopid 600mg®	I	276	0.41	274	0.43	263	0.40	244	0.37	212	0.35	195	0.31
Probucol	Lurselle®	I	53	0.08	29	0.05	26	0.04	9	0.01	6	0.01	3	0.00
Nicotinic acid	Nicotinic acid 30mg®	I	0	0	0	0	3	0.00	6	0.01	3	0.01	2	0.00
	Nicotinic acid (BT)®	I	52	0.08	41	0.06	46	0.07	41	0.06	49	0.08	35	0.06
Acipimox	Olbetam®	I	37	0.06	38	0.06	34	0.05	25	0.04	30	0.05	28	0.05
Pravastatin	Prava 10mg®	I	1595	2.39	1539	2.44	1626	2.47	1589	2.38	1472	2.44	1469	2.37
	Prava 20mg®	I	1912	2.87	1818	2.88	2006	3.05	2021	3.03	1818	3.01	1894	3.06
	Prava 40mg®	I	1179	1.77	1141	1.81	1262	1.92	1290	1.93	1164	1.93	1154	1.86
Cholestyramine	Questran lite®	I	641	0.96	539	0.85	484	0.73	476	0.71	389	0.64	420	0.68
Simvastatin	Adco-simvastatin 10mg®	G	0	0	0	0	0	0	0	0	0	0	3	0.00
	Adco-simvastatin 20mg®	G	0	0	0	0	0	0	0	0	0	0	2	0.00
	Adco-simvastatin 40mg®	G	0	0	0	0	0	0	0	0	0	0	0	0
	Zocor 10mg®	I	5432	8.14	5165	8.18	5206	7.90	5150	7.72	4457	7.38	4448	7.19
	Zocor 20mg®	I	3578	5.36	3331	5.28	3418	5.19	3393	5.09	3019	5.00	2947	4.76
	Zocor 40mg®	I	982	1.47	899	1.42	937	1.42	984	1.47	853	1.41	883	1.43
Total			66692	100	63125	100	65870	100	66718	100	60418	100	61905	100

%* The quotient of the frequency of individual hypolipidemic drugs and the total number of all hypolipidemic drugs multiplied by hundred

Table B.10 The prevalence of individual hypolipidemic drugs claimed from November 2002 to April 2003

Active ingredient	Drugs		Nov2002		Dec2002		Jan2003		Feb2003		Mar2003		Apr2003	
			P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
Cerivastatin	Baycol 0.1mg®	I	0	0	0	0	0	0	0	0	0	0	0	0
	Baycol 0.2mg®	I	0	0	0	0	0	0	0	0	0	0	0	0
	Baycol 0.3mg®	I	0	0	0	0	0	0	0	0	0	0	0	0
	Baycol 0.4mg®	I	0	0	0	0	0	0	0	0	0	0	0	0
Bezafibrate	Bezalip 200mg®	I	102	0.17	97	0.16	152	0.22	120	0.20	123	0.19	96	0.15
	Bezalip 400mg®	I	79	0.13	80	0.13	76	0.11	57	0.10	47	0.07	40	0.06
	Rolab bezafibrate 400mg®	G	779	1.32	850	1.43	1009	1.44	833	1.39	865	1.34	921	1.48
Fluvastatin	Lescol 20mg®	I	1379	2.33	1359	2.29	1470	2.10	1243	2.08	1277	1.98	1180	1.89
	Lescol 40mg®	I	1196	2.02	1130	1.90	1352	1.93	1045	1.75	1160	1.80	1110	1.78
	Lescol XL 80mg®	I	843	1.43	1018	1.71	1517	2.17	1534	2.56	1687	2.62	1769	2.84
Clofibrate	Lipaten capsules®	I	0	0	0	0	0	0	0	0	0	0	0	0
Atorvastatin	Lipitor 10mg®	I	32131	54.34	32277	54.36	35951	51.45	30288	50.63	32403	50.30	30574	49.06
	Lipitor 20mg®	I	8339	14.19	8367	14.09	10353	14.82	8786	14.69	9326	14.48	8798	14.12
	Lipitor 40mg®	I	896	1.52	989	1.67	1395	2.00	1324	2.21	1335	2.07	1378	2.21
Essential Phospho lipids	Lipostabil®	I	4	0.01	0	0	2	0.00	2	0.00	0	0	0	0
	Lipostabil 5ml®	I	10	0.02	6	0.01	3	0.00	0	0	3	0.00	1	0.00

Fenofibrate	Lipsin 300mg®	I	412	0.70	439	0.74	524	0.75	424	0.71	440	0.68	421	0.68
GemfiBrozil	Lopid 600mg®	I	184	0.31	176	0.30	252	0.36	185	0.31	164	0.25	184	0.30
Probucol	Lurselle®	I	2	0.00	3	0.01	2	0.00	2	0.00	3	0.00	0	0
Nicotinic acid	Nicotinic acid 30mg®	I	2	0.00	3	0.01	7	0.01	3	0.01	0	0	0	0
	Nicotinic acid (BT)®	I	45	0.08	59	0.10	67	0.10	48	0.08	42	0.07	47	0.08
Acipimox	Olbetam®	I	32	0.05	32	0.05	32	0.05	13	0.02	18	0.03	33	0.05
Pravastatin	Prava 10mg®	I	1389	2.35	1347	2.27	1589	2.27	1286	2.15	1376	2.14	1317	2.11
	Prava 20mg®	I	1853	3.13	1782	3.00	2047	2.93	1760	2.94	1774	2.75	1742	2.80
	Prava 40mg®	I	1137	1.92	1144	1.93	1317	1.88	1174	1.96	1234	1.92	1194	1.92
Cholestyramine	Questran lite®	I	428	0.72	372	0.63	636	0.91	514	0.86	565	0.88	579	0.93
Simvastatin	Adco-simvastatin 10mg®	G	56	0.09	1492	2.51	2590	3.71	2299	3.84	2594	4.03	2708	4.35
	Adco-simvastatin 20mg®	G	72	0.12	1250	2.11	2286	3.27	2105	3.52	2630	4.08	2871	4.61
	Adco-simvastatin 40mg®	G	41	0.07	374	0.63	712	1.02	693	1.16	906	1.41	1006	1.61
	Zocor 10mg®	I	4244	7.18	2646	4.46	2503	3.58	2228	3.72	2472	3.84	2362	3.79
	Zocor 20mg®	I	2630	4.45	1583	2.67	1531	2.19	1355	2.26	1418	2.20	1472	2.36
	Zocor 40mg®	I	794	1.34	499	0.84	506	0.72	506	0.85	553	0.86	518	0.83
Total			59129	100	59374	100	69881	100	59827	100	64415	100	62321	100

%* The quotient of the frequency of individual hypolipidemic drugs and the total number of all hypolipidemic drugs multiplied by hundred

Table B.11 Frequency of hypolipidemic drugs according to active ingredients claimed from May 2001 to October 2001

		May2001		Jun2001		Jul2001		Aug2001		Sep2001		Oct2001	
		P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
Fibrates	Bezafibrate	518	1.53	423	1.52	434	1.45	755	1.53	832	1.71	781	1.55
	Clofibrate	0	0	0	0	0	0	0	0	0	0	0	0
	Fenofibrate	340	1.00	277	1.00	306	1.02	513	1.04	468	0.96	481	0.96
	Gemfibrozil	137	0.40	116	0.42	116	0.39	172	0.35	214	0.44	182	0.36
Statins	Atorvastatin	20704	61.02	16951	60.97	18395	61.56	31930	64.71	32774	67.18	34101	67.86
	Cerivastatin	2698	7.95	2320	8.34	2592	8.67	2306	4.67	284	0.58	117	0.23
	Fluvastatin	1710	5.04	1393	5.01	1475	4.94	2399	4.86	2562	5.25	2444	4.86
	Pravastatin	1864	5.49	1541	5.54	1550	5.19	2886	5.85	3071	6.30	3210	6.39
	Simvastatin	5452	16.07	4353	15.66	4578	15.32	7714	15.64	7998	16.39	8385	16.69
Others	Acipimox	25	0.07	29	0.10	19	0.06	32	0.04	28	0.06	34	0.07
	Cholestyramine	376	1.11	314	1.13	293	0.98	450	0.91	393	0.81	331	0.66
	Essential phospholipids	7	0.02	5	0.02	7	0.02	22	0.04	15	0.03	10	0.02
	Nicotinic acid	37	0.11	42	0.15	73	0.24	77	0.16	56	0.11	80	0.16
	Probucol	62	0.18	40	0.14	44	0.15	90	0.18	89	0.18	94	0.19
Total		33930	100	27804	100	29882	100	49346	100	48784	100	50250	100

%* Prevalence of the specific active ingredient divided by the total number of hypolipidemic drugs for that month multiplied by hundred

Table B.12 Frequency of hypolipidemic drugs according to active ingredients claimed from November 2001 to April 2002

		Nov2001		Dec2001		Jan2002		Feb2002		Mar2002		Apr2002	
		P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
Fibrates	Bezafibrate	655	1.59	778	1.58	1013	1.59	1008	1.66	1192	1.81	1153	1.69
	Clofibrate	0	0	0	0	8	0.01	0	0	0	0	0	0
	Fenofibrate	367	0.89	429	0.87	529	0.83	559	0.92	562	0.85	566	0.83
	Gemfibrozil	185	0.45	191	0.39	277	0.44	272	0.45	239	0.36	302	0.44
Statins	Atorvastatin	28094	68.10	33618	68.11	43410	68.34	41429	68.18	45113	68.59	46867	68.55
	Cerivastatin	37	0.09	30	0.06	8	0.01	4	0.01	0	0	0	0
	Fluvastatin	2079	5.04	2423	4.91	3012	4.74	2982	4.91	3118	4.74	3217	4.71
	Pravastatin	2691	6.52	3283	6.65	4201	6.61	4117	6.78	4565	6.94	4860	7.11
	Simvastatin	6676	16.18	8101	16.41	10201	16.06	9576	15.76	10164	15.45	10529	15.40
Others	Acipimox	20	0.05	33	0.07	23	0.04	24	0.04	29	0.04	26	0.04
	Cholestyramine	299	0.72	343	0.69	666	1.05	627	1.03	618	0.94	691	1.01
	Essential phospholipids	16	0.04	11	0.02	27	0.04	16	0.03	14	0.02	23	0.03
	Nicotinic acid	51	0.12	48	0.10	43	0.07	43	0.07	53	0.08	46	0.07
	Probucol	87	0.21	73	0.15	101	0.16	106	0.17	104	0.16	89	0.13
Total		41257	100	49361	100	63519	100	60763	100	65771	100	68369	100

%* Prevalence of the specific active ingredient divided by the total number of hypolipidemic drugs for that month multiplied by hundred

Table B.13 Frequency of hypolipidemic drugs according to active ingredients claimed from May 2002 to October 2002

		May 2002		Jun 2002		Jul 2002		Aug 2002		Sep 2002		Oct 2002	
		P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
Fibrates	Bezafibrate	1175	1.76	1123	1.78	1165	1.77	1156	1.73	964	1.60	1033	1.67
	Clofibrate	0	0	0	0	0	0	0	0	0	0	0	0
	Fenofibrate	504	0.76	464	0.74	492	0.75	471	0.71	408	0.68	457	0.74
	Gemfibrozil	276	0.41	274	0.43	263	0.40	244	0.37	212	0.35	195	0.31
Statins	Atorvastatin	46205	69.28	43763	69.33	45848	69.60	46854	70.23	42801	70.84	43782	70.72
	Cerivastatin	0	0	0	0	0	0	0	0	0	0	0	0
	Fluvastatin	3059	4.59	2936	4.65	3036	4.61	2995	4.49	2747	4.55	3138	5.07
	Pravastatin	4686	7.03	4498	7.13	4894	7.43	4900	7.34	4454	7.37	4517	7.30
	Simvastatin	9992	14.98	9395	14.88	9561	7.43	9527	14.28	8329	13.79	8283	13.38
Others	Acipimox	37	0.06	38	0.06	34	0.05	25	0.04	30	0.05	28	0.05
	Cholestyramine	641	0.96	539	0.85	484	0.73	476	0.71	389	0.64	420	0.68
	Essential phospholipids	12	0.02	13	0.02	18	0.03	14	0.02	26	0.04	12	0.02
	Nicotinic acid	52	0.08	53	0.08	49	0.07	47	0.07	52	0.09	37	0.06
	Probucol	53	0.08	29	0.05	26	0.04	9	0.01	6	0.01	3	0.00
Total		66692	100	63125	100	65870	100	66718	100	60418	100	61905	100

%* Prevalence of the specific active ingredient divided by the total number of hypolipidemic drugs for that month multiplied by hundred

Table B.14 Frequency of hypolipidemic drugs according to active ingredients claimed from November 2001 to April 2003

		Nov 2002		Dec 2002		Jan 2003		Feb 2003		Mar 2003		Apr 2003	
		P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
Fibrates	Bezafibrate	960	1.62	1027	1.73	1237	1.77	1010	1.69	1035	1.61	1057	1.70
	Clofibrate	0	0	0	0	0	0	0	0	0	0	0	0
	Fenofibrate	412	0.70	439	0.74	524	0.75	424	0.71	440	0.68	421	0.68
	Gemfibrozil	184	0.31	176	0.30	252	0.36	185	0.31	164	0.25	184	0.30
Statins	Atorvastatin	41416	70.04	41633	70.12	47699	68.26	40398	67.52	43064	66.85	40750	65.39
	Cerivastatin	0	0	0	0	0	0	0	0	0	0	0	0
	Fluvastatin	3418	5.78	3507	5.91	4339	6.21	3882	6.39	4124	6.40	4059	6.51
	Pravastatin	4379	7.41	4273	7.20	4953	7.09	4220	7.05	4384	6.81	4253	6.82
	Simvastatin	7837	13.25	7844	13.21	10128	14.49	9186	15.35	10573	16.41	10937	17.55
Others	Acipimox	32	0.05	32	0.05	32	0.05	13	0.02	18	0.03	33	0.05
	Cholestyramine	428	0.72	372	0.63	636	0.91	514	0.86	565	0.88	579	0.93
	Essential Phospholipids	14	0.02	6	0.01	5	0.01	2	0.00	3	0.00	1	0.00
	Nicotinic acid	47	0.08	62	0.10	74	0.11	51	0.09	42	0.07	47	0.08
	Probucol	2	0.00	3	0.01	2	0.00	2	0.00	3	0.00	0	0
Total		59129	100	59374	100	69881	100	59827	100	64415	100	62321	100

%* Prevalence of the specific active ingredient divided by the total number of hypolipidemic drugs for that month multiplied by hundred

Table B.15 Prevalence of the innovator and generic drugs of the different pharmacological groups in the main pharmacological group: cardiovascular drugs claimed from May 2001 to October 2001

		May 2001		Jun 2001		Jul 2001		Aug 2001		Sep 2001		Oct 2001	
		P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
Antianginal drugs	I	8594	31.88	6829	30.73	7214	30.30	11468	30.18	11015	30.12	10912	29.23
	G	18366	68.12	15395	69.27	16593	69.70	26526	69.82	25553	69.88	26417	70.77
Antiarrhythmic drugs	I	964	75.85	752	69.31	793	69.81	1493	71.78	1282	68.16	1333	65.34
	G	307	24.15	333	30.69	343	30.19	587	28.22	599	31.84	707	34.66
Antihypertensive drugs	I	91432	86.60	74813	86.15	80051	85.75	128788	84.90	125540	84.64	127647	84.58
	G	14151	13.40	12030	13.85	13303	14.25	22902	15.10	22784	15.36	23276	15.42
Hypolipidemic drugs	I	33742	99.45	27624	99.35	29719	99.45	48983	99.47	48344	99.10	49817	99.14
	G	188	0.55	180	0.65	163	0.55	363	0.53	440	0.90	433	0.86
Other vasodilators	I	671	100	512	100	782	100	804	100	548	100	600	100
	G	0	0	0	0	0	0	0	0	0	0	0	0
+ inotropic drugs	I	2797	79.17	2126	77.51	2365	79.60	3796	78.80	3713	77.78	3862	78.77
	G	736	20.83	617	22.49	606	20.40	1021	21.20	1061	22.22	1041	21.23
Vasoconstrictors	I	1183	100	863	100	810	100	1452	100	1335	100	1445	100
	G	0	0	0	0	0	0	0	0	0	0	0	0

%* Prevalence of either the innovator or generic drugs divided by the total number of all items for the particular pharmacological group claimed per month multiplied by hundred

Table B.16 The prevalence of the innovator and generic drugs of the different pharmacological groups in the main pharmacological group: cardiovascular drugs claimed from November 2001 to April 2002

		Nov 2001		Dec 2001		Jan 2002		Feb 2002		Mar 2002		Apr 2002	
		P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
Antianginal drugs	I	8871	29.91	9964	27.96	13378	28.29	12575	28.14	13383	28.00	13303	27.14
	G	21741	71.02	25676	72.04	33915	71.71	32106	71.86	34413	72.00	35708	72.86
Antiarrhythmic drugs	I	992	62.35	1085	60.21	1647	59.07	1597	60.56	1651	57.78	1624	57.90
	G	599	37.65	717	39.79	1141	40.93	1040	39.44	1207	42.23	1181	42.10
Antihypertensive drugs	I	104844	84.17	125180	84.07	158124	83.54	149991	83.37	162749	83.48	166820	83.39
	G	19714	15.83	23714	15.93	31162	16.46	29912	16.63	32203	16.52	33223	16.61
Hypolipidemic drugs	I	40887	99.10	48954	99.18	62911	99.04	60135	98.97	65037	98.88	67656	98.96
	G	370	0.90	416	0.82	608	0.96	628	1.03	734	1.12	713	1.04
Other vasodilators	I	403	100	408	100	945	100	701	100	754	100	705	100
	G	0	0	0	0	0	0	0	0	0	0	0	0
+ inotropic drugs	I	3238	79.11	3670	80.00	4765	79.05	4481	79.24	4631	78.16	4871	78.83
	G	855	20.89	917	20.00	1263	20.95	1174	20.76	1294	21.84	1303	21.17
Vasoconstrictors	I	1092	100	1257	100	2598	100	2476	100	2271	100	1938	100
	G	0	0	0	0	0	0	0	0	0	0	0	0

%* Prevalence of either the innovator or generic drugs divided by the total number of all items for the particular pharmacological group claimed per month multiplied by hundred

Table B.17 Prevalence of the innovator and generic drugs of the different pharmacological groups in the main pharmacological group: cardiovascular drugs claimed from May 2002 to October 2002

		May2002		Jun2002		Jul2002		Aug2002		Sep2002		Oct2002	
		P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
Antianginal drugs	I	5423	24.99	10450	23.24	10680	22.62	10578	22.41	9366	22.23	9136	21.41
	G	16278	75.01	34510	76.76	36537	77.38	36623	77.59	32758	77.77	33540	78.59
Antiarrhythmic drugs	I	706	57.21	1447	56.26	1452	56.24	1404	55.60	1294	57.43	1187	54.45
	G	528	42.79	1125	43.74	1130	43.76	1121	44.40	959	42.57	993	45.55
Antihypertensive drugs	I	72259	82.12	153948	82.41	161685	81.95	164032	81.76	148759	84.61	152071	81.41
	G	15738	17.88	32849	17.59	35600	18.05	36588	18.24	33708	15.39	34729	18.59
Hypolipidemic drugs	I	29626	98.66	62278	98.66	64966	98.63	65803	98.63	59658	98.74	61056	98.63
	G	401	1.34	847	1.34	904	1.37	915	1.37	760	1.26	849	1.37
Other vasodilators	I	339	100	830	100	970	100	661	100	560	100	557	100
	G	0	0	0	0	0	0	0	0	0	0	0	0
+ inotropic drugs	I	2090	79.74	4407	78.49	4681	78.73	4574	77.86	3783	76.27	3964	76.38
	G	531	20.26	1208	21.51	1265	21.27	1301	22.14	1177	23.73	1226	23.62
Vasoconstrictors	I	818	100	1393	100	1451	100	1557	100	1415	100	1744	100
	G	0	0	0	0	0	0	0	0	0	0	0	0

%* Prevalence of either the innovator or generic drugs divided by the total number of all items for the particular pharmacological group claimed per month multiplied by hundred

Table B.18 Prevalence of the innovator and generic drugs of the different pharmacological groups in the main pharmacological group: cardiovascular drugs claimed from November 2002 to April 2003

		Nov 2002		Dec 2002		Jan 2003		Feb 2003		Mar 2003		Apr 2003	
		P	%*	P	%*	P	%*	P	%*	P	%*	P	%*
Antianginal drugs	I	8794	21.86	8352	21.18	10744	22.48	8977	21.52	9085	20.49	8991	20.66
	G	31440	78.14	31087	78.82	37052	77.52	32733	78.48	35243	79.51	34522	79.34
Antiarrhythmic drugs	I	1152	54.52	1141	55.12	1400	50.22	1125	49.28	1236	49.64	1169	48.71
	G	961	45.48	929	44.88	1388	49.78	1158	51.72	1254	50.36	1231	51.29
Antihypertensive drugs	I	144988	81.25	145061	81.17	168857	80.76	145465	80.62	156843	80.43	151969	80.10
	G	33449	18.75	33654	18.83	40230	19.24	34964	19.38	38174	19.57	37766	19.90
Hypolipidemic drugs	I	58181	98.40	55408	93.32	63284	90.56	53897	90.09	57420	89.14	54815	87.96
	G	948	1.60	3966	6.68	6597	9.44	5930	9.91	6995	10.86	7506	12.04
Other vasodilators	I	488	100	372	100	656	100	502	100	525	100	487	100
	G	0	0	0	0	0	0	0	0	0	0	0	0
+ inotropic drugs	I	3673	77.70	3732	78.21	4533	79.03	3685	77.29	4110	78.81	3876	77.17
	G	1054	22.30	1040	21.79	1203	20.97	1083	22.71	1105	21.19	1147	22.83
Vasoconstrictors	I	1585	100	1287	100	2405	100	2340	100	2048	100	1670	100
	G	0	0	0	0	0	0	0	0	0	0	0	0

%* Prevalence of either the innovator or generic drugs divided by the total number of all items for the particular pharmacological group claimed per month multiplied by hundred

Table B.19 Prevalence of the innovator and generic drugs of hypolipidemic drugs from May 2001 to April 2002

Months		Fibrates		Statins		"Others"	
		I	G	I	G	I	G
May	P	807	188	32428	0	507	0
2001	%*	81.11	18.89	100	0	100	0
Jun	P	636	180	26558	0	430	0
2001	%*	77.94	22.06	100	0	100	0
Jul	P	693	163	28590	0	436	0
2001	%*	80.96	19.04	100	0	100	0
Aug	P	1077	363	47235	0	671	0
2001	%*	74.79	25.21	100	0	100	0
Sep	P	1074	440	46689	0	581	0
2001	%*	70.94	29.06	100	0	100	0
Oct	P	1011	433	48257	0	549	0
2001	%*	70.01	29.99	100	0	100	0
Nov	P	837	370	39577	0	473	0
2001	%*	69.35	30.65	100	0	100	0
Dec	P	982	416	47455	0	508	0
2001	%*	70.50	29.50	100	0	100	0
Jan	P	1219	608	60832	0	860	0
2002	%*	66.72	33.28	100	0	100	0
Feb	P	1211	628	58108	0	816	0
2002	%*	65.85	34.15	100	0	100	0
Mar	P	1259	734	62960	0	818	0
2002	%*	63.17	36.83	100	0	100	0
Apr	P	1308	713	65473	0	875	0
2002	%*	64.72	35.28	100	0	100	0

%* Prevalence of either generic or innovator drugs divided by total number of hypolipidemic drugs multiplied by hundred. "Others" refer to other hypolipidemic drugs as listed on paragraph 5.4.

Table B.20 Prevalence of the innovator and generic drugs of hypolipidemic drugs from May 2002 to April 2003

Months		Fibrates		Statins		Others	
		I	G	I	G	I	G
May 2002	P	494	401	28758	0	374	0
	%*	55.20	44.80	100	0	100	0
Jun 2002	P	1014	847	60592	0	672	0
	%*	54.49	45.51	100	0	100	0
Jul 2002	P	1016	904	63339	0	611	0
	%*	52.92	47.08	100	0	100	0
Aug 2002	P	956	915	64276	0	571	0
	%*	51.10	48.90	100	0	100	0
Sep 2002	P	824	760	58331	0	503	0
	%*	52.02	47.98	100	0	100	0
Oct 2002	P	841	849	59715	0	500	0
	%*	49.76	50.24	100	0	100	0
Nov 2002	P	777	948	56881	0	523	0
	%*	45.04	54.96	100	0	100	0
Dec 2002	P	792	850	54141	3116	475	0
	%*	48.23	51.77	94.56	5.44	100	0
Jan 2003	P	1004	1009	61531	5588	749	0
	%*	49.88	50.12	91.67	8.33	100	0
Feb 2003	P	786	833	52529	5097	582	0
	%*	48.55	51.45	91.16	8.84	100	0
Mar 2003	P	774	865	56015	6130	631	0
	%*	47.22	52.78	90.14	9.86	100	0
Apr 2003	P	741	921	53414	6585	660	0
	%*	44.58	55.42	89.02	10.98	100	0

%* Prevalence of either generic or innovator drugs divided by total number of hypolipidemic drugs multiplied by hundred. "Others" refer to other hypolipidemic drugs as listed on paragraph 5.4.

APPENDIX C

Table C.1 Average cost of medicine items according to the different pharmacological groups of the cardiovascular drugs claimed from May 2001 to October 2001

		May 2001	Jun 2001	Jul 2001	Aug 2001	Sep 2001	Oct 2001
Total number of items (R)	+ inotropic drugs	3533	2743	2971	4817	4774	4903
	Antiarrythmic drugs	1271	1085	1136	2080	1881	2040
	Antihypertensive drugs	105583	86843	93354	151690	148324	150923
	Antianginal drugs	26960	22224	23807	37994	36568	37329
	Other vasodilators	671	512	782	804	548	600
	Vaso-constrictors	1183	863	810	1452	1335	1445
	Hypolipidemic drugs	33930	27804	29882	49346	48784	50250
Average cost and Standard deviation (R)	+ inotropic drugs	13.59 ± 6.70	13.70 ± 7.40	14.01 ± 8.95	13.75 ± 7.83	13.49 ±7.47	13.35±6.38
	Antiarrythmic drugs	369.36 ± 254.42	361.94 ±253.07	361.77 ±267.70	378 ± 230.82	365.79 ±228.09	344.83±225.43
	Antihypertensive drugs	210.18 ± 90.40	210.11 ±90.45	209.81 ±90.87	208.70 ±90.93	209.07 ±90.48	209.12±89.85
	Antianginal drugs	121.28 ± 80.33	122.14 ± 9.67	121.40 ±76.61	121.13 ±80.18	122.00 ±80.74	124.15±80.62
	Other vasodilators	326.29 ± 197.98	334.97 ±210.63	288.35 ±189.56	324.49 ±192.61	338.92 ±195.59	334.35±198.35

	Vaso-constrictors	153.39 ± 76.96	148.93 ±74.63	146.36 ±80.25	141.75 ±75.16	149.36 ±72.14	150.08±78.74
	Hypolipidemic drugs	322.04 ± 99.51	325.19 ±91.24	326.15 ±95.76	329.64 ±92.51	331.73 ±91.68	330.97±86.46
Total cost (R)	+ inotropic drugs	48030.82	37591.28	41615.26	66237	64398.67	65475.70
	Antiarrythmic drugs	469452.38	392702.66	410967.42	786738	688042.11	703454.78
	Antihypertensive drugs	22191207.79	18246645.56	19586985.20	31657485.98	31009590.49	31560856.83
	Antianginal drugs	32690715.53	2714378.62	2890141.84	4612246.05	4461609.50	4634560.15
	Other vasodilators	218940.13	171506.26	225493.10	260886.56	185730.39	200612.00
	Vaso-constrictors	181464.32	128524.37	118552.56	205820.12	199396.25	216868.06
	Hypolipidemic drugs	10926921.30	904159.73	9746284.96	16266345.60	16183259.02	16631320.20

Table C.2 Average cost of medicine items according to the different pharmacological groups of cardiovascular drugs claimed from November 2001 to April 2002

		Nov 2001	Dec 2001	Jan 2002	Feb 2002	Mar 2002	Apr 2002
Total number of items (R)	+ inotropic drugs	4093	4587	6028	5655	5925	6179
	Antiarrythmic drugs	1591	1802	2788	2637	2858	2805
	Antihypertensive drugs	124558	148894	189286	179903	194952	200043
	Antianginal drugs	30612	35640	47293	44681	47796	49011
	Other vasodilators	403	408	945	701	754	705
	Vaso-constrictors	1092	1257	2598	2476	2271	1938
	Hypolipidemic drugs	41257	49361	63519	60763	65771	38369
Average cost and Standard deviation (R)	+ inotropic drugs	13.90±7.22	14.21 ±8.18	14.03 ±8.18	14.40 ±10.16	14.47 ±9.6	14.31 ±7.65
	Antiarrythmic drugs	350.40±218.31	351.08 ±228.09	350.18 ±224.90	353.19 ±238.31	400.82 ±194.64	413.24 ±186.51
	Antihypertensive drugs	208.61±90.30	210.20 ±87.11	216.55 ±89.19	218.11 ±89.53	216.24 ±92.15	217.87 ±92.79
	Antianginal drugs	124.88±80.83	125.49 ±81.82	123.77 ±84.98	127.68 ±88.44	131.42 ±92.	134.16 ±93.62
	Other vasodilators	346.12±195.19	368.26 ±218.34	384.62 ±232.82	404.60 ±239.86	382.38 ±226.99	412.93 ±249.63
	Vaso-constrictors	153.07±74.45	157.06 ±74.33	161.91 ±82.81	157.52 ±81.77	170.81 ±87.97	174.34 ±93.61
	Hypolipidemic agents	330.30±86.11	330.73 ±87.16	333.09 ±88.45	336.08 ±88.64	341.98 ±90.16	340.18 ±89.43

Total cost (R)	+ inotropic drugs	56880.25	65191.18	84590	81450.10	85760.85	88445.98
	Antiarrythmic drugs	557489.32	632654.94	976298.96	931360.80	1145552.41	1159150.52
	Antihypertensive drugs	25984523.71	31297540.77	40989254.54	39238728.03	42155919.07	43584306.70
	Antianginal drugs	3822702.30	4472515.09	5853266.83	5704849.29	6281542.11	6575522.90
	Other vasodilators	139480.70	150249.08	363462.82	283622.73	288318.23	291114.33
	Vaso-constrictors	167156.96	197423.05	420637.72	390030.70	387903.36	337871.04
	Hypolipidemic drugs	13627130.63	16325039.08	21157235.95	20421149.75	22492220.33	23257550.41

Table C.3 Average cost of medicine items according to the different pharmacological groups of cardiovascular drugs claimed from May 2002 to October 2002

		May 2002	Jun 2002	Jul 2002	Aug 2002	Sep 2002	Oct 2002
Total number of items (R)	+ inotropic drugs	2621	5615	5946	5875	4960	5190
	Antiarrythmic drugs	1234	2572	2582	2525	2253	2180
	Antihypertensive drugs	87997	186797	197285	200620	182467	186800
	Antianginal drugs	21701	44960	47217	47201	42124	42676
	Other vasodilators	339	830	970	661	560	557
	Vaso-constrictors	818	1393	1451	1557	1415	1744
	Hypolipidemic drugs	30027	63125	65870	66718	60418	61905
Average cost and Standard deviation (R)	+ inotropic drugs	14.94 ± 9.95	15.17 ±10.14	15.07 ±10.80	15.38 ±12.75	15.09 ±10.88	15.54 ±15.19
	Antiarrythmic drugs	417.18 ±174.94	409.02 ±175.23	412.15 ±179.77	405.20 ±170.76	406.73 ±165.75	411.46 ±171.36
	Antihypertensive drugs	215.14 ±92.11	216.12 ±91.04	214.98 ±90.63	214.57 ±89.87	215.32 ±90.71	215.98 ±90.93
	Antianginal drugs	129.61 ±87.71	129.70 ±86.79	129.42 ±86.43	125.89 ±80.56	125.30 ±81.17	123.33 ±79.59
	Other vasodilators	408.44 ±236.04	439.22 ±250.61	391.64 ±236.44	416.18 ±232.82	418.81 ±230.93	418.41 ±231.41
	Vaso-constrictors	172.41 ±85.94	174.33 ±92.64	170.92 ±87.09	168.70 ±93.76	182.66 ±99.77	174.19 ±92.12
	Hypolipidemic drugs	339.54 ±87.90	339.70 ±86.12	338.90 ±84.58	337.84 ±83.86	338.08 ±81.73	337.14 ±81.68

Total cost (R)	+ inotropic drugs	39180.87	85203.60	89625.23	90396.72	74866.01	80648.47
	Antiarrythmic drugs	514798.68	1052009.86	1064167.55	1023121.41	916355.28	896983.78
	Antihypertensive drugs	18931813.18	40370311.85	42411844.30	43046398.05	39288160.43	40344361.54
	Antianginal drugs	2812569.15	5831341.09	6110590.84	5942069.37	5278172.48	5263039.65
	Other vasodilators	138462.22	364553.92	379887.89	275091.68	234535.51	233055.71
	Vaso-constrictors	141031.42	242835.68	247999.71	262672.36	258458.69	303779.08
	Hypolipidemic drugs	10195489.10	21443714.22	22323123.39	22540037.17	20426407.64	20870923.58

Table C.4 Average cost of medicine items according to different the different pharmacological groups of cardiovascular drugs claimed from November 2002 to April 2003

		Nov 2002	Dec 2002	Jan 2003	Feb 2003	Mar 2003	Apr2003
Total number of items (R)	+ inotropic drugs	4727	4772	5736	4768	5215	5023
	Antiarrythmic drugs	2113	2070	2788	2283	2490	2400
	Antihypertensive drugs	178437	178715	209087	180429	195017	189735
	Antianginal drugs	40234	39439	47796	41710	44328	43513
	Other vasodilators	488	372	656	502	525	487
	Vaso-constrictors	1585	1287	2405	2340	2048	1670
	Hypolipidemic drugs	59129	59374	69881	59827	64415	62321
Average cost and Standard deviation (R)	+ inotropic drugs	15.48 ±11.18	15.75 ±10.04	16.01 ±9.80	16.33 ±10.21	16.56 ±14.01	16.25 ±9.94
	Antiarrythmic drugs	421.99 ±182.77	411.96 ±169.55	417.27 ±181.07	423.26 ±196.24	409.51 ±180.83	387.37 ±204.97
	Antihypertensive drugs	216.81 ±90.80	218.79 ±92.70	224.47 ±96.23	225.20 ±95.20	225.07 ±95.06	223.82 ±95.69
	Antianginal drugs	125.41 ±79.64	127.47 ±80.99	127.24 ±80.63	125.06 ±80.64	124.10 ±79.92	123.22 ±79.83
	Other vasodilators	448.43 ±246.88	499.87 ±265.42	451.59 ±245.61	478.01 ±271.59	461.96 ±235.20	457.88 ±229.64
	Vaso-constrictors	179.84 ±92.14	176.73 ±96.25	179.47 ±93.57	177.62 ±94.64	184.85 ±98.23	182.19 ±92.91
	Hypolipidemic drugs	335.43 ±81.42	329.67 ±92.96	329.52 ±100.58	325.64 ±105.31	322.73 ±107.89	320.41 ±105.86

Total cost (R)	+ inotropic drugs	73155.70	75144.54	91868.53	77847.22	86334.42	81632.59
	Antiarrythmic drugs	891674.54	852765.48	1163347.15	966306.94	1019687.50	929691.92
	Antihypertensive drugs	38687537.34	39101770.22	46934244.83	40632659.29	43892259.22	42465727.54
	Antianginal drugs	5045734.92	5027126.77	6081636.76	5216285.52	5501120.32	5361534.23
	Other vasodilators	218833.33	185957.36	296246.02	239960.60	242528.08	222987.33
	Vaso-constrictors	285044.85	227455.38	431635.19	415633.25	378573.07	304253.63
	Hypolipidemic drugs	19833709.91	19574011.71	23026915.94	19481865.79	20788639.41	19968138.27

Table C.5 Average cost of the different sub-pharmacological groups of hypolipidemic drugs claimed from May 2001 to October 2001

		May 2001	Jun 2001	Jul 2001	Aug 2001	Sep 2001	Oct 2001
Total number of items	Fibrates	995	816	856	1440	1514	1444
	Statins	32428	26558	28590	47235	46689	48257
	"Others"	507	430	436	671	581	549
Average cost (R)	Fibrates	308.83	312.01	327.10	314.76	307.08	316.68
	Statins	324.26	328.16	328.47	331.83	334.01	332.88
	"Others"	206.25	166.72	172.58	207.29	212.96	200.81
Standard deviation (R)	Fibrates	124.15	137.82	145.36	125.06	115.12	112.63
	Statins	94.37	85.13	89.74	88.03	87.93	82.50
	"Others"	221.13	169.70	187.14	186.04	183.99	186.84
Total cost (R)	Fibrates	307283.27	254597.02	279996.72	453249.84	464925.98	457284.04
	Statins	10515070.99	8715307.93	9391044.72	15674001.86	15594605.22	16063793.81
	"Others"	104567.04	71687.78	75243.52	139093.90	123727.82	110242.35

"Others" refer to other hypolipidemic drugs as listed on paragraph 5.4.

Table C.6 Average cost of the different sub-pharmacological groups of hypolipidemic drugs claimed from November 2001 to April 2002

		Nov 2001	Dec 2001	Jan 2002	Feb 2002	Mar 2002	Apr 2002
Total number of items	Fibrates	1207	1398	1827	1839	1993	2021
	Statins	39577	47455	60832	58108	62960	65473
	"Others"	473	508	860	816	818	875
Average cost (R)	Fibrates	327.46	322.91	338.04	350.34	357.49	356.93
	Statins	331.72	332.17	335.01	337.38	343.08	341.53
	"Others"	218.88	217.25	186.58	211.18	219.66	200.21
Standard deviation (R)	Fibrates	123.50	115.58	135.42	139.96	134.21	130.28
	Statins	82.17	83.60	82.60	82.51	84.35	83.96
	"Others"	174.15	188.24	186.01	200.15	215.70	194.62
Total cost (R)	Fibrates	395245.31	451423.16	617607.73	644268.87	712468.05	721364.78
	Statins	13128353.94	15763252.93	20379173.10	19604559.52	21600071.50	22361003.78
	"Others"	103531.38	110362.99	160455.12	172321.36	179680.78	175181.85

"Others" refer to other hypolipidemic drugs as listed on paragraph 5.4.

Table C.7 Average cost of the different sub-pharmacological groups of hypolipidemic drugs claimed from May 2002 to October 2002

		May 2002	Jun 2002	Jul 2002	Aug 2002	Sep 2002	Oct 2002
Total number of items	Fibrates	1955	1861	1920	1871	1584	1690
	Statins	63942	60592	63339	64276	58331	59715
	"Others"	795	672	611	571	503	500
Average cost (R)	Fibrates	329.95	334.79	336.82	336.89	339.45	341.05
	Statins	341.88	341.57	340.35	339.23	339.31	338.30
	"Others"	171.43	184.94	194.34	185.01	192.19	186.04
Standard deviation (R)	Fibrates	123.42	128.79	130.21	131.89	127.21	137.67
	Statins	81.53	81.29	80.12	79.66	77.90	77.22
	"Others"	174.73	175.24	177.60	163.86	162.01	164.25
Total cost (R)	Fibrates	645045.01	623042.57	646685.11	630327.63	537687.63	576371.88
	Statins	21860465.79	20696389.47	21557696.06	21804066.99	19792046.94	20201530.92
	"Others"	136286.76	124282.18	118742.22	105642.55	96673.07	93020.78

"Others" refer to other hypolipidemic drugs as listed on paragraph 5.4.

Table C.8 Average cost of the different sub-pharmacological groups of hypolipidemic drugs claimed from November 2002 to April 2003

		Nov 2002	Dec 2002	Jan 2003	Feb 2003	Mar 2003	Apr 2003
Total number of items	Fibrates	1725	4758	7601	1619	1639	1662
	Statins	56881	54141	61531	57626	62145	59999
	"Others"	523	475	749	582	631	660
Average cost (R)	Fibrates	350.11	258.03	240.57	368.30	366.58	369.19
	Statins	336.55	337.30	342.64	326.23	323.30	320.95
	"Others"	165.15	177.52	153.68	147.78	155.68	147.88
Standard deviation (R)	Fibrates	138.78	116.80	115.88	140.22	142.51	146.07
	Statins	76.28	85.71	89.54	101.52	104.34	101.80
	"Others"	152.66	158.18	153.80	167.85	174.23	162.61
Total cost (R)	Fibrates	603939.81	1227718.76	1828603.12	596275.68	600818.19	613592.9
	Statins	19143396.53	18261972.23	21083204.58	18799581.02	20089586.5	19256942.4
	"Others"	86373.57	84320.72	115108.24	86009.09	98234.72	97602.97

"Others" refer to other hypolipidemic drugs as listed on paragraph 5.4.

Table C.9 Average cost of hypolipidemic drugs claimed per prescription from May 2001 to April 2002

Months	Total no of prescriptions	Average cost (R)	Standard deviation (R)	Minimum cost (R)	Maximum cost (R)	Median (R)	Total cost (R)
May 2001	33552	325.67	108.18	0.77	3466.82	311.79	10926921.30
Jun 2001	27502	328.76	99.77	0.36	1820.85	321.08	9041592.73
Jul 2001	29599	329.28	104.06	2.10	1823.03	321.08	9746284.96
Aug 2001	48889	332.72	99.65	0.43	1821.04	321.08	16266345.60
Sep 2001	48300	335.06	100.28	0.36	1821.15	321.08	16183259.02
Oct 2001	49769	334.17	94.26	1.60	1821.04	312.08	16631320.20
Nov 2001	40887	333.29	94.39	1.60	2043.77	321.09	13627130.63
Dec 2001	48950	333.50	94.68	0.68	1821.04	321.09	16325039.08
Jan 2002	62944	336.13	97.19	1.60	1823.20	321.09	21157235.95
Feb 2002	60212	339.15	97.86	0.09	1837.74	321.09	20421149.75
Mar 2002	65205	344.95	99.02	1.47	2193.96	333.84	22492220.33
Apr 2002	67799	343.04	98.36	0.09	3276.40	333.84	23257550.41

Table C.10 Average cost of hypolipidemic drugs claimed per prescription from May 2002 to May 2003

Months	Total no of prescriptions	Average cost (R)	Standard deviation (R)	Minimum cost (R)	Maximum cost (R)	Median (R)	Total cost (R)
May 2002	66161	342.22	94.30	1.84	2179.01	333.84	22641797.56
Jun 2002	62610	342.50	93.70	1.63	1893.78	333.84	21443714.22
Jul 2002	65389	341.40	91.45	0.09	1848.32	333.84	22323123.39
Aug 2002	66203	340.47	91.69	1.47	1893.74	333.84	22540037.17
Sep 2002	59955	340.70	89.30	0.22	1637.21	333.84	20426407.64
Oct 2002	61434	339.73	89.01	0.30	1637.21	333.84	20870923.58
Nov 2002	58710	337.83	88.50	1.47	1665.03	333.84	19833709.91
Dec 2002	58947	332.06	99.14	1.61	1744.49	333.84	19574011.71
Jan 2003	69350	332.04	107.72	1.61	1784.16	340.39	23026915.94
Feb 2003	59449	327.71	111.05	1.00	2321.43	340.35	19481865.79
Mar 2003	64002	324.81	113.46	1.00	4184.04	330.26	20788639.41
Apr 2003	61932	322.42	112.10	1.00	2498.98	325.06	19968138.27

Table C.11 Average cost per number of hypolipidemic drugs from May 2001 to April 2002

Months	Total no of items	Average cost (R)	Standard deviation (R)	Minimum cost (R)	Maximum cost (R)	Median (R)	Total cost (R)
May 2001	33930	322.04	99.51	0.77	3466.82	311.79	10926921.30
Jun 2001	27804	325.19	91.24	0.36	1820.85	321.08	9041592.73
Jul 2001	29882	326.16	95.76	2.10	1823.03	321.08	9746284.96
Aug 2001	49346	329.64	92.51	0.43	1821.04	321.08	16266345.60
Sep 2001	48784	331.73	91.68	0.36	1821.15	321.08	16183259.02
Oct 2001	50250	330.97	86.46	1.60	1821.04	321.08	16631320.20
Nov 2001	41257	330.30	86.11	1.60	1932.80	321.08	13627130.63
Dec 2001	49361	330.73	87.16	0.68	1821.04	321.09	16325039.08
Jan 2002	63519	333.09	88.45	1.60	1823.20	321.09	21157235.95
Feb 2002	60763	336.08	88.64	0.09	1823.20	321.09	20421149.75
Mar 2002	65771	341.98	90.16	1.47	2193.96	333.84	22492220.33
Apr 2002	68369	340.18	89.43	0.09	3276.40	333.84	232575550.41

Table C.12 Average cost per number of hypolipidemic drugs from May 2002 to May 2003

Months	Total no of items	Average cost (R)	Standard deviation (R)	Minimum cost (R)	Maximum cost (R)	Median (R)	Total cost (R)
May 2002	66692	339.50	86.77	1.84	1893.74	333.84	22641797.56
Jun 2002	63125	339.70	86.12	1.63	1893.78	333.84	21443714.22
Jul 2002	65870	338.90	84.58	0.09	1848.32	333.84	22323123.39
Aug 2002	66718	337.84	83.84	1.47	1893.74	333.84	22540037.17
Sep 2002	60418	338.08	81.73	0.22	1329.59	333.84	20426407.64
Oct 2002	61905	337.14	81.68	0.30	1420.78	333.84	20870923.58
Nov 2002	59129	335.43	81.42	1.47	1316.98	333.84	19833709.91
Dec 2002	59374	329.67	92.96	1.61	1744.49	333.84	19574011.71
Jan 2003	69881	329.52	100.58	1.61	1382.74	340.35	23026915.94
Feb 2003	59827	325.64	105.31	1.00	2321.43	340.15	19481865.79
Mar 2003	64415	322.73	107.89	1.00	4184.04	325.11	20788639.41
Apr 2003	62321	320.41	105.86	1.00	1988.34	324.60	19968138.27

Table C.13 Average cost of individual hypolipidemic drugs according to active ingredients claimed from May 2001 to October 2001

Hypolipidemic group	Active ingredient	I Or G	May 2001	Jun 2001	Jul 2001	Aug 2001	Sep 2001	Oct 2001
			Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)
Fibrates	Bezafibrate	I	302.65 ± 91.04	291.70 ± 71.93	295.30 ±65.31	296.99 ±69.54	299.95 ±63.65	3265.41±93.89
	Bezafibrate	G	208.14 ± 52.61	206.71 ±46.32	200.52 ±21.78	200.08 ±26.87	197.10 ±27.84	214.59±28.71
	Clofibrate	I	0	0	0	0	0	0
	Fenofibrate	I	401.08 ±115.17	414.64 ±155.44	430.49 ±172.21	408.63±132.38	409.10±103.68	400.90±92.13
	Gemfibrozil	I	232.90 ±120.59	272.83 ±131.33	306.50 ±117.46	317.30±107.08	323.17±115.45	318.37±125.67
Statins	Atorvastatin	I	340.13 ± 102.90	345.85 ±89.46	346.70 ±95.15	346.63 ±91.89	345.95 ±90.81	343.79±85.07
	Cerivastatin	I	252.09 ±27.62	257.08 ±30.18	258.81 ±36.21	256.68 ±45.42	252.34 ±42.44	241.39±67.60
	Fluvastatin	I	265.42 ± 32.05	265.66 ±34.45	263.71 ±24.33	264.24 ±32.04	263.74 ±41.21	265.36±30.41
	Pravastatin	I	274.11 ±51.20	278.53 ±50.86	275.59 ±58.92	275.71 ±50.81	275.53 ±56.89	273.42±52.66
	Simvastatin	I	335.31 ±74.62	334.73 ±72.08	333.45 ±73.52	335.05 ±73.44	332.95 ±75.99	332.24±71.41
	Simvastatin	G	0	0	0	0	0	0
Others	Acipimox	I	240.40 ±36.67	239.73 ±36.29	235.98 ±34.95	259.27 ±59.07	254.28 ±54.81	251.07±46.02
	Cholestyramine	I	177.29 ±202.67	135.67 ±127.73	160.01 ±155.22	181.71±151.94	185.67±157.72	170.09±152.01
	Essential phospholipid	I	273.17 ±141.29	327.18 ±9.73	177.21 ±60.37	277.08 ±85.32	360.74 ±75.40	221.35±45.89
	Nicotinic acid	I	12.16 ±10.19	23.93 ±30.27	14.54 ±19.43	17.19 ±20.79	14.70 ±130.97	27.08±29.63
	Probucol	I	476.35 ± 217.68	487.38 ±203.60	490.36 ±201.18	462.31±195.60	420.30±185.11	436.46±188.68

Table C.14 Average cost of individual hypolipidemic drugs according to active ingredients claimed from November 2001 to April 2002

Hypolipidemic group	Active ingredient	I Or G	Nov 2001	Dec 2001	Jan 2002	Feb 2002	Mar 2002	Apr 2002
			Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)
Fibrates	Bezafibrate	I	357.86±110.55	343.16±102.53	342.38±97.04	371.42±124.29	382.19±111.97	372.12±126.5
	Bezafibrate	G	221.52±30.37	218.62±28.46	223.81±36.55	227.06±40.95	249.37±43.73	250.99±31.03
	Clofibrate	I	0	0	407.02 ± 0	0	0	0
	Fenofibrate	I	408.25±123.79	406.89±99.81	466.94±126.67	470.82±116.97	475.90±122.33	471.23±112.6
	Gemfibrozil	I	332.25±108.30	323.02±116.25	334.32±114.64	357.89±115.60	363.73±123.13	370.72±113.1
Statins	Atorvastatin	I	342.14±84.85	343.20±86.73	345.11±85.07	348.65±85.03	356.04±86.29	354.90±83.28
	Cerivastatin	I	259.29±11.41	260.78±12.91	259.10±7.94	256.72±10.42	0	0
	Fluvastatin	I	264.27±24.16	267.36±29.40	281.45±27.43	283.50±31.31	284.63±29.52	282.11±35.07
	Pravastatin	I	274.64±54.04	271.51±52.81	273.78±58.48	273.76±56.25	273.75±57.34	271.87±56.11
	Simvastatin	I	332.28±71.81	330.66±71.12	333.11±73.66	332.80±71.74	334.61±72.49	332.33±83.28
	Simvastatin	G	0	0	0	0	0	0
Others	Acipimox	I	244.16±49.97	253.07±39.17	214.29±117.54	187.84±129.76	196.29±119.11	219.04±104.5
	Cholestyramine	I	197.66±155.84	188.24±159.78	153.01±155.82	176.95±160.48	176.85±161.08	166.44±156.2
	Essential phospholipid	I	270.50±90.02	296.87±54.26	278.38±113.72	260.95±125.35	389.59±94.31	418.58±177.1
	Nicotinic acid	I	30.41±27.36	24.92±26.83	18.47±19.31	20.25±20.08	24.67±30.13	29.78±32.73
	Probucol	I	386.99±167.43	451.82±201.66	448.61±194.32	488.85±225.95	557.08±242.04	488.55±229.2

Table C.15 Average cost of individual hypolipidemic drugs according to active ingredients claimed from May 2002 to October 2002

Hypolipidemic group	Active ingredient	I Or G	May 2002	Jun 2002	Jul 2002	Aug 2002	Sep 2002	Oct 2002
			Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)
Fibrates	Bezafibrate	I	295.37±117.68	309.62±127.93	306.06±120.46	315.30±123.76	308.56±123.95	314.39±122.5
	Bezafibrate	G	249.93 ±36.18	252.14±33.12	249.76±32.92	252.03±31.91	255.09±39.41	255.97±51.78
	Clofibrate	I	0	0	0	0	0	0
	Fenofibrate	I	464.29±100.56	484.35±100.32	493.74±100.77	491.60±117.39	489.53±94.83	500.47±117.9
	Gemfibrozil	I	373.73±116.13	362.37±124.24	373. 00±111.19	377.82±112.26	382.80±108.11	365.05±115.7
Statins	Atorvastatin	I	354.53 ±82.66	354.21±82.39	352.69±81.04	350.86±80.51	350.38±78.58	349.54±78.10
	Cerivastatin	I	0	0	0	0	0	0
	Fluvastatin	I	289.03 ±31.21	290.45±28.85	290.00±29.31	289.77±27.14	290.44±32.38	291.42±30.79
	Pravastatin	I	272.55 ±55.53	273.11±56.46	273.36±55.13	273.53±53.90	275.94±56.32	275.35±55.23
	Simvastatin	I	332.07 ±72.50	331.42±71.72	331.47±72.75	331.32±74.09	332.41±71.53	330.96±70.79
	Simvastatin	G	0	0	0	0	0	201.78±12.69
Others	Acipimox	I	261.73 ±75.93	284.80±63.66	276.61±58.82	272.36±62.84	292.23±63.18	285.77±63.88
	Cholestyramine	I	150.62±154.81	171.77±154.80	182.55±168.24	187.35±160.67	194.22±163.78	187.74±169.0
	Essential phospholipid	I	356.41 ±58.70	332.28±92.49	384.97±29.05	328.86±87.56	329.89±97.12	312.64±44.63
	Nicotinic acid	I	27.71 ±32.21	16.36±22.45	27.80±30.53	22.43±24.59	31.22±34.53	41.33±37.87
	Probucol	I	549.17±203.50	540.81±231.49	488.16±183.38	443.87±247.89	358.92±97.44	296.03±108.9

Table C.16 Average cost of individual hypolipidemic drugs according to active ingredients claimed from November 2002 to April 2003

Hypolipidemic group	Active ingredient	I Or G	Nov 2002	Dec 2002	Jan 2003	Feb 2003	Mar 2003	Apr 2003
			Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)
Fibrates	Bezafibrate	I	338.40±133.26	326.12±132.98	311.73±121.09	292.89±107.07	295.61±109.94	287.26±108.8
	Bezafibrate	G	286.86±38.84	290.68±50.44	284.11±37.05	285.56±33.54	286.56±41.16	294.71±47.07
	Clofibrate	I	0	0	0	0	0	0
	Fenofibrate	I	531.55±115.54	530.05±111.06	550.48±130.43	541.35±118.84	543.22±121.57	549.11±143.7
	Gemfibrozil	I	360.18±115.53	378.59±118.58	420.88±123.40	416.35±128.80	388.26±137.21	390.88±136.0
Statins	Atorvastatin	I	348.04±76.69	356.40±81.01	364.18±83.45	364.72±83.40	363.43±88.61	363.34±82.83
	Cerivastatin	I	0	0	0	0	0	0
	Fluvastatin	I	293.55±36.26	295.29±48.52	311.08±33.83	312.95±33.20	312.99±33.83	315.22±32.23
	Pravastatin	I	275.84±56.11	276.38±59.05	287.93±59.55	290.38±57.06	290.00±60.35	291.33±58.89
	Simvastatin	I	328.34±72.85	255.38±82.75	206.24±53.14	201.28±69.65	198.91±37.60	199.31±37.90
	Simvastatin	G	200.97±50.03	200.12±38.20	192.62±42.71	161.11±35.37	161.97±37.27	161.72±36.12
Others	Acipimox	I	280.08±53.24	281.15±44.89	307.09±95.13	337.54±42.05	328.01±50.24	277.15±93.26
	Cholestyramine	I	165.11±153.98	190.53±162.92	159.30±155.06	155.25±171.10	156.95±175.83	150.46±165.3
	Essential phospholipid	I	346.86±115.22	281.10±87.06	269.12±154.26	91.18±0	305.70±0	305.70±0
	Nicotinic acid	I	30.24±25.74	30.21±22.47	29.12±25.83	22.98±19.04	29.51±20.96	22.08±21.52
	Probucol	I	233.13±0	296.06±108.91	233.18±0	233.18±0	499.61±0	0

Table C.17 Total cost of individual hypolipidemic drugs according to active ingredient claimed from May 2001 to October 2001

	Active ingredient	I or G	May 2001 Total cost (R)	Jun 2001 Total cost (R)	Jul 2001 Total cost (R)	Aug 2001 Total cost (R)	Sep 2001 Total cost (R)	Oct 2001 Total cost (R)
Fibrates	Bezafibrate	I	99876.10 (N=330)	70884.66 (N=243)	80026.87 (N=271)	116418.32 (N=392)	117581.90 (N=392)	113589.37 (N=348)
	Bezafibrate	G	39131.19 (N=188)	37207.99 (N=180)	32684.25 (N=163)	72628.29 (N=363)	86725.99 (N=440)	92919 (N=433)
	Clofibrate	I	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
	Fenofibrate	I	136368.32 (N=340)	114856.59 (N=277)	131731.25 (N=3060	209627.35 (N=513)	191458.34 (N=468)	192832.31 (N=481)
	Gemfibrozil	I	31907.66 (N=137)	31647.78 (N=116)	35554.35 (N=116)	54575.88 (N=172)	69159.95 (N=214)	57943.20 (N=182)
Statins	Atorvastatin	I	7042008.82 (N=20704)	5862529.94 (N=16951)	6377519.80 (N=18395)	11067907.50 (N=31930)	11338179.32 (N=32774)	11723511.05 (N=54101)
	Cerivastatin	I	680152.18 (N=2698)	596418.37 (N=2320)	670837.28 (N=2592)	591902.02 (N=2306)	71664.30 (N=284)	28242.34 (N=117)
	Fluvastatin	I	453870.92 (N=1710)	370064.84 (N=1393)	388967.21 (N=1475)	633906.56 (N=2399)	675698.14 (N=2562)	648543.26 (N=2444)
	Pravastatin	I	510947.91 (N=1864)	429221.16 (N=1541)	427168.43 (N=1550)	795712.66 (N=2886)	846159.94 (N=3071)	877677.22 (N=3210)

	Simvastatin	I	1828091.16 (N=5452)	1457073.62 (N=4353)	1526552.00 (N=4578)	2584573.12 (N=7714)	2662903.52 (N=7998)	2785819.94 (N=8385)
	Simvastatin	G	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
Others	Acipimox	I	6009.94 (N=25)	6952.28 (N=29)	4483.60 (N=19)	8296.62 (N=32)	7119.97 (N=28)	8536.24 (N=34)
	Cholestyramine	I	66661.67 (N=376)	42599.07 (N=314)	46881.87 (N=293)	81770.41 (N=450)	72966.83 (N=393)	56298.77 (N=331)
	Essential phospholipids	I	1912.19 (N=70	1635.91 (N=5)	1240.47 (N=7)	6095.77 (N=22)	5411.12 (N=15)	2213.50 (N=10)
	Nicotinic acid	I	449.76 (N=37)	1005.27 (N=42)	1061.64 (N=73)	1323.44 (N=77)	823.27 (N=56)	2166 (N=80)
	Probucol	I	29533.48 (N=62)	19495.25 (N=40)	21575.94 (N=44)	41607.66 (N=90)	37406.63 (N=89)	41027.24 (N=94)

Table C.18 Total cost of individual hypolipidemic drugs according to active ingredient claimed from November 2001 to April 2002

	Active ingredient	I or G	Nov 2001 Total cost (R)	Dec 2001 Total cost (R)	Jan 2002 Total cost (R)	Feb 2002 Total cost (R)	Mar 2002 Total cost (R)	Apr 2002 Total cost (R)
Fibrates	Bezafibrate	I	101989.39 (N=285)	124223.84 (N=362)	138663.16 (N=405)	141140.67 (N=380)	175041.30 (N=458)	163730.62 (N=440)
	Bezafibrate	G	81962.68 (N=370)	90946.68 (N=416)	136070.93 (N=608)	142595.16 (N=628)	1803040.91 (N=734)	178959.69 (N=713)
	Clofibrate	I	0 (N=0)	0 (N=0)	3256.16 (N=8)	0 (N=0)	0 (N=0)	0 (N=0)
	Fenofibrate	I	149827.85 (N=367)	174556.40 (N=429)	247010.73 (N=529)	263186.28 (N=559)	267454.52 (N=562)	266716.21 (N=566)
	Gemfibrozil	I	61465.39 (N=185)	61696.24 (N=191)	92606.75 (N=277)	97346.76 (N=272)	86931.31 (N=239)	111958.26 (N=302)
Statins	Atorvastatin	I	9612014.35 (N=28094)	11537569.67 (N=33618)	14981092.83 (N=43410)	14444131.09 (N=41429)	16061920.57 (N=45113)	16633090.29 (N=46867)
	Cerivastatin	I	9593.61 (N=37)	7823.32 (N=30)	2072.84 (N=8)	1026.86 (N=4)	0 (N=0)	0 (N=0)
	Fluvastatin	I	549421.56 (N=2079)	647815.30 (N=2423)	847733.90 (N=3012)	845408.14 (N=2982)	887476.43 (N=3118)	907535.80 (N=3217)
	Pravastatin	I	739052.89 (N=2691)	891367.68 (N=3283)	1150168.44 (N=4201)	1127074.13 (N=4117)	1249658.64 (N=4565)	1321312.13 (N=4860)

	Simvastatin	I	2218271.53 (N=6676)	2678676.96 (N=8101)	3398105.09 (N=10201)	3186919.30 (N=9576)	3401015.86 (N=10164)	3499065.56 (N=10529)
	Simvastatin	G	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
Others	Acipimox	I	4883.13 (N=20)	8351.15 (N=33)	4928.77 (N=23)	4508.16 (N=24)	5692.33 (N=29)	5695.13 (N=26)
	Cholestyramine	I	59101.59 (N=299)	64567.44 (N=343)	101905.95 (N=666)	110949.31 (N=627)	109290.55 (N=618)	115008.70 (N=691)
	Essential phospholipids	I	4328.04 (N=16)	3265.57 (N=11)	7516.36 (N=27)	4175.17 (N=16)	5454.24 (N=14)	9627.38 (N=23)
	Nicotinic acid	I	1550.80 (N=51)	1195 (N=48)	794.21 (N=43)	870.91 (N=43)	1307.73 (N=53)	1370.06 (N=46)
	Probucol	I	33667.82 (N=87)	32982.84 (N=73)	45309.83 (N=101)	51817.81 (N=106)	57935.93 (N=104)	43480.58 (N=89)

Table C.19 Total cost of individual hypolipidemic drugs according to active ingredient claimed from May 2002 to October 2002

	Active ingredient	I or G	May 2002	Jun 2002	Jul 2002	Aug 2002	Sep 2002	Oct 2002
			Total cost (R)	Total cost (R)	Total cost (R)	Total cost (R)	Total cost (R)	Total cost (R)
Fibrates	Bezafibrate	I	92541.71 (N=313)	85454.51 (N=276)	79880.51 (N=261)	75988.49 (N=241)	62929.86 (N=204)	59418.98 (N=189)
	Bezafibrate	G	215439.68 (N=862)	213559.21 (N=847)	225785.62 (N=904)	230608.66 (N=915)	193865.87 (N=760)	216040.98 (N=844)
	Clofibrate	I	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
	Fenofibrate	I	234003.85 (N=504)	224739.55 (N=464)	242919.81 (N=492)	231541.45 (N=471)	199727.82 (N=408)	228718.90 (N=457)
	Gemfibrozil	I	103149.77 (N=276)	99289.30 (N=274)	98099.17 (N=263)	92189.03 (N=244)	81154.08 (N=212)	71184.75 (N=195)
Statins	Atorvastatin	I	16381125.63 (N=46205)	15501461.54 (N=43763)	16170247.28 (N=45848)	16439369.53 (N=46854)	14996512.14 (N=42801)	15303605.41 (N=43782)
	Cerivastatin	I	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	914467.63 (N=3138)
	Fluvastatin	I	884132.60 (N=3059)	852759.02 (N=2936)	880433.94 (N=3036)	867863.87 (N=2995)	797843.03 (N=2747)	1243764.77 (N=4517)
	Pravastatin	I	1277149.13 (N=4686)	1228439.00 (N=4498)	1337817.61 (N=4894)	1340309.81 (N=4900)	1229035.01 (N=4454)	2739693.11 (N=8278)

	Simvastatin	I	3318058.43 (N=9992)	3113729.91 (N=9395)	3169197.23 (N=9561)	3156523.78 (N=9527)	2768656.76 (N=8329)	1008.92 (N=5)
	Simvastatin	G	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
Others	Acipimox	I	9684.07 (N=37)	10826.22 (N=38)	9404.81 (N=34)	6808.95 (N=25)	8766.76 (N=30)	8001.47 (N=28)
	Cholestyramine	I	96548.43 (N=641)	92586.07 (N=539)	88353.69 (N=484)	89180.30 (N=476)	75552.34 (N=389)	78850.44 (N=420)
	Essential phospholipids	I	4276.87 (N=12)	4319.60 (N=13)	6929.54 (N=18)	4604.05 (N=14)	8577.11 (N=26)	3751.68 (N=12)
	Nicotinic acid	I	1441.25 (N=52)	866.86 (N=53	1362.00 (N=49)	1054 (N=47)	1623.30 (N=52)	1529.11 (N=37)
	Probucol	I	24336.14 (N=53)	15683.43 (N=29)	12692.18 (N=26)	3994.86 (N=9)	2153.54 (N=6)	888.08 (N=3)

Table C.20 Total cost of individual hypolipidemic drugs according to active ingredient claimed from November 2002 to April 2003

	Active ingredient	I or G	Nov 2002 Total cost (R)	Dec 2002 Total cost (R)	Jan 2003 Total cost (R)	Feb 2003 Total cost (R)	Mar 2003 Total cost (R)	Apr 2003 Total cost (R)
Fibrates	Bezafibrate	I	61244.95 (N=181	57723.51 (N=177)	71073.31 (N=228)	51841.81 (N=177)	50252.85 (N=170)	39067.52 (N=136)
	Bezafibrate	G	223460.09 (N=779)	247079.97 (N=850)	286670.08 (N=1009)	237874.81 (N=833)	247873.88 (N=865)	271426.90 (N=921)
	Clofibrate	I	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
	Fenofibrate	I	218996.96 (N=412)	232693.64 (N=439)	288452.14 (N=524)	229533.70 (N=424)	239016.93 (N=440)	231176.81 (N=421)
	Gemfibrozil	I	66273.61 (N=184)	66632.42 (N=176)	106061.09 (N=252)	77025.36 (N=185)	63674.53 (N=164)	71921.67 (N=184)
Statins	Atorvastatin	I	14414417.64 (N=41416)	14838021.94 (N=41633)	17370985.41 (N=47699)	14733857.64 (N=40398)	15650827.03 (N=43064)	14806116.84 (N=40750)
	Cerivastatin	I	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
	Fluvastatin	I	1003364.85 (N=3418)	1035571.35 (N=3507)	1349775.75 (N=4339)	1196082.05 (N=3822)	1290771.31 (4124)N=	1279494.98 (N=4059)
	Pravastatin	I	1207889.12 (N=4379)	1180950.72 (N=4273)	1426095.62 (N=4953)	1225418.19 (N=4220)	1271347.42 (N=4384)	1239028.34 (N=4253)

	Simvastatin	I	2517724.92 (N=7668)	1207428.22 (N=4728)	936347.80 (N=4540)	823051.12 (N=4089)	883749.74 (N=4443)	867391.45 (N=4352)
	Simvastatin	G	33964.20 (N=169)	623589.32 (N=3116)	1076346 (N=5588)	821172.02 (N=5097)	992891.00 (N=6130)	1064910.79 (N=6585)
Others	Acipimox	I	8962.44 (N=32)	8996.82 (N=32)	9826.75 (N=32)	4387.99 (N=13)	5904.26 (18)N=	9145.99 (N=33)
	Cholestyramine	I	70667.43 (N=428)	70876.09 (N=372)	101314.56 (N=636)	79800.64 (N=514)	88675.28 (N=565)	87113.56 (N=579)
	Essential phospholipids	I	4856.09 (N=14)	1686.60 (N=6)	1345.62 (N=5)	182.36 (N=2)	917.10 (N=3)	305.70 (N=1)
	Nicotinic acid	I	1421.35 (N=47)	1873.03 (N=62)	2154.95 (N=74)	1171.74 (N=51)	1239.25 (N=42)	1037.72 (N=47)
	Probucol	I	466.26 (N=2)	888.18 (N=3)	466.36 (N=2)	466.36 (N=2)	1498.23 (N=3)	0 (N=0)

Table C.21 Average cost of individual hypolipidemic drugs claimed from May 2001 to April 2002

Individual agents	May 2001	Jun 2001	Jul 2001	Aug 2001	Sep 2001	Oct 2001	Nov 2001	Dec 2001	Jan 2002	Feb 2002	Mar 2002	April 2002
	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)
Adco-Simv 10mg®	0	0	0	0	0	0	0	0	0	0	0	0
Adco-Simv 20mg®	0	0	0	0	0	0	0	0	0	0	0	0
Adco-Simv 40mg®	0	0	0	0	0	0	0	0	0	0	0	0
Baycol 0.1mg®	241.15 ± 16.69	248.64 ± 19.98	247.03 ±41.03	246.62 ±50.38	256.18 ±10.00	246.01 ±0	246.03 ±0	0	0	0	0	0
Baycol 0.2mg®	242.93 ± 30.91	250.18 ± 33.68	252.08 ±42.02	247.33 ±54.76	247.99 ±49.11	224.67 ±83.02	256.57 ±9.83	255.57 ±9.91	259.70 ±9.31	256.72 ±10.42	0	0
Baycol 0.3mg®	268.72 ± 11.89	268.51 ± 12.92	267.69 ±21.03	269.43 ±11.68	271.80 ±9.53	275.41 ±6.81	277.74 ±0.15	277.88 ±0	0	0	0	0
Baycol 0.4mg®	264.72 ± 17.98	267.22 ± 29.35	268.71 ±26.77	268.31 ±34.89	247.80 ±45.70	262.79 ±9.11	257.30 ±0	277.85 ±0	257.31 ±0	0	0	0
Bezalip 200mg®	189.83 ± 76.62	193.38 ± 78.98	216.06 ±73.60	218.08 ±78.11	208.28 ±77.20	226.39 ±98.46	217.17 ±86.96	250.35 ±95.23	219.83 ±94.09	243.77 ±101.53	248.31 ±102.62	237.87 ±105.92
Bezalip 400mg®	336.41 ± 62.71	323.24 ± 27.35	322.90 ±30.44	328.15 ±30.22	324.95 ±24.95	367.30 ±52.02	404.53 ±70.88	382.62 ±76.96	389.80 ±39.74	428.21 ±85.25	436.39 ±56.20	432.17 ±80.56
Lescol 20mg®	265.75 ± 25.80	265.23 ± 27.17	264.62 ±19.67	263.91 ±31.33	263.43 ±46.99	264.56 ±24.73	264.94 ±17.52	266.91 ±21.16	281.73 ±21.03	283.42 ±27.80	283.99 ±24.98	283.15 ±24.38
Lescol 40mg®	265.03 ± 38.33	266.21 ± 41.98	262.48 ±29.38	264.62 ±32.86	264.11 ±32.94	266.34 ±36.17	263.39 ±30.76	267.91 ±37.11	281.10 ±33.70	283.60 ±35.09	285.39 ±34.16	280.88 ±44.39
Lescol XL 80mg®	0	0	0	0	0	0	0	0	0	0	0	0
Lipaten® Cap	0	0	0	0	0	0	0	0	407.02 ±0	0	0	0
Lipitor 10mg®	303.04 ± 31.76	309.39 ± 32.45	309.68 ±34.45	309.27 ±33.33	308.66 ±34.67	308.11 ±34.23	307.96 ±35.00	308.23 ±33.55	308.95 ±32.53	313.10 ±33.53	320.32 ±34.91	320.13 ±36.34
Lipitor 20mg®	456.97 ± 150.97	434.14 ± 110.83	466.83 ±123.15	464.73 ±110.22	459.11 ±102.93	456.78 ±92.06	456.51 ±93.83	456.96 ±100.83	454.81 ±89.64	460.56 ±88.10	468.81 ±92.17	465.67 ±81.20
Lipitor 40mg®	586.25 ± 0	561.33 ± 21.64	606.75 ±169.96	578.93 ±176.90	616.29 ±203.73	565.73 ±138.96	568.28 ±153.81	565.17 ±150.97	556.11 ±169.03	547.81 ±181.31	541.71 ±171.67	528.96 ±171.97

Lipostabil cap®	233.36 ± 138.45	334.29 ± 0	168.14 ±60.69	300.89 ±53.68	335.85 ±62.11	220.37 ±48.57	276.27 ±95.21	321.89 ±39.77	311.72 ±110.03	241.26 ±145.02	300.51 ±155.25	461.78 ±244.67
Lipostabil 5ml®	372.69 ± 123.92	316.52 ± 0	231.63 ±	242.69 ±111.97	460.29 ±0	230.14 ±0	230.15 ±0	230.14 ±0	247.43 ±112.01	304.26 ±54.21	413.88 ±60.93	378.98 ±68.71
Lipsin 300mg®	401.08 ± 115.17	414.64 ± 155.44	430.49 ±172.21	408.63 ±132.39	409.10 ±103.68	400.90 ±92.13	408.25 ±123.79	406.89 ±99.81	466.94 ±126.67	470.82 ±116.97	475.90 ±122.33	471.23 ±112.63
Lopid 600mg®	232.90 ± 120.59	272.83 ± 131.33	306.50 ±117.46	317.30 ±107.08	323.18 ±115.45	318.37 ±125.67	332.25 ±108.30	323.02 ±116.25	334.32 ±114.64	357.89 ±115.60	363.73 ±123.13	370.72 ±113.11
Lurselle®	476.35 ± 217.68	487.38 ± 203.60	490.36 ±201.11	462.31 ±195.60	420.30 ±185.11	436.46 ±188.68	386.99 ±167.43	451.82 ±201.66	448.61 ±194.32	488.85 ±225.95	557.08 ±242.04	488.55 ±229.20
Nicotinic acid tab®	12.16 ± 10.89	23.94 ± 30.28	14.71 ±19.52	16.97 ±20.83	14.92 ±14.00	28.65 ±29.25	30.41 ±0	25.39 ±0	18.27 ±20.02	20.25 ±20.08	24.67 ±30.13	29.78 ±32.73
Nicotinic acid 30mg®	0	0	2.75 ±	33.89 ±	2.66 ±	3.51 ±0.78	0	2.66 ±0	21.19 ±0	0	0	0
Olbetam 250mg®	240.40 ± 36.67	239.73 ± 36.29	235.98 ±34.95	259.27 ±59.07	254.28 ±54.81	251.07 ±46.02	244.16 ±49.97	253.07 ±39.17	214.29 ±117.54	187.84 ±129.76	196.29 ±119.11	219.04 ±104.52
Prava 10mg®	239.83 ± 7.92	238.99 ± 12.16	237.00 ±20.43	238.97 ±16.28	239.12 ±15.84	238.76 ±16.28	238.57 ±13.52	238.27 ±15.55	240.37 ±21.51	239.91 ±19.65	239.20 ±16.35	237.61 ±21.70
Prava 20mg®	296.90 ± 36.57	300.14 ± 26.61	297.78 ±41.89	297.08 ±30.16	300.86 ±44.49	296.12 ±32.77	298.64 ±41.28	295.51 ±35.44	295.60 ±41.37	295.96 ±37.06	295.85 ±38.74	294.67 ±38.49
Prava 40mg®	304.44 ± 80.52	313.20 ± 72.55	312.26 ±87.90	306.88 ±77.47	291.48 ±82.04	289.80 ±79.60	295.43 ±79.87	283.02 ±82.15	290.74 ±90.02	285.12 ±87.51	284.09 ±87.29	284.04 ±82.79
Questran Lite®	177.29 ± 202.67	135.67 ± 127.73	160.00 ±155.22	181.71 ±151.95	185.67 ±157.73	170.09 ±152.00	197.66 ±155.83	188.24 ±159.78	153.01 ±155.82	176.95 ±160.48	176.85 ±161.08	166.44 ±156.22
Rolab-bezafibrate®	208.14 ± 52.61	323.24 ± 46.32	200.52 ±21.78	200.08 ±26.87	197.10 ±27.85	214.59 ±28.70	221.52 ± 30.37	218.62 ±28.46	223.80 ±36.55	227.06 ±40.95	249.37 ±43.73	251.00 ±31.03
Zocor 10mg®	283.88 ± 36.24	285.09 ± 38.46	283.66 ±31.62	283.95 ±33.22	283.45 ±39.85	283.31 ±33.39	284.09 ±30.87	284.23 ±29.06	285.59 ±35.39	285.58 ±28.68	286.41 ±32.44	285.59 ±64.25
Zocor 20mg®	408.81 ± 46.78	406.58 ± 37.36	407.44 ±44.30	406.38 ±42.83	404.71 ±51.40	402.63 ±42.07	402.59 ±42.96	403.06 ±48.23	402.50 ±52.39	402.07 ±51.17	403.24 ±49.67	401.29 ±50.63
Zocor 40mg®	368.68 ± 84.06	362.15 ± 87.26	369.24 ±79.49	372.78 ±94.20	364.95 ±90.32	358.14 ±90.87	361.97 ±101.80	349.11 ±91.47	350.58 ±92.78	345.34 ±93.06	344.62 ±92.25	339.27 ±94.94

Refer to table C.23 for active ingredients of individual hypolipidemic medicine items

Table C.22 Average cost of individual hypolipidemic drugs claimed from May 2002 to April 2003

Individual agents	May 2002	Jun 2002	Jul 2002	Aug 2002	Sep 2002	Oct 2002	Nov 2002	Dec 2002	Jan 2003	Feb 2003	Mar 2003	April 2003
	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)	Average cost (R)
Adco-Simv 10mg®	0	0	0	0	0	192.52 ±0	192.75 ±0.57	189.45 ±15.79	184.10 ±23.00	151.18 ±13.70	150.99 ±13.95	151.48 ±15.62
Adco-Simv 20mg®	0	0	0	0	0	215.68 ±0	197.69 ±57.46	208.66 ±31.34	196.61 ±40.59	160.41 ±32.07	160.72 ±32.96	160.30 ±31.70
Adco-Simv 40mg®	0	0	0	0	0	0	217.96 ±65.13	214.11 ±83.68	210.78 ±80.41	196.17 ±62.47	197.06 ±64.14	193.33 ±61.10
Baycol 0.1mg®	0	0	0	0	0	0	0	0	0	0	0	0
Baycol 0.2mg®	0	0	0	0	0	0	0	0	0	0	0	0
Baycol 0.3mg®	0	0	0	0	0	0	0	0	0	0	0	0
Baycol 0.4mg®	0	0	0	0	0	0	0	0	0	0	0	0
Bezalip 200mg®	247.57 ±113.13	254.10 ±112.62	249.94 ±113.01	257.85 ±108.66	254.18 ±103.87	248.94 ±106.96	259.33 ±103.90	256.04 ±104.64	282.11 ±114.00	276.48 ±105.82	277.39 ±110.30	259.77 ±101.24
Bezalip 400mg®	332.59 ±107.53	354.91 ±121.97	359.24 ±102.02	384.88 ±103.90	377.40 ±113.01	379.14 ±100.92	440.42 ±91.03	411.10 ±112.89	370.95 ±113.49	327.44 ±102.18	343.28 ±94.48	353.23 ±98.52
Lescol 20mg®	283.28 ±25.52	284.10 ±23.51	284.13 ±25.38	283.65 ±21.15	283.34 ±26.91	283.22 ±23.37	279.69 ±37.57	279.38 ±45.76	297.77 ±27.42	298.88 ±28.89	297.90 ±33.43	298.66 ±29.27
Lescol 40mg®	295.97 ±35.73	297.85 ±32.51	296.82 ±31.98	297.02 ±31.86	298.39 ±36.40	296.27 ±32.21	297.24 ±29.33	297.22 ±39.68	312.95 ±39.88	313.21 ±38.34	312.90 ±33.88	312.34 ±39.23
Lescol XL 80mg®	0	0	0	0	317.50 ±11.81	308.51 ±41.08	311.00 ±34.14	314.38 ±53.52	322.31 ±28.75	324.16 ±28.00	324.47 ±29.32	328.08 ±22.21
Lipaten Cap®	0	0	0	0	0	0	0	0	0	0	0	0
Lipitor 10mg®	320.87 ±36.58	320.72 ±35.90	320.47 ±37.61	319.73 ±36.29	320.01 ±36.21	319.95 ±36.55	319.64 ±36.84	326.99 ±40.20	333.77 ±39.03	334.43 ±38.48	334.38 ±54.51	334.16 ±38.52
Lipitor 20mg®	463.65 ±83.42	463.86 ±83.34	458.33 ±77.40	455.98 ±80.99	450.86 ±78.94	446.83 ±82.25	444.09 ±81.98	455.65 ±87.82	453.50 ±94.29	451.21 ±93.72	447.26 ±95.66	446.30 ±97.45
Lipitor 40mg®	517.83 ±172.41	506.86 ±179.26	530.62 ±179.26	497.43 ±194.34	486.38 ±188.86	477.20 ±177.21	467.12 ±175.69	476.56 ±179.76	484.99 ±187.86	483.63 ±187.99	482.94 ±182.85	481.11 ±180.73
Lipostabil cap®	404.00 ±1.59	314.32 ±111.68	404.83 ±1.88	325.30 ±156.07	341.61 ±139.99	302.98 ±22.30	357.61 ±171.65	0	100.14 ±0	91.18 ±0	0	0
Lipostabil 5ml®	322.41 ±55.50	361.01 ±46.45	372.34 ±31.31	330.29 ±54.28	327.10 ±88.48	317.47 ±53.26	342.57 ±96.35	281.10 ±87.06	381.78 ±0	0	305.70 ±0	305.70 ±0

Lipsin 300mg®	464.29 ±100.56	484.35 ±100.32	493.74 ±100.76	491.60 ±117.39	489.53 ±94.83	500.48 ±117.18	531.54 ±115.54	530.05 ±111.06	550.48 ±130.43	541.35 ±118.84	543.22 ±121.57	549.11 ±143.77
Lopid 600mg®	373.73 ±116.13	362.37 ±124.24	373.00 ±111.19	377.82 ±112.26	382.80 ±108.11	365.05 ±115.70	360.18 ±115.53	378.59 ±118.58	420.88 ±123.40	416.35 ±128.80	388.26 ±137.21	390.88 ±136.01
Lurselle®	459.17 ±203.50	540.81 ±231.48	488.16 183.38	443.87 ±247.89	358.92 ±97.44	296.03 ±108.94	233.13 ±0	296.06 ±108.91	233.18 ±0	233.18 ±0	499.61 ±0	0
Nicotinic acid tab®	27.72 ±32.21	21.20 ±24.25	29.40 ±30.84	25.33 ±25.05	32.85 ±34.93	42.66 ±38.53	30.79 ±26.09	31.61 ±22.13	31.45 ±26.05	24.09 ±19.08	29.51 ±20.96	22.08 ±21.52
Nicotinic acid 30mg®	0	3.23 ±0.57	3.18 ±0.90	2.62 ±0	4.59 ±0.85	18.01 ±0	18.01 ±0	2.67 ±0	6.82 ±2.94	5.19 ±0	0	0
Olbetam 250mg®	261.73 ±75.93	284.90 ±63.65	276.61 ±58.82	272.36 ±62.84	292.23 ±63.18	285.77 ±63.88	280.08 ±53.24	281.15 ±44.89	307.09 ±95.13	337.54 ±42.05	328.01 ±50.24	277.15 ±93.26
Prava 10mg®	239.09 ±14.86	239.46 ±13.17	238.76 ±12.86	239.13 ±12.73	239.09 ±18.12	238.88 ±14.56	239.84 ±19.35	240.18 ±18.29	250.96 ±20.85	252.02 ±17.74	252.33 ±19.37	252.87 ±12.92
Prava 20mg®	294.97 ±40.39	295.44 ±41.92	296.50 ±35.29	295.62 ±32.21	297.96 ±36.77	298.48 ±34.88	298.12 ±37.65	301.78 ±39.77	310.96 ±41.12	313.74 ±30.14	312.04 ±37.22	312.25 ±39.40
Prava 40mg®	281.44 ±83.10	282.91 ±84.38	281.16 ±84.52	281.30 ±83.25	288.15 ±83.63	283.83 ±83.87	283.50 ±83.13	279.41 ±87.26	296.71 ±87.41	297.39 ±86.73	300.03 ±90.27	303.23 ±86.58
Questran lite®	150.62 ±154.81	171.77 ±154.79	182.55 ±168.24	187.35 ±160.67	194.22 ±163.78	187.74 ±169.03	165.11 ±153.98	190.53 ±162.92	159.30 ±155.06	155.25 ±171.10	156.95 ±175.83	150.45 ±165.34
Rolab-bezafibrate®	249.53 ±36.18	252.14 ±33.12	249.76 ±32.92	252.03 ±31.91	255.09 ±39.41	255.97 ±51.77	286.86 ±38.84	290.68 ±50.44	284.11 ±37.05	285.56 ±33.54	286.56 ±41.16	294.71 ±47.07
Zocor 10mg®	285.34 ±29.72	285.30 ±31.78	285.32 ±31.41	285.44 ±31.33	285.23 ±31.16	284.97 ±32.09	284.77 ±33.85	227.25 ±52.98	192.95 ±44.06	189.87 ±81.16	186.51 ±21.89	186.57 ±23.68
Zocor 20mg®	402.18 ±51.08	401.34 ±47.89	401.45 ±50.70	399.41 ±55.75	402.34 ±41.13	399.30 ±44.29	397.86 ±51.51	294.48 ±97.36	216.32 ±45.46	207.01 ±22.31	207.34 ±23.36	206.37 ±22.35
Zocor 40mg®	335.12 ±95.36	337.39 ±95.34	332.65 ±97.22	336.67 ±101.31	331.47 ±99.82	334.57 ±94.87	331.00 ±100.95	280.50 ±101.68	241.54 ±84.11	236.20 ±83.70	232.71 ±76.25	237.32 ±76.01

Refer to table C.23 for active ingredients of individual hypolipidemic medicine items

Table C.23 Total cost of individual hypolipidemic drugs claimed from May 2001 to October 2001

Active ingredient	Individual agents	May 2001 Total cost (R)	Jun 2001 Total cost (R)	Jul 2001 Total cost (R)	Aug 2001 Total cost (R)	Sep 2001 Total cost (R)	Oct 2001 Total cost (R)
Simvastatin	Adco-Simv 10mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
	Adco-Simv 20mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
	Adco-Simv 40mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
Cerivastatin	Baycol 0.1mg®	45335.50 (N=188)	33317.73 (N=134)	34337.10 (N=139)	27128.49 (N=110)	8453.95 (N=33)	738.03 (N=3)
	Baycol 0.2mg®	356147.40 (N=1466)	318484.70 (N=1273)	334260.80 (N=1326)	287897.36 (N=1164)	37446.24 (N=151)	15727.21 (N=70)
	Baycol 0.3mg®	165265.05 (N=615)	134255.53 (N=500)	156596.69 (N=585)	128788.13 (N=478)	11143.74 (N=41)	4681.87 (N=17)
	Baycol 0.4mg®	116404.23 (N=429)	110360.41 (N=413)	145642.69 (N=542)	148088.04 (N=554)	14620.37 (N=59)	7095.23 (N=27)
Bezafibrate	Bezalip 200mg®	14427.04 (N=76)	11409.16 (N=59)	15124.51 (N=70)	24207.24 (N=111)	17495.93 (N=84)	22865.62 (N=101)
	Bezalip 400mg®	85449.06 (N=254)	59475.50 (N=184)	64902.36 (N=201)	92211.08 (N=281)	100085.89 (N=308)	90723.75 (N=247)
Fluvastatin	Lescol 20mg®	249530.72 (N=939)	207408.16 (N=782)	223077.80 (N=843)	342561.42 (N=1298)	368538.27 (N=1399)	356098.87 (N=1346)
	Lescol 40mg®	204340.20 (N=771)	162656.68 (N=611)	165889.41 (N=632)	291345.14 (N=1101)	307159.87 (N=1163)	292444.39 (N=1098)
	Lescol XL 80mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
Clofibrate	Lipaten Cap®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
Atorvastatin	Lipitor 10mg®	4763169.10 (N=15718)	4006905.9 (N=12951)	4370266.8 (N=14112)	7548329.32 (N=24407)	7684337.9 (N=24896)	8049984.49 (N=26127)

	Lipitor 20mg®	2277080.97 (N=4983)	1838222.9 (N=3969)	1973274.8 (N=4227)	3400896.58 (N=7318)	3509012.9 (N=7643)	3511728.36 (N=7688)
	Lipitor 40mg®	1758.75 (N=3)	17401.17 (N=31)	33978.21 (N=56)	118681.60 (N=205)	144828.49 (N=235)	161798.20 (N=286)
Essential phospholipids	Lipostabil capsules®	1166.82 (N=5)	1002.87 (N=3)	1008.84 (N=6)	3911.54 (N=13)	4030.25 (N=12)	1983.36 (N=9)
	Lipostabil 5ml®	745.37 (N=2)	633.04 (N=2)	231.63 (N=1)	2184.23 (N=9)	1380.87 (N=3)	230.14 (N=1)
Fenofibrate	Lipsin 300mg®	136368.32 (N=340)	114856.59 (N=277)	131731.25 (N=306)	209627.35 (N=513)	191458.34 (N=468)	192832.21 (N=481)
Gemfibrozil	Lopid 600mg®	31907.66 (N=137)	31647.78 (N=116)	35554.35 (N=116)	54575.88 (N=172)	69159.95 (N=214)	57943.20 (N=182)
Probucol	Lurselle®	29533.48 (N=62)	19495.25 (N=40)	21575.94 (N=44)	41607.66 (N=90)	37406.63 (N=89)	41027.24 (N=94)
Nicotinic acid	Nicotinic acid®	449.76 (N=37)	1005.27 (N=42)	1058.89 (N=72)	1289.55 (N=76)	820.61 (N=55)	2149.01 (N=75)
	Nicotinic acid 30mg®	0 (N=0)	0 (N=0)	2.75 (N=1)	33.89 (N=1)	2.66 (N=1)	17.59 (N=5)
Acipimox	Olbetam 250mg®	6009.94 (N=25)	6952.28 (N=29)	4483.60 (N=19)	8296.62 (N=32)	7119.97 (N=28)	8536.24 (N=34)
Pravastatin	Prava 10mg®	189467.93 (N=790)	147932.24 (N=619)	151683.17 (N=640)	276723.60 (N=1158)	275464.30 (N=1152)	284358.43 (N=1191)
	Prava 20mg®	216144.31 (N=728)	171983.16 (N=573)	178372.87 (N=599)	342532.85 (N=1153)	363745.32 (N=1209)	384369.65 (N=1298)
	Prava 40mg®	105335.67 (N=346)	109305.76 (N=349)	97112.39 (N=311)	176456.21 (N=575)	206950.32 (N=710)	208949.14 (N=721)
Cholestyramine	Questran Lite®	66661.67 (N=376)	42599.07 (N=314)	46881.87 (N=293)	81770.41 (N=450)	72966.83 (N=393)	56298.77 (N=331)
Bezafibrate	Rolab-bezafibrate®	39131.19 (N=188)	37207.99 (N=180)	32684.25 (N=163)	72628.29 (N=363)	86725.89 (N=440)	92919.16 (N=433)
Simvastatin	Zocor 10mg®	878071.11 (N=3093)	703597.07 (N=2468)	748308.00 (N=2638)	1228091.03 (N=4325)	1283450.1 (N=4528)	1330413.99 (N=4696)

	Zocor 20mg®	818033.72 (N=2001)	648092.02 (N=1594)	660454.98 (N=1621)	1126103.57 (N=2771)	1150993.0 (N=2844)	1214734.02 (N=3017)
	Zocor 40mg®	131986.33 (N=358)	105384.53 (N=291)	117789.02 (N=319)	230378.52 (N=618)	228460.42 (N=626)	240671.93 (N=672)

Table C.24 Total cost of individual hypolipidemic drugs claimed from November 2001 to April 2002

Active ingredient	Individual agents	Nov 2001 Total cost (R)	Dec 2001 Total cost (R)	Jan 2002 Total cost (R)	Feb 2002 Total cost (R)	Mar 2002 Total cost (R)	April 2002 Total cost (R)
Simvastatin	Adco-Simv 10mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
	Adco-Simv 20mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
	Adco-Simv 40mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
Cerivastatin	Baycol 0.1mg®	738.09 (N=3)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
	Baycol 0.2mg®	5387.98 (N=21)	5878.22 (N=23)	1558.22 (N=6)	1026.86 (N=4)	0 (N=0)	0 (N=0)
	Baycol 0.3mg®	1666.44 (N=6)	1389.40 (N=5)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
	Baycol 0.4mg®	1801.10 (N=7)	555.70 (N=2)	514.62 (N=2)	0 (N=0	0 (N=0)	0 (N=0)
Bezafibrate	Bezalip 200mg®	15419.06 (N=71)	27037.75 (N=108)	24841.27 (N=113)	28520.99 (N=117)	32777.48 (N=132)	32349.74 (N=136)
	Bezalip 400mg®	86570.33 (N=214)	97186.09 (N=254)	113821.89 (N=292)	112619.68 (N=263)	142263.82 (N=326)	131380.88 (N=304)
Fluvastatin	Lescol 20mg®	312896.61 (N=1181)	356593.59 (N=1336)	468810.55 (N=1664)	462535.28 (N=1632)	481934 (N=1697)	490423.13 (N=1732)
	Lescol 40mg	236524.95 (N=898)	291221.71 (N=1087)	378923.35 (N=1348)	382872.86 (N=1350)	405541.73 (N=1421)	417112.67 (N=1485)
	Lescol XL 80mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
Clofibrate	Lipaten Cap®	0 (N=0)	0 (N=	3256.16 (N=8)	0 (N=0)	0 (N=0)	0 (N=0)
Atorvastatin	Lipitor 10mg®	6716335.75 (N=21809)	7991475.4 (N=25927)	10197112.7 (N=33006)	9941500.00 (N=31752)	11069946.97 (N=34559)	11516831.50 (N=35975)
	Lipitor 20mg®	2760996.32 (N=6048)	3381065.3 (N=7399)	4497585.94 (N=9889)	4215029.19 (N=9152)	4663694.56 (N=9948)	4747044.27 (N=10194)

	Lipitor 40mg®	134682.28 (N=237)	165028.96 (N=292)	286394.24 (N=515)	287601.90 (N=525)	328279.04 (N=606)	369214.52 (N=698)
Essential phospholipids	Lipostabil capsules®	3867.74 (N=14)	2575.15 (N=8)	4052.32 (N=13)	2653.88 (N=11)	901.52 (N=3)	5079 (N=11)
	Lipostabil 5ml®	460.30 (N=2)	690.42 (N=3)	3464.04 (N=14)	1521.29 (N=5)	4552.72 (N=11)	4547.76 (N=12)
Fenofibrate	Lipsin 300mg®	149827.68 (N=367)	174556.40 (N=429)	247010.73 (N=529)	263186.28 (559)N=	267454.52 (N=562)	266716.21 (N=566)
Gemfibrozil	Lopid 600mg®	61465.39 (N=185)	61696.24 (N=191)	92606.75 (N=277)	97346.76 (N=272)	86931.32 (N=239)	111958.26 (N=302)
Probucol	Lurselle®	33667.82 (N=87)	32982.84 (N=73)	45309.83 (N=101)	51817.81 (N=106)	57935.93 (N=104)	43480.58 (N=89)
Nicotinic acid	Nicotinic acid BT®	1550.80 (N=51)	1193.33 (N=47)	794.21 (N=40)	870.91 (N=43)	1307.73 (N=53)	1370.06 (N=46)
	Nicotinic acid 30mg®	0 (N=0)	2.66 (N=1)	63.57 (N=3)	0 (N=0)	0 (N=0)	0 (N=0)
Acipimox	Olbetam 250mg®	4883.13 (N=20)	8351.15 (N=33)	4928.77 (N=23)	4508.16 (N=24)	5692.33 (N=29)	5695.13 (N=26)
Pravastatin	Prava 10mg®	249305.08 (N=1045)	289498.33 (N=1215)	377853.84 (N=1572)	345463.55 (N=1440)	367646.02 (N=1537)	406557.66 (N=1711)
	Prava 20mg®	322827.37 (N=1081)	392434.84 (N=1328)	484482.76 (N=1639)	500769.46 (N=1692)	547917.06 (N=1852)	563117.34 (N=1911)
	Prava 40mg®	166920.44 (N=565)	209434.51 (N=740)	287831.84 (N=990)	280841.12 (N=985)	334095.56 (N=1176)	35163713 (N=1238)
Cholestyramine	Questran Lite®	59101.59 (N=299)	64567.44 (N=343)	10190595 (N=666)	110949.31 (N=627)	109290.55 (N=618)	115008.70 (N=691)
Bezafibrate	Rolab-bezafibrate®	81962.68 (N=370)	90946.68 (N=416)	136070.93 (N=608)	142595.16 (N=628)	183040.91 (N=734)	178959.69 (N=713)
Simvastatin	Zocor® 10mg	1073305.95 (N=3778)	1313700.8 (N=4622)	1618164.35 (N=5666)	1503012.22 (N=5263)	1574081.91 (N=5496)	1638148.97 (N=5736)
	Zocor® 20mg	951313.28 (N=2363)	1123740.6 (N=2788)	1473534.98 (N=3661)	1378282.44 (N=3428)	1501265.19 (N=3723)	1519268.80 (N=3786)

	Zocor 40mg®	193652.30 (N=535)	241235.57 (N=691)	306405.76 (N=874)	305624.64 (N=885)	325668.76 (N=945)	341647.79 (N=1007)

Table C.25 Total cost of individual hypolipidemic drugs claimed from May 2002 to October 2002

Active ingredient	Individual agent	May 2002	Jun 2002	Jul 2002	Aug 2002	Sep 2002	Oct 2002
		Total cost (R)	Total cost (R)	Total cost (R)	Total cost (R)	Total cost (R)	Total cost (R)
Simvastatin	Adco-Simv 10mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	577.56 (N=3))
	Adco-Simv 20mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	431.36 (N=2))
	Adco-Simv 40mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
Cerivastatin	Baycol 0.1mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
	Baycol 0.2mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
	Baycol 0.3mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
	Baycol 0.4mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
Bezafibrate	Bezalip 200mg®	33916.42 (N=137)	31508.45 (N=124)	31742.67 (N=127	34036.83 (N=132)	28976.62 (N=114)	23400.24 (N=94)
	Bezalip 400mg®	58535.29 (N=176)	53946.06 (N=152)	48137 (N=134)	41951.66 (N=109)	33963.24 (N=90)	36018.74 (N=95)

Fluvastatin	Lescol 20mg®	474209.81 (N=1674)	448875.50 (N=1580)	463693.89 (N=1632)	460356.15 (N=1623)	423026.02 (N=1493)	422004.73 (N=1490)
	Lescol 40mg®	409922.79 (N=1385)	403883.52 (N=1356)	416740.05 (N=1404)	407507.72 (N=1372)	364339.40 (N=1221)	386335.28 (N=1304)
	Lescol XL 80mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	10477.61 (N=33)	106127.65 (N=344)
Clofibrate	Lipaten Cap®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
Atorvastatin	Lipitor 10mg®	11419301.75 (N=35589)	10824126.36 (N=33749)	11392587.61 (N=35550)	11642880.44 (N=36415)	10591803.43 (N=33098)	10814547.03 (N=33801)
	Lipitor 20mg®	4582255.63 (N=9883)	4297696.19 (N=9265)	4353696.93 (N=9499)	4358747.44 (N=9559	3993716.83 (N=8858)	4029032.85 (N=9017)
	Lipitor 40mg®	379568.25 (N=733)	379638.99 (N=749)	423962.74 (N=799)	437741.65 (N=880)	410991.88 (N=845)	460025.53 (N=964)
Essential phospholipids	Lipostabil cap®	2020.01 (N=5)	2514.57 (N=8)	0 (N=0)	1301.19 (N=4)	1708.04 (N=5)	1211.92 (N=4)
	Lipostabil 5ml®	2256.86 (N=7)	1805 (N=5)	4095 (N=11)	3302.86 (N=10)	6869.07 (N=21)	2539.76 (N=8)
Fenofibrate	Lipsin 300mg®	234003.85 (N=504)	224739.55 (N=464)	242919.81 (N=492)	231541.45 (N=471)	199727.82 (N=408)	228718.90 (N=457)
Gemfibrozil	Lopid 600mg®	103149.77 (N=276)	99289.30 (N=274)	98099.17 (N=263)	92189.03 (N=244)	81154.08 (N=212)	71184.75 (N=195)

Probucol	Lurselle®	24336.14 (N=53)	15683.43 (N=29)	12692.18 (N=26)	3994.86 (N=9)	2153.54 (N=6)	888.08 (N=3)
Nicotinic acid	Nicotinic acid BT®	1441.25 (N=52)	828.13 (N=41)	1352.46 (N=46)	1038.67 (N=41)	1609.52 (N=49)	1493.09 (N=35)
	Nicotinic acid 30mg®	0 (N=0)	38.73 (N=12)	9.54 (N=3)	15.72 (N=6)	13.78 (N=3)	36.02 (N=2)
Acipimox	Olbetam 250mg®	9684.07 (N=37)	10826.22 (N=38)	9404.81 (N=34)	6808.95 (N=25)	8766 (N=30)	8001.47 (N=28)
Pravastatin	Prava 10mg®	381345.71 (N=1595)	368530.71 (N=1539)	388224.27 (N=1626)	379980.04 (N=1589)	351945.28 (N=1472)	350909.82 (N=1469)
	Prava 20mg®	563986.87 (N=1912)	537102.99 (N=1818)	594774.54 (N=2006)	597455.82 (N=2021)	541685.86 (N=1818)	565320.32 (N=1894)
	Prava 40mg®	331816.55 (N=1179)	322805.30 (N=1141)	354818.80 (N=1262)	362873.95 (N=1290)	335403.87 (N=1164)	327534.63 (N=1154)
Cholestyramine	Questran Lite®	96548.43 (N=641)	92586.07 (N=539)	88353.69 (N=484)	89180.30 (N=476)	75552.34 (N=389)	78850.44 (N=420)
Bezafibrate	Rolab-bezafibrate®	215439.68 (N=862)	213559.21 (N=847)	225785.62 (N=904)	230608.66 (N=915)	193865.87 (N=760)	216040.33 (N=844)
Simvastatin	Zocor 10mg®	1549969.19 (N=5432)	1473550.99 (N=5165)	1485357.57 (N=5206)	1470023.03 (N=5150)	1271249.15 (N=4457)	126547.36 (N=4448)
	Zocor 20mg®	1439001.16 (N=3578)	1336863.51 (N=3331)	1372149.24 (N=3418)	1355213.88 (N=3393)	1214660.15 (N=3019)	1176724.35 (N=2947)

	Zocor 40mg®	329088.08 (N=982)	303315.41 (N=899)	311690.42 (N=937)	331286.87 (N=984)	282747.46 (N=853)	295421.40 (N=883)

Table C.26 Total cost of individual hypolipidemic drugs claimed from November 2002 to April 2003

Active ingredient	Individual agent	Nov 2002	Dec 2002	Jan 2003	Feb 2003	Mar 2003	April 2003
		Total cost (R)	Total cost (R)	Total cost (R)	Total cost (R)	Total cost (R)	Total cost (R)
Simvastatin	Adco-Simv 10mg®	10794.03 (N=56)	282665.75 (N=1492)	476822.19 (N=2590)	347559.74 (N=2299)	391671.13 (N=2594)	410202.30 (N=2708)
	Adco-Simv 20mg®	14233.74 (N=72)	260844.93 (N=1250)	449452.24 (N=2286)	337667.92 (N=2105)	422681.33 (N=2630)	460221.58 (N=2871)
	Adco-Simv 40mg®	8936.43 (N=41)	80078.64 (N=374)	150072.07 (N=712)	135944.36 (N=693)	178538.54 (N=906)	194486.91 (N=1006)
Cerivastatin	Baycol 0.1mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
	Baycol 0.2mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
	Baycol 0.3mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
	Baycol 0.4mg®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
Bezafibrate	Bezalip 200mg®	26451.71 (N=102)	24835.81 (N=97)	42881.35 (N=152)	33177.83 (N=120)	34118.81 (N=123)	24938.13 (N=96)
	Bezalip 400mg®	34793.24 (N=79)	327887.70 (N=80)	28191.96 (N=76)	18663.98 (N=57)	16134.04 (N=47)	14129.39 (N=40)

Fluvastatin	Lescol 20mg®	385694.20 (N=1379)	379676.27 (N=1359)	437718.66 (N=1470)	371509.34 (N=1243)	380424.60 (N=1277)	352423.21 (N=1180)
	Lescol 40mg®	355501.49 (N=1196)	335856.42 (N=1130)	423106.95 (N=1352)	327304.26 (N=1045)	362966.53 (N=1160)	346695.60 (N=1110)
	Lescol XL 80mg®	262169.16 (N=843)	320038.66 (N=1018)	488950.14 (N=1517)	497268.45 (N=1534)	547380.18 (N=1687)	580376.17 (N=1769)
Clofibrate	Lipaten Caps®	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)	0 (N=0)
Atorvastatin	Lipitor 10mg®	10270439.78 (N=32131)	10554290.60 (N=32277)	11999354.69 (N=35951)	10129187.83 (N=30288)	10834928.19 (N=32403)	10216633.49 (N=30574)
	Lipitor 20mg®	3725439.04 (N=8389)	3812412.61 (N=8367)	4695067.63 (N=10353)	3964339.97 (N=8786)	4171168.76 (N=9326)	3926516.85 (N=8798)
	Lipitor 40mg®	418538.82 (N=896)	471318.73 (N=989)	676563.09 (N=1395)	640329.84 (N=1324)	644730.08 (N=1335)	662966.50 (N=1378)
Essential phospholipids	Lipostabil capsules®	1430.43 (N=4)	0 (N=0)	200.28 (N=2)	182.36 (N=2)	0 (N=0)	0 (N=0)
	Lipostabil 5ml®	3425.66 (N=10)	1686.60 (N=6)	1145.34 (N=3)	0 (N=0)	917.10 (N=3)	305.70 (N=1)
Fenofibrate	Lipsin 300mg®	218996.96 (N=412)	232693.54 (N=439)	288452.14 (N=524)	229533.70 (N=424)	239016.93 (N=440)	231176.81 (N=421)
Gemfibrozil	Lopid 600mg®	66273.61 (N=184)	66632.42 (N=176)	106061 (N=252)	77025.36 (N=185)	63674.53 (N=164)	71921.67 (N=184)

Probucol	Lurselle®	466.26 (N=2)	888.18 (N=3)	466.36 (N=2)	466.36 (N=2)	1498.83 (N=3)	0 (N=0)
Nicotinic acid	Nicotinic acid BT®	1385.33 (N=45)	1865.02 (N=59)	2107.24 (N=67)	1156.17 (N=48)	1239.25 (N=42)	1037.72 (N=47)
	Nicotinic acid 30mg®	36.02 (N=2)	8.01 (N=3)	47.71 (N=7)	15.57 (N=3)	0 (N=0)	0 (N=0)
Acipimox	Olbetam 250mg®	8962.44 (N=32)	8996.82 (N=32)	9826.75 (N=32)	4387.99 (N=13)	5904.26 (N=18)	9145.99 (N=33)
Pravastatin	Prava 10mg®	333140.42 (N=1389)	323522.15 (N=1347)	398781.68 (N=1589)	324097.12 (N=1286)	347209.44 (N=1376)	333024.89 (N=1317)
	Prava 20mg®	552410.86 (N=1853)	537780.00 (N=1782)	636543.67 (N=2047)	552188.39 (N=1760)	553567.12 (N=1774)	543945.19 (N=1742)
	Prava 40mg®	322337.84 (N=1137)	319648.57 (N=1144)	390770.27 (N=1317)	349132.68 (N=1174)	370570.86 (N=1234)	362058.26 (N=1194)
Cholestyramine	Questran Lite®	70667.43 (N=428)	70876.09 (N=372)	101314.56 (N=636)	79800.64 (N=514)	88675.28 (N=565)	87113.56 (N=579)
Bezafibrate	Rolab-bezafibrate®	223460.09 (N=779)	247079.97 (N=850)	286670.08 (N=1009)	237874.81 (N=833)	247873.88 (N=865)	271426.90 (N=921)
Simvastatin	Zocor 10mg®	1208543.27 (N=4244)	601295.27 (N=2646)	482949.21 (N=2503)	423039.72 (N=2228)	461048.99 (N=2472)	440680.54 (N=2362)
	Zocor 20mg®	1046364.96 (N=2630)	466161.94 (N=1583)	331178.89 (N=1531)	280495.13 (N=1355)	294013.69 (N=1418)	303781.71 (N=1472)

	Zocor 40mg®	262816.69 (N=794)	139971.01 (N=499)	122219.70 (N=506)	119516.27 (N=506)	128687.06 (N=553)	122929.20 (N=518)

Table C.27 Average cost of all generic and innovator hypolipidemic drugs claimed from May 2001 to April 2002

Months	Innovator			Generic		
	Total no of items	Average cost (R)	Total cost (R)	Total no of items	Average cost (R)	Total cost (R)
May 2001	33742	322.68 ±99.35	10887790.11	188	208.14 ±52.61	39131.19
Jun 2001	27624	325.96 ±90.96	9004384.74	180	206.71 ±46.32	37207.99
Jul 2001	29719	326.85 ±95.55	9713600.71	163	200.52 ±21.78	32684.25
Aug 2001	48983	330.60 ±92.14	16193717.31	363	200.08 ±26.87	72628.29
Sep 2001	48344	332.96 ±91.15	16096533.13	440	197.10 ±27.84	86725.89
Oct 2001	49817	331.98 ±86.11	16538401.04	433	214.59 ±28.75	92919.16
Nov 2001	40887	331.29 ±85.82	13545167.95	370	221.52 ±30.37	81962.68
Dec 2001	48945	331.68 ±86.87	16234092.40	416	218.62 ±28.46	90946.68
Jan 2002	62911	334.14 ±88.14	21021165.02	608	223.80 ±36.54	136070.93
Feb 2002	60135	337.22 ±88.30	20278554.59	628	227.06 ±40.95	142595.16
Mar 2002	65037	343.02 ±90.01	22309179.42	734	249.37 ±43.73	183040.91
Apr 2002	67656	341.12 ±89.37	23078590.72	713	251.00 ±31.03	178959.69

Table C.28 Average cost of all generic and innovator hypolipidemic drugs claimed from May 2002 to April 2003

Months	Innovator			Generic		
	Total no of items	Average cost (R)	Total cost (R)	Total no of items	Average cost (R)	Total cost (R)
May 2002	65830	340.67 ±86.62	22426357.88	862	249.93 ±36.18	215439.68
Jun 2002	62278	340.89 ±86.01	21230155.01	847	252.14 ±33.12	213559.21
Jul 2002	64966	340.14 ±84.42	22097337.77	904	249.76 ±32.92	225785.62
Aug 2002	65803	339.03 ±83.74	22309428.51	915	252.03 ±31.91	230608.66
Sep 2002	59658	339.14 ±81.58	20232541.77	760	255.09 ±39.41	193865.87
Oct 2002	61056	338.28 ±81.45	20653874.33	849	255.65 ±51.79	217049.25
Nov 2002	58181	336.47 ±81.39	19576285.62	948	271.54 ±52.58	257424.29
Dec 2002	55408	337.56 ±90.05	18703342.42	3966	219.53 ±55.43	870669.29
Jan 2003	63284	342.33 ±95.58	21663899.36	6597	206.61 ±53.28	1363016.58
Feb 2003	53897	341.82 ±96.58	18422818.96	5930	178.59 ±55.71	1059046.83
Mar 2003	57420	340.44 ±98.95	19547874.53	6995	177.38 ±55.76	1240764.58
Apr 2003	54815	339.90 ±95.55	18631800.58	7506	178.04 ±57.62	1336337.69

APPENDIX D

Table D.1 MPL price of bezafibrate claimed from May 2002 to October 2002

Months	Description	Bezalip retard 400mg®	Rolab-bezafibrate 400mg®
May 2002	MPL price (R)	253.00	253.00
	MPL size	30	30
	Cost per unit* (R)	8.43	8.43
Jun 2002	MPL price (R)	253.00	253.00
	MPL size	30	30
	Cost per unit* (R)	8.43	8.43
Jul 2002	MPL price (R)	253.00	253.00
	MPL size	30	30
	Cost per unit* (R)	8.43	8.43
Aug 2002	MPL price (R)	253.00	253.00
	MPL size	30	30
	Cost per unit* (R)	8.43	8.43
Sep 2002	MPL price (R)	253.00	253.00
	MPL size	30	30
	Cost per unit* (R)	8.43	8.43
Oct 2002	MPL price (R)	253.00	253.00
	MPL size	30	30
	Cost per unit* (R)	8.43	8.43

Cost per unit* is the MPL price divided by the MPL size.

Table D.2 MPL price of bezafibrate claimed from November 2002 to April 2003

Months	Description	Bezalip retard 400mg®	Rolab-bezafibrate 400mg®
Nov 2002	MPL price (R)	284.00	284.00
	MPL size	30	30
	Cost per unit* (R)	9.47	9.47
Dec 2002	MPL price (R)	284.00	284.00
	MPL size	30	30
	Cost per unit* (R)	9.47	9.47
Jan 2003	MPL price (R)	284.00	284.00
	MPL size	30	30
	Cost per unit* (R)	9.47	9.47
Feb 2003	MPL price (R)	284.00	284.00
	MPL size	30	30
	Cost per unit* (R)	9.47	9.47
Mar 2003	MPL price (R)	284.00	284.00
	MPL size	30	30
	Cost per unit* (R)	9.47	9.47
Apr 2003	MPL price (R)	284.00	284.00
	MPL size	30	30
	Cost per unit* (R)	9.47	9.47

Cost per unit* is the MPL price divided by the MPL size.

Table D.3 MPL price of simvastatin claimed from December 2002 to April 2003

		Adco simvastatin 10mg	Adco simvastatin 20mg	Adco simvastatin 30mg	Zocor 10mg	Zocor 20mg	Zocor 40mg
December 2002	MPL price (R)	192.00	215.00	290.00	192.00	215.00	290.00
	MPL size	30	30	30	30	30	30
	Cost per unit* (R)	6.40	7.17	9.67	6.40	7.17	9.67
Jan 2003	MPL price (R)	192.00	215.00	290.00	192.00	215.00	290.00
	MPL size	30	30	30	30	30	30
	Cost per unit* (R)	6.40	7.17	9.67	6.40	7.17	9.67
Feb 2003	MPL price (R)	192.00	215.00	290.00	192.00	215.00	290.00
	MPL size	30	30	30	30	30	30
	Cost per unit* (R)	6.40	7.17	9.67	6.40	7.17	9.67
Mar 2003	MPL price (R)	192.00	215.00	290.00	192.00	215.00	290.00
	MPL size	30	30	30	30	30	30
	Cost per unit* (R)	6.40	7.17	9.67	6.40	7.17	9.67
Apr 2003	MPL price (R)	192.00	215.00	290.00	192.00	215.00	290.00
	MPL size	30	30	30	30	30	30
	Cost per unit* (R)	6.40	7.17	9.67	6.40	7.17	9.67

Cost per unit* is the MPL price divided by the MPL size.

Table D.5 Average MPL prices of the total cost of individual medicine items containing bezafibrate as an active ingredient claimed from May 2002 to April 2002

Months	Description	Bezalip retard 400mg	Rolab-bezafibrate 400mg
May 2002 to Aug 2002	Average cost (R)	8.43 ± 0	8.43 ± 0
Sep 2002 to Dec 2002	Average cost (R)	8.95 ± 0.60	8.95 ± 0.60
Jan 2003 to Apr 2003	Average cost (R)	9.47 ± 0	9.47 ± 0

Table D.6 Average MPL prices of the total cost of medicine items containing simvastatin as an active ingredient from Sept 2002 to Jan 2003

Simvastatin	Sep 2002 to Dec 2002		Jan 2003 to Apr 2003	
	Average cost (R)	Standard deviation	Average cost (R)	Standard deviation
Adco-simvastatin 10mg	6.40	0	6.40	0
Adco-simvastatin 20mg	7.17	0	7.17	0
Adco-simvastatin 40mg	9.67	0	9.67	0
Zocor 10mg	6.40	0	6.40	0
Zocor 20mg	7.17	0	7.17	0
Zocor 40mg	9.67	0	9.67	0

APPENDIX E

BEZAFIBRRATE

Table E.1 Calculated prescribed daily dose of Bezalip 200mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
15	2	0.1	30	162	0.2	30	260	0.2
25	2	0.17	60	131	0.4	60	169	0.4
30	121	0.2	90	71	0.6	90	69	0.6
60	127	0.4						
90	64	0.6						

Table E.2 Calculated prescribed daily dose of Bezalip 200mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
24	6	0.16	14	3	0.09	14	2	0.09
30	256	0.2	28	3	0.19	15	3	0.10
60	186	0.4	31	2	0.21	30	249	0.20
90	72	0.6	30	225	0.20	60	187	0.40
			60	133	0.40	69	2	0.46
			90	41	0.60	90	48	0.60

Table E.3 Calculated prescribed daily dose of Bezalip retard 400mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
12	1	0.16	5	3	0.07	7	3	0.09
15	2	0.20	15	8	0.20	10	5	0.13
20	3	0.27	30	988	0.40	15	9	0.20
45	4	0.60	60	24	0.80	30	1148	0.40
30	887	0.40				60	20	0.80
60	23	0.80						

Table E.4 Calculated prescribed daily dose of Bezalip retard 400mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
10	1	0.13	5	1	0.07	8	4	0.11
15	6	0.20	8	4	0.11	30	213	0.40
20	2	0.27	10	2	0.13	60	3	0.80
30	556	0.40	15	2	0.20			
60	6	0.80	23	1	0.31			
			30	334	0.40			

Table E.5 Calculated prescribed daily dose of Rolab-bezafibrate 400mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
15	10	0.20	7	3	0.09	6	2	0.08
28	15	0.37	10	1	0.13	10	2	0.13
30	836	0.40	15	24	0.20	14	1	0.19
45	4	0.60	28	9	0.37	15	33	0.20
60	29	0.80	30	1601	0.40	20	8	0.27
			60	21	0.80	22	1	0.29
						26	4	0.35
						28	9	0.37
						30	2561	0.40
						45	3	0.60
						60	59	0.80

Table E.6 Calculated prescribed daily dose of Rolab-bezafibrate 400mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
6	1	0.08	7	4	0.09	5	3	0.07
15	36	0.20	9	1	0.12	15	44	0.20
20	3	0.27	13	3	0.17	20	6	0.27
22	3	0.29	14	1	0.19	25	4	0.33
23	3	0.31	15	26	0.20	30	3514	0.40
28	18	0.37	25	3	0.33	45	3	0.60
38	1	0.51	28	4	0.37	60	54	0.80
30	3386	0.40	30	3096	0.40			
60	76	0.80	60	95	0.80			
90	1	1.20						

CLOFIBRATE

Table E.7 Calculated prescribed daily dose of Lipaten 200mg® from January 2002 to April 2002

Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (g)
60	8	0.4

FENOFIBRATE

Table E.8 Calculated prescribed daily dose of Lipsin 300mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
5	3	0.05	6	2	0.06	15	40	0.15
15	39	0.15	15	53	0.15	20	6	0.20
25	2	0.25	20	3	0.20	25	2	0.25
25	5	0.28	28	1	0.28	29	4	0.29
30	1285	0.30	29	2	0.29	30	1999	0.30
31	6	0.31	30	1575	0.30	60	165	0.60
45	1	0.45	31	3	0.31			
60	83	0.60	45	1	0.45			
120	12	1.20	60	104	0.60			
			150	1	1.50			

Table E.9 Calculated prescribed daily dose of Lipsin 300mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
13	1	0.13	8	1	0.08	8	3	0.08
15	31	0.15	10	3	0.10	15	39	0.15
20	5	0.20	15	37	0.15	28	3	0.28
27	5	0.27	16	2	0.16	30	1661	0.30
30	1799	0.30	20	3	0.20	60	103	0.60
50	1	0.50	28	1	0.28			
60	87	0.60	30	1594	0.30			
90	1	0.90	60	75	0.60			

GEMFIBROZIL

Table E.10 Calculated prescribed daily dose of Lopid 600mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
15	34	0.3	15	69	0.3	15	60	0.3
20	3	0.4	16	1	0.32	30	416	0.6
30	255	0.6	30	280	0.6	45	9	0.9
45	3	0.9	45	3	0.9	60	594	1.2
60	246	1.2	60	410	1.2	90	11	1.8
			90	9	1.8			

Table E.11 Calculated prescribed daily dose of Lopid 600mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
5	2	0.1	15	33	0.3	15	34	0.3
10	2	0.2	20	2	0.4	30	285	0.6
15	56	0.3	29	1	0.58	60	464	1.2
23	1	0.46	30	289	0.6	90	2	1.8
30	360	0.6	45	3	0.9			
45	6	0.9	60	436	1.2			
60	624	1.2	90	3	1.8			
90	6	1.8						

ATORVASTATIN

Table E.12 Calculated prescribed daily dose of Lipitor 10mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
1	5	0.33	2	8	0.67	1	2	0.33
2	10	0.67	3	7	1.00	2	12	0.67
3	6	1.00	4	7	1.33	3	8	1.00
4	5	1.33	5	18	1.67	4	7	1.33
5	10	1.67	6	16	2.00	5	23	1.67
7	47	2.33	7	59	2.33	6	5	2.00
8	9	2.67	8	18	2.67	7	70	2.33
10	29	3.33	9	10	3.00	8	13	2.67
11	9	3.67	10	65	3.33	9	7	3.00
12	41	4.00	11	6	3.67	10	75	3.33
13	6	4.33	12	29	4.00	11	3	3.67
14	391	4.67	13	16	4.33	12	33	4.00
15	1797	5.00	14	770	4.67	13	17	4.33
16	7	5.33	15	2742	5.00	14	1113	4.67
17	7	5.67	16	23	5.33	15	3944	5.00
20	42	6.67	17	5	5.67	16	23	5.33
21	12	7.00	18	13	6.00	17	10	5.67
22	3	7.33	19	7	6.33	18	7	6.00
23	16	7.67	20	72	6.67	19	3	6.33
24	7	8.00	21	18	7.00	20	24	6.67
26	11	8.67	22	7	7.33	21	25	7.00
27	2	9.00	23	21	7.67	22	3	7.33
28	16616	9.33	24	7	8.00	23	36	7.67
29	3	9.67	25	3	8.33	24	12	8.00
30	47933	10.00	26	4	8.67	25	6	8.33
31	18	10.33	28	28561	9.33	26	1	8.67
32	7	10.67	29	5	9.67	27	1	9.00
33	3	11.00	30	66032	10.00	28	37358	9.33
35	8	11.67	31	35	10.33	30	92192	10.00
42	2	14.00	32	3	10.67	31	46	10.33
45	44	15.00	35	4	11.67	36	1	12.00
56	19	18.67	45	60	15.00	40	6	13.33
60	57	20.00	56	46	18.67	45	88	15.00
84	3	28.00	60	49	20.00	56	40	18.67
90	3	30.00	84	4	28.00	60	68	20.00
			90	8	30.00	84	3	28.00
			168	1	56.00	90	6	30.00
						168	1	56.00

Table E.13 Calculated prescribed daily dose of Lipitor 10mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
2	4	0.67	2	4	0.67	1	4	0.33
3	2	1.00	3	3	1.00	2	6	0.67
4	5	1.33	4	6	1.33	3	6	1.00
5	15	1.67	5	25	1.67	4	10	1.33
6	8	2.00	6	2	2.00	5	6	1.67
7	94	2.33	7	72	2.33	6	10	2.00
8	26	2.67	8	19	2.67	7	71	2.33
9	4	3.00	9	16	3.00	8	25	2.67
10	86	3.33	10	130	3.33	9	8	3.00
12	27	4.00	11	1	3.67	10	66	3.33
13	17	4.33	12	37	4.00	11	5	3.67
14	1186	4.67	13	23	4.33	12	16	4.00
15	4763	5.00	14	1198	4.67	13	11	4.33
16	23	5.33	15	4639	5.00	14	1459	4.67
18	23	6.00	16	30	5.33	15	4916	5.00
20	64	6.67	17	2	5.67	16	13	5.33
21	26	7.00	18	18	6.00	17	3	5.67
22	2	7.33	19	13	6.33	18	13	6.00
23	29	7.67	20	79	6.67	19	4	6.33
25	15	8.33	21	51	7.00	20	52	6.67
25	19	8.33	22	5	7.33	21	35	7.00
26	5	8.67	23	36	7.67	22	13	7.33
27	4	9.00	24	3	8.00	23	38	7.67
28	37226	9.33	25	12	8.33	24	3	8.00
29	5	9.67	27	7	9.00	25	8	8.33
30	97345	10.00	28	35358	9.33	26	6	8.67
31	42	10.33	29	8	9.67	28	37458	9.33
32	28	10.67	30	89297	10.00	30	84799	10.00
33	1	11.00	31	26	10.33	31	15	10.33
36	2	12.00	32	1	10.67	36	3	12.00
40	8	13.33	35	2	11.67	37	4	12.33
42	1	14.00	36	8	12.00	40	2	13.33
45	86	15.00	40	8	13.33	42	3	14.00
56	36	18.67	45	71	15.00	45	59	15.00
60	51	20.00	56	22	18.67	56	15	18.67
84	2	28.00	60	63	20.00	60	43	20.00
90	20	30.00	80	3	26.67	90	2	30.00
168	3	56.00	84	2	28.00	180	3	60.00
			90	2	30.00	360	3	120.00
			112	1	37.33			
			120	2	40.00			
			150	2	50.00			

Table E.14 Calculated prescribed daily dose of Lipitor 20mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
1	3	0.67	1	3	0.67	1	6	0.67
5	3	3.33	2	1	1.33	3	1	2.00
6	9	4.00	3	1	2.00	4	4	2.67
7	11	4.67	4	5	2.67	5	11	3.33
10	8	6.67	5	7	3.33	7	40	4.67
11	2	7.33	7	20	4.67	8	4	5.33
12	10	8.00	8	1	5.33	9	2	6.00
13	12	8.67	10	16	6.67	10	29	6.67
14	27	9.33	12	16	8.00	11	6	7.33
15	205	10.00	13	15	8.67	12	12	8.00
16	2	10.67	14	121	9.33	13	11	8.67
17	2	11.33	15	322	10.00	14	260	9.33
20	12	13.33	18	6	12.00	15	686	10.00
21	2	14.00	20	33	13.33	16	12	10.67
22	1	14.67	21	5	14.00	17	2	11.33
23	3	15.33	22	2	14.67	18	5	12.00
26	3	17.33	23	7	15.33	20	19	13.33
27	2	18.00	24	9	16.00	21	8	14.00
28	5005	18.67	25	5	16.67	22	3	14.67
30	14170	20.00	26	3	17.33	23	6	15.33
31	3	20.67	28	8422	18.67	25	6	16.67
33	2	22.00	29	3	19.33	26	3	17.33
35	2	23.33	30	18758	20.00	28	10266	18.67
38	3	25.33	31	3	20.67	29	4	19.33
42	12	28.00	32	3	21.33	30	26784	20.00
45	52	30.00	37	3	24.67	31	1	20.67
56	162	37.33	38	6	25.33	35	2	23.33
60	685	40.00	40	7	26.67	37	1	24.67
84	22	56.00	42	24	28.00	42	29	28.00
90	11	60.00	43	2	28.67	45	97	30.00
112	17	74.67	45	61	30.00	56	170	37.33
120	31	80.00	56	187	37.33	60	649	40.00
240	3	160.00	60	628	40.00	65	1	43.33
			70	3	46.67	84	21	56.00
			84	25	56.00	90	7	60.00
			90	12	60.00	120	14	80.00
			112	10	74.67	140	1	93.33
			120	23	80.00			

Table E.15 Calculated prescribed daily dose of Lipitor 20mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
1	1	0.67	1	2	0.67	1	3	0.67
2	4	1.33	3	3	2.00	3	6	2.00
3	1	2.00	4	4	2.67	4	5	2.67
4	5	2.67	5	6	3.33	5	3	3.33
5	9	3.33	6	8	4.00	6	3	4.00
6	9	4.00	7	39	4.67	7	32	4.67
7	49	4.67	8	7	5.33	8	13	5.33
8	1	5.33	9	3	6.00	9	9	6.00
9	6	6.00	10	51	6.67	10	49	6.67
10	32	6.67	11	1	7.33	12	23	8.00
12	13	8.00	12	8	8.00	13	15	8.67
13	11	8.67	13	16	8.67	14	1264	9.33
14	464	9.33	14	742	9.33	15	5184	10.00
15	1275	10.00	15	2555	10.00	16	32	10.67
16	5	10.67	16	9	10.67	18	10	12.00
17	4	11.33	17	5	11.33	20	19	13.33
18	9	12.00	18	7	12.00	21	29	14.00
19	3	12.67	19	5	12.67	22	3	14.67
20	33	13.33	20	26	13.33	23	6	15.33
21	9	14.00	21	19	14.00	24	4	16.00
23	4	15.33	22	7	14.67	25	2	16.67
24	8	16.00	24	3	16.00	28	9225	18.67
25	1	16.67	25	2	16.67	30	21076	20.00
27	2	18.00	28	8566	18.67	31	19	20.67
28	9600	18.67	29	5	19.33	32	2	21.33
29	3	19.33	30	22198	20.00	35	8	23.33
30	26033	20.00	31	3	20.67	42	15	28.00
42	44	28.00	32	3	21.33	45	42	30.00
45	80	30.00	33	3	22.00	46	1	30.67
56	100	37.33	35	6	23.33	56	57	37.33
60	365	40.00	42	17	28.00	60	89	40.00
84	10	56.00	45	50	30.00	84	10	56.00
90	6	60.00	56	59	37.33	90	3	60.00
120	7	80.00	60	185	40.00	120	2	80.00
			84	7	56.00			
			90	1	60.00			

Table E.16 Calculated prescribed daily dose of Lipitor 40mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
7	2	9.33	8	6	10.67	5	6	6.67
14	3	18.67	14	19	18.67	7	13	9.33
15	6	20.00	15	19	20.00	10	5	13.33
28	119	37.33	28	409	37.33	14	88	18.67
30	147	40.00	30	495	40.00	15	272	20.00
56	8	74.67	56	22	74.67	20	2	26.67
60	10	80.00	60	40	80.00	23	1	30.67
						28	839	37.33
						30	988	40.00
						38	1	50.67
						45	12	60.00
						56	39	74.67
						60	78	80.00

Table E.17 Calculated prescribed daily dose of Lipitor 40mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
1	1	1.33	5	3	6.67	3	2	4.00
5	3	6.67	7	33	9.33	5	2	6.67
7	22	9.33	8	11	10.67	7	42	9.33
8	10	10.67	10	13	13.33	8	25	10.67
10	2	13.33	13	5	17.33	10	5	13.33
12	2	16.00	14	355	18.67	14	551	18.67
13	2	17.33	15	1114	20.00	15	2100	20.00
14	225	18.67	20	3	26.67	18	2	24.00
15	616	20.00	21	4	28.00	22	2	29.33
16	1	21.33	27	1	36.00	23	4	30.67
20	4	26.67	28	921	37.33	28	1086	37.33
21	1	28.00	30	1063	40.00	30	1397	40.00
26	3	34.67	42	13	56.00	42	23	56.00
28	936	37.33	45	37	60.00	45	59	60.00
30	1160	40.00	54	4	72.00	56	59	74.67
42	7	56.00	56	52	74.67	60	73	80.00
45	30	60.00	60	62	80.00			
56	53	74.67						
60	83	80.00						

CERIVASTATIN

Table E.18 Calculated prescribed daily dose of Baycol 0.1mg® from May 2001 to Dec 2001

May 2001 to Aug 2001			Sep 2001 to Dec 2001		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
7	1	0.02	28	22	0.09
14	1	0.05	30	17	0.10
15	6	0.05			
20	1	0.07			
28	294	0.09			
30	268	0.10			

Table E.19 Calculated prescribed daily dose of Baycol 0.2mg® from May 2001 to Dec 2001

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
4	1	0.03	15	5	0.10	28	4	0.19
5	4	0.03	28	113	0.19	30	6	0.20
7	2	0.05	30	147	0.20			
14	13	0.09						
15	25	0.10						
18	3	0.12						
20	15	0.13						
23	3	0.15						
24	6	0.16						
26	2	0.17						
28	2260	0.19						
30	2872	0.20						
31	4	0.21						
60	18	0.40						
112	1	0.75						

Table E.20 Calculated prescribed daily dose of Baycol 0.3mg® from May 2001 to Dec 2001

May 2001 to Aug 2001			Sep 2001 to Dec 2001		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
2	3	0.02	28	14	0.28
14	5	0.14	30	55	0.30
28	928	0.28			
30	1242	0.30			

Table E.21 Calculated prescribed daily dose of Baycol 0.4mg® from May 2001 to Dec 2001

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
10	2	0.13	8	3	0.11	28	2	0.37
14	12	0.19	18	5	0.24			
15	4	0.20	28	62	0.37			
28	1052	0.37	30	25	0.40			
30	855	0.40						
56	1	0.75						
60	12	0.80						

FLUVASTATIN

Table E.22 Calculated prescribed daily dose of Lescol 20mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
1	4	0.67	1	4	0.67	7	5	4.67
4	3	2.67	5	4	3.33	13	3	8.67
10	5	6.67	9	3	6.00	14	13	9.33
14	8	9.33	10	2	6.67	15	20	10.00
15	1	10.00	14	7	9.33	20	3	13.33
20	3	13.33	15	1	10.00	25	1	16.67
22	3	14.67	16	1	10.67	27	1	18.00
28	1142	18.67	20	3	13.33	28	2217	18.67
30	2678	20.00	24	1	16.00	29	3	19.33
56	9	37.33	25	1	16.67	30	4433	20.00
60	6	40.00	28	1827	18.67	35	1	23.33
			29	2	19.33	56	7	37.33
			30	3392	20.00	60	18	40.00
			60	13	40.00			
			168	1	112.00			

Table E.23 Calculated prescribed daily dose of Lescol 20mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
7	3	4.67	7	4	4.67	7	1	4.67
10	1	6.67	8	1	5.33	14	21	9.33
14	17	9.33	10	2	6.67	15	23	10.00
15	33	10.00	12	1	8.00	17	3	11.33
20	3	13.33	14	19	9.33	20	3	13.33
21	1	14.00	15	25	10.00	28	2007	18.67
23	1	15.33	21	1	14.00	30	3089	20.00
28	2069	18.67	27	3	18.00	56	3	37.33
30	4354	20.00	28	1958	18.67	60	20	40.00
32	3	21.33	30	3689	20.00			
35	1	23.33	60	18	40.00			
56	4	37.33						
60	19	40.00						

Table E.24 Calculated prescribed daily dose of Lescol 40mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
7	1	9.33	10	4	13.33	5	4	6.67
14	4	18.67	12	5	16.00	7	3	9.33
15	31	20.00	14	5	18.67	14	8	18.67
28	1208	37.33	15	28	20.00	15	31	20.00
30	1837	40.00	22	2	29.33	16	3	21.33
56	4	74.67	26	2	34.67	20	1	26.67
60	30	80.00	28	1695	37.33	28	2122	37.33
			30	2457	40.00	30	3378	40.00
			31	1	41.33	56	4	74.67
			56	19	74.67	60	50	80.00
			60	28	80.00			

Table E.25 Calculated prescribed daily dose of Lescol 40mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
7	3	9.33	2	3	2.67	5	2	6.67
10	4	13.33	4	2	5.33	7	2	9.33
14	4	18.67	7	1	9.33	14	25	18.67
15	43	20.00	10	2	13.33	15	48	20.00
17	1	22.67	12	1	16.00	18	3	24.00
20	4	26.67	14	6	18.67	20	3	26.67
21	1	28.00	15	42	20.00	28	1817	37.33
28	2037	37.33	16	4	21.33	30	2729	40.00
30	3374	40.00	20	1	26.67	33	2	44.00
32	1	42.67	26	1	34.67	56	21	74.67
56	13	74.67	28	1770	37.33	60	15	80.00
60	32	80.00	30	2976	40.00			
			56	17	74.67			
			60	25	80.00			

Table E.26 Calculated prescribed daily dose of Lescol XL 80mg® from Sep 2002 to April 2003

Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
7	11	18.67	1	6	2.67
10	1	26.67	4	4	10.67
14	11	37.33	5	3	13.33
15	4	40.00	6	2	16.00
18	4	48.00	7	6	18.67
20	3	53.33	10	3	26.67
21	3	56.00	14	24	37.33
23	3	61.33	15	38	40.00
26	5	69.33	18	11	48.00
28	1589	74.67	20	2	53.33
30	599	80.00	21	27	56.00
56	2	149.33	23	6	61.33
84	3	224.00	25	2	66.67
			28	4097	74.67
			30	2271	80.00
			56	2	149.33
			60	3	160.00

PRAVASTATIN

Table E.27 Calculated prescribed daily dose of Prava 10mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
10	8	3.33	10	1	3.33	5	3	1.67
15	39	5.00	14	2	4.67	7	4	2.33
20	4	6.67	15	74	5.00	10	5	3.33
25	2	8.33	20	3	6.67	14	3	4.67
28	12	9.33	22	2	7.33	15	93	5.00
30	3138	10.00	28	47	9.33	20	3	6.67
45	4	15.00	30	4465	10.00	23	3	7.67
			34	1	11.33	28	19	9.33
			45	8	15.00	30	6098	10.00
						45	16	15.00
						60	13	20.00

Table E.28 Calculated prescribed daily dose Prava 10mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
7	4	2.33	5	2	1.67	10	6	3.33
14	6	4.67	6	2	2.00	14	12	4.67
15	66	5.00	10	8	3.33	15	86	5.00
20	6	6.67	14	5	4.67	28	25	9.33
25	1	8.33	15	61	5.00	30	5435	10.00
28	19	9.33	20	8	6.67	60	4	20.00
30	6239	10.00	25	1	8.33			
45	8	15.00	28	23	9.33			
			30	5557	10.00			
			60	10	20.00			

Table E.29 Calculated prescribed daily dose of Prava 20mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
5	3	3.33	3	3	2.00	3	12	2.00
11	3	7.33	5	3	3.33	4	1	2.67
15	80	10.00	7	1	4.67	7	2	4.67
18	2	12.00	8	3	5.33	10	3	6.67
20	1	13.33	10	3	6.67	13	3	8.67
24	4	16.00	11	1	7.33	14	8	9.33
25	1	16.67	13	1	8.67	15	315	10.00
28	6	18.67	15	166	10.00	20	4	13.33
30	2935	20.00	20	9	13.33	28	13	18.67
45	2	30.00	28	15	18.67	30	6689	20.00
56	6	37.33	30	4675	20.00	45	2	30.00
60	10	40.00	60	35	40.00	60	42	40.00
			90	1	60.00			

Table E.30 Calculated prescribed daily dose Prava 20mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
2	2	1.33	5	5	3.33	5	4	3.33
3	6	2.00	6	4	4.00	7	2	4.67
5	2	3.33	10	6	6.67	10	5	6.67
7	5	4.67	12	4	8.00	12	2	8.00
10	4	6.67	13	2	8.67	15	265	10.00
15	334	10.00	15	213	10.00	17	2	11.33
16	1	10.67	20	3	13.33	20	7	13.33
20	3	13.33	23	4	15.33	23	6	15.33
21	2	14.00	27	3	18.00	24	3	16.00
28	11	18.67	28	23	18.67	28	42	18.67
30	7340	20.00	30	7014	20.00	30	6946	20.00
35	3	23.33	32	1	21.33	32	2	21.33
45	1	30.00	45	7	30.00	45	20	30.00
60	43	40.00	60	58	40.00	60	17	40.00

Table E.31 Calculated prescribed daily dose of Prava 40mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
10	3	13.33	5	2	6.67	5	8	6.67
15	488	20.00	7	3	9.33	7	9	9.33
20	1	26.67	8	6	10.67	8	37	10.67
30	1085	40.00	10	4	13.33	10	19	13.33
60	4	80.00	12	3	16.00	14	41	18.67
			14	37	18.67	15	1864	20.00
			15	1102	20.00	20	5	26.67
			20	7	26.67	28	10	37.33
			28	12	37.33	30	2380	40.00
			30	1558	40.00	60	16	80.00
			32	2	42.67			

Table E.32 Calculated prescribed daily dose Prava 40mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
1	2	1.33	2	1	2.67	4	3	5.33
3	2	4.00	5	2	6.67	5	4	6.67
4	1	5.33	7	18	9.33	6	6	8.00
6	3	8.00	8	43	10.67	7	6	9.33
7	12	9.33	10	14	13.33	8	36	10.67
8	39	10.67	12	13	16.00	10	19	13.33
10	13	13.33	14	13	18.67	12	12	16.00
12	19	16.00	15	1970	20.00	14	21	18.67
14	38	18.67	16	2	21.33	15	2141	20.00
15	2132	20.00	22	9	29.33	16	9	21.33
20	3	26.67	23	3	30.67	21	2	28.00
22	6	29.33	24	1	32.00	22	15	29.33
23	1	30.67	25	3	33.33	24	2	32.00
25	1	33.33	26	2	34.67	25	3	33.33
26	1	34.67	28	4	37.33	28	8	37.33
28	3	37.33	30	2501	40.00	30	2629	40.00
29	1	38.67				60	3	80.00
30	2595	40.00						

SIMVASTATIN

Table E.33 Calculated prescribed daily dose of Zocor 10mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
1	5	0.33	2	2	0.67	2	3	0.67
4	1	1.33	5	6	1.67	7	6	2.33
7	2	2.33	6	4	2.00	10	16	3.33
10	4	3.33	8	3	2.67	13	6	4.33
11	2	3.67	10	7	3.33	14	222	4.67
12	6	4.00	12	9	4.00	15	563	5.00
13	12	4.33	13	9	4.33	16	6	5.33
14	82	4.67	14	169	4.67	20	12	6.67
15	451	5.00	15	484	5.00	21	2	7.00
20	5	6.67	16	6	5.33	22	2	7.33
21	2	7.00	18	6	6.00	23	3	7.67
23	1	7.67	20	7	6.67	24	2	8.00
28	3010	9.33	21	2	7.00	27	2	9.00
29	3	9.67	23	2	7.67	28	6369	9.33
30	8910	10.00	25	2	8.33	30	14856	10.00
31	2	10.33	28	5656	9.33	31	4	10.33
39	2	13.00	29	3	9.67	34	3	11.33
45	14	15.00	30	11197	10.00	36	3	12.00
56	3	18.67	39	2	13.00	42	16	14.00
60	7	20.00	42	22	14.00	45	40	15.00
			45	14	15.00	56	9	18.67
			56	3	18.67	60	7	20.00
			60	8	20.00	84	3	28.00
						90	1	30.00
						112	3	37.33
						336	2	112.00

Table E.34 Calculated prescribed daily dose of Zocor 10mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
1	3	0.33	4	2	1.33	5	2	1.67
3	2	1.00	7	3	2.33	6	3	2.00
7	3	2.33	8	6	2.67	7	5	2.33
8	6	2.67	10	11	3.33	10	9	3.33
10	5	3.33	14	142	4.67	12	3	4.00
11	1	3.67	15	438	5.00	14	87	4.67
12	13	4.00	16	6	5.33	15	220	5.00
13	12	4.33	19	1	6.33	16	6	5.33
14	192	4.67	20	14	6.67	20	9	6.67
15	578	5.00	22	19	7.33	22	8	7.33
16	3	5.33	25	1	8.33	28	3556	9.33
18	3	6.00	28	4680	9.33	30	5587	10.00
20	6	6.67	30	10396	10.00	45	49	15.00
26	1	8.67	31	6	10.33	56	14	18.67
28	5743	9.33	32	7	10.67	60	1	20.00
30	14302	10.00	40	2	13.33	180	3	60.00
32	6	10.67	42	18	14.00	360	3	120.00
42	18	14.00	45	21	15.00			
45	32	15.00	56	10	18.67			
54	2	18.00	60	10	20.00			
56	18	18.67	90	2	30.00			
60	4	20.00						

Table E.35 Calculated prescribed daily dose of Zocor 20mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
3	3	2.00	7	3	4.67	3	2	2.00
9	2	6.00	8	3	5.33	4	1	2.67
10	8	6.67	10	11	6.67	5	10	3.33
12	2	8.00	11	3	7.33	7	6	4.67
14	45	9.33	14	87	9.33	8	14	5.33
15	110	10.00	15	227	10.00	10	26	6.67
20	11	13.33	20	12	13.33	11	3	7.33
22	3	14.67	21	1	14.00	12	6	8.00
23	1	15.33	23	1	15.33	14	146	9.33
25	2	16.67	28	3600	18.67	15	379	10.00
26	3	17.33	29	1	19.33	16	2	10.67
28	2122	18.67	30	6983	20.00	20	19	13.33
30	5622	20.00	31	21	20.67	23	6	15.33
31	3	20.67	45	16	30.00	24	3	16.00
40	3	26.67	56	18	37.33	26	1	17.33
45	14	30.00	60	25	40.00	28	4308	18.67
56	13	37.33				30	9571	20.00
60	20	40.00				31	15	20.67
						39	2	26.00
						45	14	30.00
						56	23	37.33
						60	39	40.00
						84	1	56.00
						90	1	60.00

Table E.36 Calculated prescribed daily dose of Zocor 20mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
3	3	2.00	2	3	1.33	6	2	4.00
4	2	2.67	3	1	2.00	8	12	5.33
5	9	3.33	4	2	2.67	10	1	6.67
6	2	4.00	5	2	3.33	14	56	9.33
7	7	4.67	7	7	4.67	15	194	10.00
8	12	5.33	10	9	6.67	20	2	13.33
10	16	6.67	12	2	8.00	23	3	15.33
12	4	8.00	14	85	9.33	24	4	16.00
14	111	9.33	15	337	10.00	28	2323	18.67
15	445	10.00	16	3	10.67	30	3170	20.00
16	5	10.67	20	23	13.33	31	9	20.67
20	9	13.33	24	5	16.00			
21	1	14.00	25	6	16.67			
23	1	15.33	26	2	17.33			
25	5	16.67	28	3117	18.67			
27	3	18.00	30	6556	20.00			
28	4056	18.67	45	7	30.00			
30	8954	20.00	56	3	37.33			
31	9	20.67	60	9	40.00			
45	11	30.00						
56	17	37.33						
60	38	40.00						

Table E.37 Calculated prescribed daily dose of Zocor 40mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD(mg)	Quantity	Number of scripts	PDD(mg)	Quantity	Number of scripts	PDD(mg)
7	3	9.33	4	3	5.33	3	2	4.00
8	3	10.67	5	3	6.67	8	29	10.67
10	1	13.33	7	3	9.33	10	7	13.33
14	5	18.67	8	22	10.67	14	36	18.67
15	385	20.00	10	2	13.33	15	1310	20.00
16	2	21.33	14	13	18.67	19	6	25.33
20	11	26.67	15	721	20.00	20	7	26.67
27	3	36.00	17	1	22.67	22	2	29.33
28	3	37.33	20	3	26.67	28	27	37.33
30	1163	40.00	28	6	37.33	30	2273	40.00
60	7	80.00	30	1738	40.00	40	3	53.33
			60	9	80.00	45	9	60.00

Table E.38 Calculated prescribed daily dose of Zocor 40mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
3	1	4.00	2	2	2.67	2	3	2.67
4	1	5.33	7	2	9.33	3	2	4.00
8	37	10.67	8	44	10.67	8	26	10.67
10	6	13.33	10	4	13.33	14	8	18.67
14	43	18.67	14	11	18.67	15	841	20.00
15	1533	20.00	15	1257	20.00	21	3	28.00
20	6	26.67	28	19	37.33	28	9	37.33
24	1	32.00	30	1676	40.00	30	1154	40.00
28	12	37.33	45	8	60.00	40	1	53.33
30	2141	40.00	60	6	80.00	45	18	60.00
32	1	42.67				60	18	80.00
45	16	60.00						
56	1	74.67						
60	3	80.00						

Table E.39 Calculated prescribed daily dose of Adco-Simvastatin 10mg® from Sep 2002 to April 2003

Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
14	5.00	4.67	7	2.00	2.33
15	46.00	5.00	10	9.00	3.33
28	192.00	9.33	14	26.00	4.67
30	1308.00	10.00	15	362.00	5.00
			23	3.00	7.67
			28	666.00	9.33
			30	9113.00	10.00
			60	9.00	20.00
			84	1.00	28.00

Table E.40 Calculated prescribed daily dose of Adco-Simvastatin 20mg® from Sep 2002 to April 2003

Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
5	3.00	3.33	7	3.00	4.67
14	6.00	9.33	10	7.00	6.67
15	111.00	10.00	14	60.00	9.33
28	166.00	18.67	15	1448.00	10.00
30	1030.00	20.00	20	2.00	13.33
60	8.00	40.00	21	4.00	14.00
			23	2.00	15.33
			28	720.00	18.67
			30	7587.00	20.00
			45	2.00	30.00
			60	57.00	40.00

Table E.41 Calculated prescribed daily dose of Adco-Simvastatin 40mg® from Sep 2002 to April 2003

Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (mg)	Quantity	Number of scripts	PDD (mg)
14	2	10.00	5	2	3.57
20	3	21.43	11	2	7.86
28	3	30.00	10	4	14.29
60	3	64.29	25	2	17.86
15	227	1216.07	14	9	45.00
30	177	1896.43	8	25	71.43
			28	20	200.00
			60	15	321.43
			15	1835	9830.36
			30	1403	15032.14

ACIPIMOX

Table E.42 Calculated prescribed daily dose of Olbetam 250 mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
30	1	0.25	30	2	0.25	60	63	0.50
60	64	0.50	60	60	0.50	90	34	0.75
65	1	0.54	90	51	0.75	120	5	1.00
90	37	0.75	120	2	1.00			
120	2	1.00						

Table E.43 Calculated prescribed daily dose of Olbetam 250 mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
21	3	0.18	30	3	0.25	10	2	0.08
30	5	0.25	60	67	0.50	30	8	0.25
60	80	0.50	90	50	0.75	60	36	0.50
80	6	0.67	120	2	1.00	70	3	0.58
90	36	0.75				90	45	0.75
120	4	1.00				120	2	1.00

CHOLESTYRAMINE

Table E.44 Calculated prescribed daily dose of Questran lite® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
1	9	0.13	1	8	0.13	1	14	0.13
2	18	0.27	2	21	0.27	2	41	0.27
3	88	0.40	3	70	0.40	3	168	0.40
4	52	0.53	4	65	0.53	4	134	0.53
5	340	0.67	5	298	0.67	5	618	0.67
6	50	0.80	6	36	0.80	6	86	0.80
7	17	0.93	7	9	0.93	7	23	0.93
8	16	1.07	8	18	1.07	8	42	1.07
9	9	1.20	9	3	1.20	9	15	1.20
10	97	1.33	10	54	1.33	10	196	1.33
12	24	1.60	12	12	1.60	11	3	1.47
14	2	1.87	13	1	1.73	12	21	1.60
15	29	2.00	14	5	1.87	14	14	1.87
16	15	2.13	15	13	2.00	15	28	2.00
20	41	2.67	16	9	2.13	16	19	2.13
21	6	2.80	20	44	2.67	18	3	2.40
24	3	3.20	25	1	3.33	19	1	2.53
25	2	3.33	28	1	3.73	20	107	2.67
28	9	3.73	30	249	4.00	21	12	2.80
30	190	4.00	35	1	4.67	24	3	3.20
32	3	4.27	40	2	5.33	28	5	3.73
40	4	5.33	50	200	6.67	29	1	3.87
42	2	5.60	60	189	8.00	30	420	4.00
50	214	6.67	70	1	9.33	32	1	4.27
60	149	8.00	90	40	12.00	33	3	4.40
90	25	12.00	100	16	13.33	35	3	4.67
100	15	13.33				40	12	5.33
240	4	32.00				42	5	5.60
						44	1	5.87
						50	300	6.67
						60	225	8.00
						90	66	12.00
						100	12	13.33

Table E.45 Calculated prescribed daily dose of Questran lite® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
1	18	0.13	1	1	0.13	1	11	0.13
2	55	0.27	2	31	0.27	2	55	0.27
3	130	0.40	3	92	0.40	3	162	0.40
4	121	0.53	4	78	0.53	4	125	0.53
5	458	0.67	5	329	0.67	5	595	0.67
6	67	0.80	6	43	0.80	6	79	0.80
7	24	0.93	7	10	0.93	7	25	0.93
8	39	1.07	8	35	1.07	8	47	1.07
9	12	1.20	9	4	1.20	9	3	1.20
10	151	1.33	10	121	1.33	10	204	1.33
12	24	1.60	12	7	1.60	11	1	1.47
14	8	1.87	14	9	1.87	12	18	1.60
15	41	2.00	15	26	2.00	14	18	1.87
16	22	2.13	16	9	2.13	15	53	2.00
18	2	2.40	20	47	2.67	16	23	2.13
20	61	2.67	21	6	2.80	19	2	2.53
21	11	2.80	25	7	3.33	20	114	2.67
25	8	3.33	28	19	3.73	21	3	2.80
28	4	3.73	30	301	4.00	23	2	3.07
30	346	4.00	35	3	4.67	24	4	3.20
40	6	5.33	40	6	5.33	25	7	3.33
42	1	5.60	42	1	5.60	26	3	3.47
44	1	5.87	50	248	6.67	28	12	3.73
45	6	6.00	60	115	8.00	30	323	4.00
50	268	6.67	90	53	12.00	32	3	4.27
60	193	8.00	100	8	13.33	36	2	4.80
90	52	12.00				40	5	5.33
100	11	13.33				42	4	5.60
						43	3	5.73
						45	4	6.00
						47	3	6.27
						50	246	6.67
						56	1	7.47
						60	97	8.00
						63	2	8.40
						90	21	12.00
						100	5	13.33
						180	9	24.00

NICOTINIC ACID

Table E.46 Calculated prescribed daily dose of Nicotinic acid (BT) 50 mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
10	6	0.03	10	23	0.03	15	5	0.05
15	21	0.05	15	8	0.05	30	36	0.10
20	18	0.07	20	1	0.07	45	4	0.15
21	1	0.07	23	3	0.08	60	25	0.20
23	2	0.08	30	26	0.10	90	30	0.30
30	42	0.10	45	6	0.15	120	12	0.40
40	2	0.13	60	36	0.20	180	15	0.60
45	8	0.15	90	23	0.30	240	8	0.80
50	5	0.17	120	16	0.40	270	8	0.90
60	24	0.20	180	35	0.60	300	10	1.00
90	18	0.30	270	6	0.90	425	4	1.42
100	4	0.33	300	11	1.00	450	6	1.50
120	3	0.40	400	9	1.33	900	4	3.00
180	19	0.60	425	4	1.42	1000	15	3.33
200	4	0.67	450	11	1.50			
240	8	0.80	600	4	2.00			
270	2	0.90	720	3	2.40			
300	12	1.00	90	4	0.30			
450	11	1.50	1000	19	3.33			
900	8	3.00						
1000	9	3.33						

Table E.47 Calculated prescribed daily dose of Nicotinic acid (BT) 50 mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
15	2	0.05	10	1	0.03	15	9	0.05
30	48	0.10	30	26	0.10	30	25	0.10
45	6	0.15	40	3	0.13	60	26	0.20
50	1	0.17	60	20	0.20	90	24	0.30
60	21	0.20	90	27	0.30	120	15	0.40
90	23	0.30	120	18	0.40	180	50	0.60
100	1	0.33	180	7	0.60	270	3	0.90
120	15	0.40	200	6	0.67	300	12	1.00
180	5	0.60	270	8	0.90	360	8	1.20
200	3	0.67	300	5	1.00	425	4	1.42
270	4	0.90	360	27	1.20	450	8	1.50
300	4	1.00	425	4	1.42	500	3	1.67
360	6	1.20	450	8	1.50	600	15	2.00
425	4	1.42	500	6	1.67	1000	2	3.33
450	11	1.50	600	8	2.00			
540	3	1.80	840	2	2.80			
600	6	2.00	900	2	3.00			
900	2	3.00	1000	10	3.33			
1000	15	3.33						

Table E.48 Calculated prescribed daily dose of Nicotinic acid 30 mg® from May 2001 to April 2002

May 2001 to Aug 2001			Sep 2001 to Dec 2001			Jan 2002 to Apr 2002		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
30	1	0.03	30	4	0.03	540	3	0.54
1000	1	1.00	60	3	0.06			

Table E.49 Calculated prescribed daily dose of Nicotinic acid 30 mg® from May 2002 to April 2003

May 2002 to Aug 2002			Sep 2002 to Dec 2002			Jan 2003 to Apr 2003		
Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)	Quantity	Number of scripts	PDD (g)
10	1	0.01	30	3	0.03	30	2	0.03
30	16	0.03	60	2	0.06	90	4	0.09
60	4	0.06	100	1	0.10	200	4	0.20
			450	4	0.45			