Retrospective analysis of the prescribing patterns of calcium channel blockers in a section of the private health care sector of South Africa

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“For my part I know nothing with any certainty, but the sight of the stars makes me dream.”
Vincent Van Gogh

This dissertation is dedicated in remembrance of Mr J.J. Smit.

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ABSTRACT

Title: Retrospective analysis of the prescribing patterns of calcium channel blockers in a section of the private health care system of South Africa.

Keywords: Angina pectoris, calcium channel blockers, cardiovascular medicine, generic substitution, hypertension, medicine cost, pharmaco-ecomomy, prevalence.

Background: Calcium channel blockers are mainly divided into antihypertensive and anti-anginal treatment agents. In 2000 it was estimated that 972 million adults worldwide were living with hypertension and it is expected to affect 1.56 billion patients by 2025. The incremental expenditure for the antihypertensive therapeutic group in the United States of America was estimated at $US 55 billion per annum in 2006.

It was stated that around seven million people in the United States of America suffered from angina, with around 400 000 new reports every year.

Objective: To determine the prescribing patterns of calcium channel blocker medicine items during 2005 to 2008 in a section of the private health care sector of South Africa.

Methods: A retrospective quantitative drug utilisation review was done using a medicine claims database ranging over four years from 1 January 2005 to 31 December 2008. The total medicine claims database was divided into cardiovascular medicine items and then into calcium channel blockers. These were analysed according to age as well as gender. Further analysis included adherence of calcium channel blockers as well as an analysis of prescribers of these items during the study period.

Results: The total number of patients on the medicine claims database consisted of 1 509 621 patients in 2005. This number decreased to 974 497 patients in 2008. The most medicine items were dispensed in 2006 (n = 21 113 422) with an average cost of R 92.82 (SD = 196.42) per medicine item.

It was noted that 16.05% (n = 242 264) of patients used at least one cardiovascular item in 2005. The percentage of cardiovascular medicine item users increased by 4.36% during the study period to 20.41% (n = 198 847) in 2008. In 2008 the cardiovascular medicine items dispensed were responsible for 19.18% (R 342 565 308.41) of the total cost of all medicine items claimed.

In 2005 the results revealed that 1.63% (n = 318 258) of all medicine items dispensed were calcium channel blocker medicine items. The percentage of calcium channel blockers increased to 2.24% (n = 367 437) of the total number of medicine items in 2008. The cost prevalence index was calculated for the calcium channel blockers and the value declined from 1.5 in 2005 to 1.22 in 2008, which indicated that the items dispensed were relatively expensive, but less than in 2005. An increase of 16.17% in the usage of generic medicine items were noted from 2005 to 2008.

More female patients than male patients claimed medicine items during the study period. A higher percentage of male patients used a cardiovascular medicine item as well as calcium channel blockers during the study period compared to females and a larger percentage of their medicine expenditure was used on cardiovascular medicine items as well as calcium channel blockers compared to females.

The usage of cardiovascular medicine items as well as calcium channel blocker medicine items increased with patient age. In 2008, 17.98% of patients older than 65 years of age used a calcium channel blocker compared to 0.97% of patients aged > 25 ≤ 35 years. Only 60.34% of calcium channel blockers items were used with acceptable refill adherence rates during the study. More than a third of the calcium channel blockers medicine items used had unacceptable low adherence rates from 2005 to 2008.

In each of the study years the highest potential saving with generic substitution was seen with amlodipine containing items. It was also observed that some generic substitutions could be relatively more expensive than the innovator products and an increased cost instead of a saving through generic substitution may have occurred.

Conclusion: This study highlighted the prescribing patterns and cost implications of calcium channel blockers in the private health care sector of South Africa.

It is recommended that a more in-depth study of the adherence of calcium channel blockers be done. This study should also include the cost strategies of generic substitution of calcium channel blockers in South Africa.

OPSOMMING

Titel: Retrospektiewe analise van die voorskryfpatrone van kalsiumkanaalblokkeerders in ’n deel van die gesondheidsorgsisteem van Suid-Afrika.

Sleutelwoorde: *Angina pectoris*, kalsium kanaal blokkeerders, kardiovaskulêre medisyne, generiese vervanging, Hipertensie, medisynekoste, farmako-ekonomie, voorkoms.

Agtergrond: Kalsiumkanaalblokkeerders word hoofsaaklik gebruik vir die behandeling van hipertensie en angina. In 2000 is ’n geskatte 972 miljoen volwassenes wêreldwyd met hipertensie gediagnoseer. Daar word verwag dat hierdie syfer verder sal styg na ’n beraamde 1.56 biljoen pasiënte wêreldwyd teen 2025. Die inkrementele uitgawes wat aan antihipertensiewe middels gespandeer was in die Verenigde State van Amerika was VSA$ 55 biljoen vir 2006.

Ongeveer 7 miljoen mense in die Verenigde State ly aan angina met ongeveer 400 000 nuwe gevalle per jaar.

Doelstelling: Die bepaling van die voorskryfpatrone vir kalsiumkanaalblokkeerders gedurende 2005 tot 2008 in ’n deel van die private gesondheidsorgsektor van Suid-Afrika.

Metode: ’n Retrospektiewe, kwantitatiewe, medisyneverbruikstudie is gedoen deur ’n medisyne-eise databasis wat oor vier jaar strek, vanaf 1 Januarie 2005 tot 31 Desember 2008, na te vors. Die totale medisyne-eise databasis is ingedeel in kardiovaskulêre middels met ’n verdere onderverdeling in kalsiumkanaalblokkeerders. Verdere analise is volgens ouderdom en geslag van die pasiënt gedoen. Nog analises sluit hervul-meewerkendheidskoers sowel as ’n analise van verskillende voorskrywers van hierdie items gedurende die studieperiode in.

Resultate: Die totale aantal pasiënte op die medisyne-eise databasis was 1 509 621 in 2005. Hierdie getal het afgeneem tot 974 497 pasiënte in 2008. Die meeste medisyne-items is uitgereik in 2006 (n = 21 113 422) met ’n gemiddelde koste van R 92.82 (SD = 196.42) per medisyne-item.

Daar is waargeneem dat 16.05% (n = 242 264) van die pasiënte op die medisyne-eise databasis minstens een kardiovaskulêre item in 2005 gebruik het. Die persentasie van kardiovaskulêre medisyne-item gebruikers het met 4.36% toegeneem tot 20.41% (n = 198 847) in 2008. Die kardiovaskulêre items wat in 2008 uitgereik is, het 19.18%

(R 342 565 308.41) van die totale koste van die medisyne-items wat in daardie jaar uitgereik is, beloop.

In 2005 is opgemerk dat kalsiumkanaalblokkeerders 1.63% (n = 318 258) van die totale medisyne uitgereik gedurend 2005 beslaan het. Die persentasie van kalsiumkanaalblokkeerders het toegeneem tot 2.24% (n = 367 437) van die totale medisyne-items wat uitgereik is in 2008. Die koste-voorkoms indeks van kalsium kanaal blokkeerders is ook bereken. Die waarde hiervan het afgeneem van 1.5 in 2005 tot 1.22 in 2008. Dit toon dat hierdie groep middels steeds relatief duur was in 2008, maar goedkoper was as in 2005. ’n Toename van 16.17% in die gebruik van generiese kalsiumkanaalblokkeerders vanaf 2005 tot 2008 is waargeneem.

Meer vrouens as mans het middels gedurend die studie tydperk ontvang. Hiervan was ’n groter persentasie manlike pasiënte wat gedurende die studieperiode ’n kardiovaskulêre medisyne-item sowel as ’n kalsium kanaal blokkeerder gebruik in vergelyking met vroulike pasiënte. Manlike pasiënte het ook ’n groter persentasie van hul totale medisynekostes daaraan bestee.

Die verbruik van kardiovaskulêre medisyne items sowel as kalsiumkanaalblokkers het met toenemende pasiënt ouderdom gedurende die studie tydperk toegeneem. In 2008 het 17.98% van pasiënte ouer as 65 jaar ’n kalsium kanaal blokkeerder ontvang in vergelyking met 0.97% van pasiënte > 25 ≤ 35 jaar. Slegs 60.34% van kalsium kanaal blokkeerders is volgens ’n aanvaarbare hervul-meewerkendheidskoers gebruik. Vir meer as ’n derde van die kalsium kanaal blokkeerders is daar ’n onaanvaarbare lae hervul-meewerkendheidskoers vanaf 2005 tot 2008 gevind.

Die grootste moontlike besparing met generiese vervanging is gevind in amlodipien bevattende middels in elk van die jare gedurende die studie tydperk. Daar is ironies ook opgemerk dat van die generiese middels relatief duurder as die oorspronklike middel kan kos. Dit lei tot ’n onnodige verhoogde koste in medisyneverbruik.

Gevolgtrekking: Hierdie studie het die voorskryfpatrone en die koste-implikasies van die kalsiumkanaalblokkeerders in die private gesondheidsorgsektor in Suid-Afrika uitgelig.

Dit word aanbeveel dat ’n meer in diepte studie oor die hervul-meewerkendheidskoers van pasiënte op kalsium kanaal blokkeerders gedoen word. Hierdie studie behoort ook kostestrategieë van generiese vervanging van kalsiumkanaalblokkeerders in Suid-Afrika in te sluit.

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ABBREVIATIONS AND DEFINITIONS

1 Abbreviations used in this study

ACE:	Angiotensin-converting enzyme
ARV:	Antiretroviral
AV:	Atrioventricular
BP:	Blood pressure. Measured Systolic BP over Diastolic BP such as 120/80 mmHg
CAD:	Coronary artery disease. Also known as CHD
CBA:	Cost-benefit analysis
CCB:	Calcium channel blocker
CDL:	Chronic disease list
CHD:	Coronary heart disease. Also known as CAD
CMA:	Cost-minimisation analysis
CMS:	Council of Medical Schemes
CPI:	Cost prevalence index
CUA:	Cost-utility analysis
DUR:	Drug utilisation review
GP:	General (medical) practitioner
HBP:	High blood pressure. Also known as hypertension
HIV:	Human immunodeficiency virus
IHD:	Ischemic heart disease
MCC:	Medicine control council

Abbreviations used in this study (continued)

MIMS®:	Monthly index of medical specialities
NAPPI:	National pharmaceutical product interface (codes)
NHI:	National health insurance
PBM:	Pharmacy benefit management (company)
PDD:	Prescribed daily dosage
PMB:	Prescribed minimum benefits
QALY:	Quality-adjusted life-years
RDD:	Recommended daily dosage
R.S.A.:	Republic of South Africa
Rx:	Prescription
S.A.:	South Africa
TB:	Tuberculosis
U.S.A.:	United States of America

2 Definitions used in this study

Bioequivalent: The absence of significant difference in the rate and extent to which the active ingredient in pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study (Chen, 2001:1646).

Chronotropy: Term used for the conductivity of the heart (Sweetman, 2010) e.g. a negative chronotroic agent causes a reduction in the conductivity of the heart and resulting in a reduced heart tempo.

Combination therapy: Any antihypertensive medication prescribed in combination with other antihypertensive medication e.g. a CCB together with a β-blocker.

Diastolic blood pressure: The pressure while the heart is at rest, between beats (National Heart Lung and Blood Institute, 2008).

Direct medical cost: Expenses directly related to specific goods, products or medical care (Waning & Montagne, 2001: 144).

DUR: a study of the distribution, marketing, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences thereof (WHO, 2003:33).

Generic equivalent: A drug that is no longer under patent protection, which may be produced by any manufacturer who follows good manufacturing protocols. Also known as 'Me-too' drugs (Segen, 2006:264).

Indirect cost: Expenses related to the loss of productivity and associated with morbidity and mortality of a certain disease (Waning & Montagne, 2001:145).

Incidence: The frequency with which something, such as a disease, appears in a particular population or area.

Inotropy: A term used for the contracting force of the myocardium (Sweetman, 2010) e.g. positive inotropic agents increase the contraction of the myocardium.

Non-medical costs: Cost of all other resources used relevant to the disease or prevention thereof e.g. transportation costs (Wang *et al.,* 2005:2).

Prescription: Document from a prescriber containing one or more medicine items and their usage directions in a format required by law.

Definitions used in this study (continued)

Prevalence:	Probability of the existence or occurrence of a condition in a specific population (Waning & Montagne, 2001:21).
Quantitative:	Refers to a measurable quantity.
Retrospective:	Type of study done with data recorded previously (Waning & Montagne, 2001:46)
Sustained formulations:	Formulation gradually releasing small amounts of the active ingredients to be absorbed (Segen, 2006:227).
Systolic blood pressure:	The blood pressure as the heart beats, as it pumps blood (National Heart Lung and Blood Institute, 2008).
Tachycardia:	Increased heart tempo.
Vasodilatation:	Dilating (opening) of blood vessels.

3 Synonyms to be noted throughout the study

Drugs = medicine = medication = medicine items = items.

Original = innovator.

Usage = prevalence.

PBM = pharmacy benefit management company = medicine claims database.

These terminologies are used interchangeably throughout this study unless stated otherwise.

Medical scheme benefit options = drug status.

CHAPTER 1

Introduction

1.1 Introduction

The pharmacological group of CCBs (calcium channel blockers) is mainly divided into antihypertensive and anti-anginal treatment agents (Donald & Warkentin., 2009:1; Snyman, 2009:103) and include the following pharmacological active ingredients: nifedipine, amlodipine, israpidine, felodipine, lercanidipine, verapamil and diltiazem (Snyman, 2009:103). The usage and cost of products containing above-mentioned ingredients were the focus of the study.

1.2 Problem statement

This study focused on prescribing patterns of CCBs (calcium channel blockers) in a section of the private health care sector of South Africa. CCBs are regarded as a relatively expensive group of medication items (Avorn & Fisher., 2009:1853).

- It is estimated by the International Society of Hypertension (2005) that approximately 972 million adults were living with HBP (high blood pressure) in the year 2000 and will increase to an estimated 1.56 billion by 2025 (International Society of Hypertension, 2005; Kearney *et al.*, 2005:4).
- Balu and Thomas (2006:810) stated that the incremental expenditure for the antihypertensive therapeutic group in the United States of America was estimated at $US 55 billion per annum.
- According to Kearney *et al.* (2005:3) 23.1% of South Africans have high blood pressure which includes 22.9% of male South Africans and 23.4% of females.
- In South Africa antihypertensive medication was the therapeutic group that used the highest percentage of the total expenditure of Mediscor, a PBM (Pharmacy Benefit Management) company in 2007 with 11.4% (Bester & Hammann, 2007:1) as well as in the year 2008 during which it used 11% of the total expenditure (Bester & Badenhorst, 2008:14).
- Calcium channel blockers are most the effective mono-therapy agents for treating hypertension in African Americans (Adigun *et al*., 2003). Donald and Warkentin (2009:1) stated that they can be used for treating angina as well.
- Adalat® is a nifedipine containing product and Adalat XL® 30mg was 28th among the Top 50 products ranked by contribution to total medicine expenditure of Mediscor for

2007 (Bester & Hammann, 2007:12) and 27th in the year 2008 (Bester & Badenhorst, 2008:18).

- Norvasc® is the original product on the market containing amlodipine and was 5th among the top 10 pharmaceuticals by sales globally in 2006 (Anon., 2006) but dropped dramatically to 52nd in 2007 in the U.S. (Anon., 2009). This could be because of generic equivalents that entered the market after the patent had expired late 2007 (Smith & Ashiya., 2007:598).
- Amloc® is an amlodipine generic on the market and was 33rd among the Top 50 products ranked by contribution to total medicine expenditure of Mediscor, in 2007 (Bester & Hammann., 2007:12) and 39th in the year 2008 (Bester & Badenhorst, 2008:18).

Calcium channel blockers are mainly used for their registered medicinal effect on the cardiac system (e.g. anti-angina and antihypertensive). Because of the CCB's effect to slow down the heart it is also used in some cases of arrhythmias such as atrial fibrillation (Ogbru, 2009) but also for a number of unregistered uses that include the following: anti-migraine (Donald & Warkentin., 2009:1), after myocardial infarct to counter the iron overload that causes tissue damage (Oudit., 2005:73) and in the near future it could be of great use in asthma patients (Barnes, 1983:4; Boushey, 2009: 340; Gomes *et al.*, 2007:1117). Amlodipine has a very useful effect in patients with atherosclerosis as it reduces the intimae-media thickness of the carotid artery (Ikeda *et al*., 2009:52). Opie and the team of researchers *(*2000:9) mentioned that verapamil lowers blood cholesterol slightly if taken for a minimum of two years.

On the basis of previous problems stated the following research questions could be formulated:

- Are there any conditions for which the use of CCBs is favoured?
- Have any pharmaco-economic studies been done on CCBs?
- Is combination therapy available and more cost-effective?
- Is it used as monotherapy or combination therapy and which other medication is found in combination with a CCB on a prescription?
- Are there potential savings that can be generated through generic substitution of calcium channel blockers in the private health care sector of South Africa?
- What are the current prescribing patterns of CCBs in the private health care sector according to demographical factors such as age, gender, prescriber and geographical area?

1.3 Study objectives

The research objectives consisted of two phases namely a literature review and an empirical investigation. The following objectives needed to be achieved from each of the phases respectively:

1.3.1 Phase 1: Literature review objectives

The specific research objectives of the literature review include the following:

- To determine the general indications and future uses of CCB medicine products.
- To determine conditions for which the use of CCB medication is considered as the preferred therapy.
- To determine the possible uses of drug utilisation review (DUR), pharmaco-economic, pharmaco-epidemiology, prescribed daily dosages (PDD) and cost analysis with regard to CCB usage.

1.3.2 Phase 2: Empirical investigation objectives

The specific research objectives of the empirical study included the following:

- To analyse the general prescribing patterns of CCBs and the identification of possible changes from 2005 to 2008.
- To determine the possible differences in the prescribing patterns between various age groups and genders of patients using CCBs.
- To determine the differences in the prescribing patterns of CCBs between general practitioners and specialists.
- To establish refill-adherence rates with regard to CCBs using data from a medicine claims database.
- To establish potential savings that could be generated by means of generic substitution of CCBs in the private health care sector of South Africa.

1.4 Research method

A retrospective drug utilisation study was done by using a medicine claims database of a PBM (pharmacy benefit management) company in the private health care sector of South Africa from 1 January 2005 to 31 December 2008.

The study population consisted of the total medicine database, CV (cardiovascular) medicine section and CCB medicine section as expressed in Table 3.1.

The following measuring instruments (Section 3.3.5) were used in this study:

- **Prevalence**: In this study, prevalence was used to indicate the number of medicine items or prescriptions claimed during a specific time period as recorded on a database of a PBM (Section 3.3.5.1).
- **Cost** of CCBs, divided as **member contributions** and **medical aid contributions** (Section 3.3.5.2).
- **Cost saving**: The cost of medicine that can potentially be saved if a medicine item (e.g. innovator) were to be substituted for a less expensive generic equivalent as specified in Section 3.3.5.3.
- **Cost prevalence index (CPI)**: It indicates the relationship between the cost and prevalence of specific items and the CPI is used to investigate drug utilisation patterns (Section 3.3.5.4).
- **Medicine refill-adherence rate**: In this study compliance was calculated by refill-adherence of the patients on the database as specified in Section 3.3.5.5.

The following selection criteria (Section 3.3.6) were used in this study:

- **Year division**: The data used in this study were divided as per year of submission and ranged from 2005 to 2008.
- **Age groups**: Patients who received the medicine items analysed were divided into seven age groups as specified in Section 3.3.6.2.
- **Gender groups**: Patients who received the medicine items analysed were divided into their specific gender as specified in Section 3.3.6.3.
- **Prescribers**: A classification into different prescribers was used to analyse the CCB prescribing patterns (Section 3.3.6.4).
- **Geographical distribution**: CCB usage was analysed provincially (Section 3.3.6.5).
- **Classification of medication**: Different classification systems were used to categorise the medicine items analysed as specified in Section 3.3.6.6.
- **Medicine benefit options**: This referred to the usage of medicine items being classified as chronic, acute or as a PMB (prescribed minimum benefits) condition (Section 3.3.6.7).

Data analysis was done by using the Statistical Analysis System® (SAS for Windows 9.1, 2005) and tables and graphs were drawn by using Microsoft® Excel® (2007).

1.5 Chapter division

Chapter 1: Introduction and Background of the study

Chapter 2: An overview of CCBs and therapeutic uses

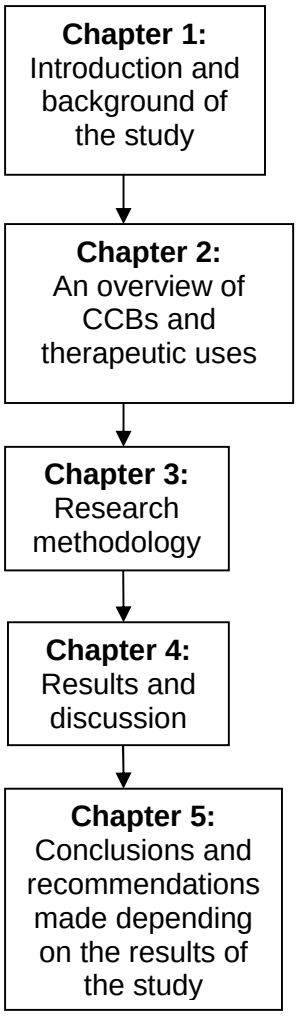
Chapter 3: Research methodology

Chapter 4: Results (Results were calculated and tabulated.)

Chapter 5: Conclusion and recommendations: (Conclusions were formulated depending on the results and recommendations given depending on the results and conclusions made.)

Appendix: Tabulation of additional results.

1.6 Algorithm of the layout of the study



Refer to Figure 4.1

Figure 1.1: Algorithm of the study layout

1.7 Chapter summary

In this chapter an introduction as well as a brief overview of the study was given. The problem statement, research questions, research objectives and the research method were also discussed.

The next chapter (Chapter 2) will report on a literature overview of CCBs, the conditions they are indicated for, adherence discussion and a brief overview of the health care sector of South Africa.

CHAPTER 2

An overview of CCBs and their therapeutic uses

2.1 Introduction

In this chapter a background of the study will be given. CCBs and their usage as well as the prevalence of hypertension and angina will be discussed briefly. However, this discussion is limited to some aspects that may be useful in the interpretation of the empirical chapter and is not intended to be a complete theoretical discussion and practical application of all the pharmacological aspects. The approach of this study is the usage of CCBs in the private health sector of S.A. (South Africa).

2.2 Background

The group of CCBs (calcium channel blockers) is mainly divided into antihypertensive and anti-anginal treatment agents (Snyman, 2009:103) and includes the following active ingredients: nifedipine, amlodipine, isradipine, felodipine, lercanidipine, verapamil and diltiazem (Snyman, 2009:103). The focus of this study was on the usage and cost of the products containing the above mentioned pharmacological active ingredients.

CCBs are classified as vasoselective drugs that block the L-type voltage gated calcium channel (Trevor *et al.*, 2005:541). This is the most important ion channel in the cardiac- and other smooth muscle. By decreasing the calcium influx during an action potential into the cell it decreases the intra-cellular calcium concentration and results in a decreased contractibility (Trevor *et al.*, 2005: 109). Calcium channel blockers have a vasodilator effect as well as a cardiac depressant effect (Ogbru, 2009; Trevor *et al.*, 2005:105).

In the year 2000 it was estimated that 972 million adults worldwide were living with HBP (high blood pressure) (International Society of Hypertension, 2005). Hypertension is expected to reach 1.56 billion patients by 2025 (International Society of Hypertension, 2005; Kearney *et al.*, 2005:4). It has been estimated that 1 in 3 adults in America has HBP (National Heart Lung and Blood Institute, 2008). Balu and Thomas (2006:810) stated that the incremental expenditure for the antihypertensive therapeutic group in the USA (United States of America) was estimated at $US 55 billion per annum in 2006.

Mediscor®, a PBM (Pharmacy Benefit Management) company, stated in its medicine review (Bester & Hammann, 2007:9) that 11.4% of the total expenditure was used for the antihypertensive therapeutic group in the year 2007 and 11% in 2008 (Bester & Badenhorst,

2008:14). This was the therapeutic group that used the highest percentage of the total expenditure for both 2007 and 2008 and it was predicted that it would stay the therapeutic group that would use the highest percentage of the total expenditure in 2009 (Bester & Badenhorst, 2008:14).

The National Heart, Lung and Blood Institute (2007) stated that around 7000 000 people in the U.S.A. suffered from angina, with around four hundred thousand new reports every year . Anti-anginal agents were in the 16th and 18th position of the annual expenditure per therapeutic group list for 2007 (Bester & Hammann, 2007:9) and 2008 (Bester & Badenhorst, 2008:14) respectively. In the year 2007 anti-anginal agents used 1.6% of the total expenditure (Bester & Hammann, 2007:9) and 1.5% in 2008 (Bester & Badenhorst, 2008:14). It was also noted by Bester and Badenhorst (2008:15) that the average cost per item in the antihypertensive therapeutic group decreased by 0.6% in the year 2008 compared to 2007.

It is clear that the antihypertensive market in SA is not only an important one for the pharmaceutical manufacturers but also a competitive market. The competitive problem has escalated due to the implementation of the single exit price and other pricing regulations and as maximum prices is controlled, creative marketing needed to alter the CCB market, as with other pharmaceutical products, and the cost cut might be the only marketing tool to use. This is supported by the so-called refine pricing compiled by the CMS as well as medicine administrators of PBMs (Serfontein, 2010).

Adalat® is a nifedipine containing product and Adalat XL® 30mg was 28th among the Top 50 products ranked according to contribution to total medicine expenditure of Mediscor for 2007 (Bester & Hammann, 2007:12). Adalat XL® 30mg was in the 27th position among the Top 50 products ranked by contribution to total medicine expenditure of Mediscor® in the year 2008 (Bester & Badenhorst, 2008:18).

Norvasc® (amlodipine besylate) is the innovator product on the market containing amlodipine and was 5th among the top 10 pharmaceuticals by sales globally in 2006 (Anon., 2006) but dropped dramatically to 52nd in 2007 in the U.S.A. (Drugs.com, 2009).

Pharma Dynamics® launched a product (Amloc®) containing amlodipine maleate because amlodipine besylate was still patented by Pfizer® (Anon., 2005). Amloc® 5mg was 33rd among the Top 50 products ranked by contribution to total medicine expenditure of Mediscor® in 2007 (Bester & Hammann, 2007:12) and ranked 34th in the year 2008 (Bester & Badenhorst, 2008:18). A generic equivalent of Norvasc® was registered in September 2005 by a company called Pharmacia® with the name Lomanor®. Like Norvasc® it contains amlodipine besylate

as the active ingredient (Pharmacia, 2005). More amlodipine generic products are currently on the S.A. market in different salt forms (Snyman, 2009:103).

The antihypertensive group of medication uses the highest percentage of the total expenditure in South Africa (Bester & Hammann, 2007:9). Adalat® and Norvasc® are both calcium channel blockers and among the top selling pharmaceuticals (Drugs.com, 2009; Bester & Badenhorst, 2008:18; Bester & Hammann, 2007:12). More Amloc® generics (amlodipine besylate) are entering the South African market as well as other amlodipine salts (e.g. amlodipine maleate) (Anon., 2005; Miginini *et al.*, 2007:2; Pharmacia, 2005; PharmaDynamics, 2008).

2.3 Medicinal aspects of the CCBs

In this section the group of CCBs will be defined, classified and the mechanism of action discussed.

2.3.1 Definition and mechanism of action

Calcium channel blockers are drugs that block the entry of calcium into the muscle cells of arteries and the heart by blocking the L-type voltage gated calcium channel (Trevor *et al.*, 2005:541). Calcium in these muscle cells have a contracting effect and causes the heart to contract and arteries to narrow (MedicineNet.com, 2004). By blocking the calcium influx into muscle cells (with calcium channel blockers) it decreases the contraction of the heart and a dilation in arteries which causes these arteries to widen (MedicineNet.com, 2004; Trevor *et al.*, 2005:109). This mechanism by effect lowers the BP and decreases the workload on the heart which causes the heart to need less oxygen and it relieves angina (MedicineNet.com, 2004; Trevor *et al.*, 2005:109).

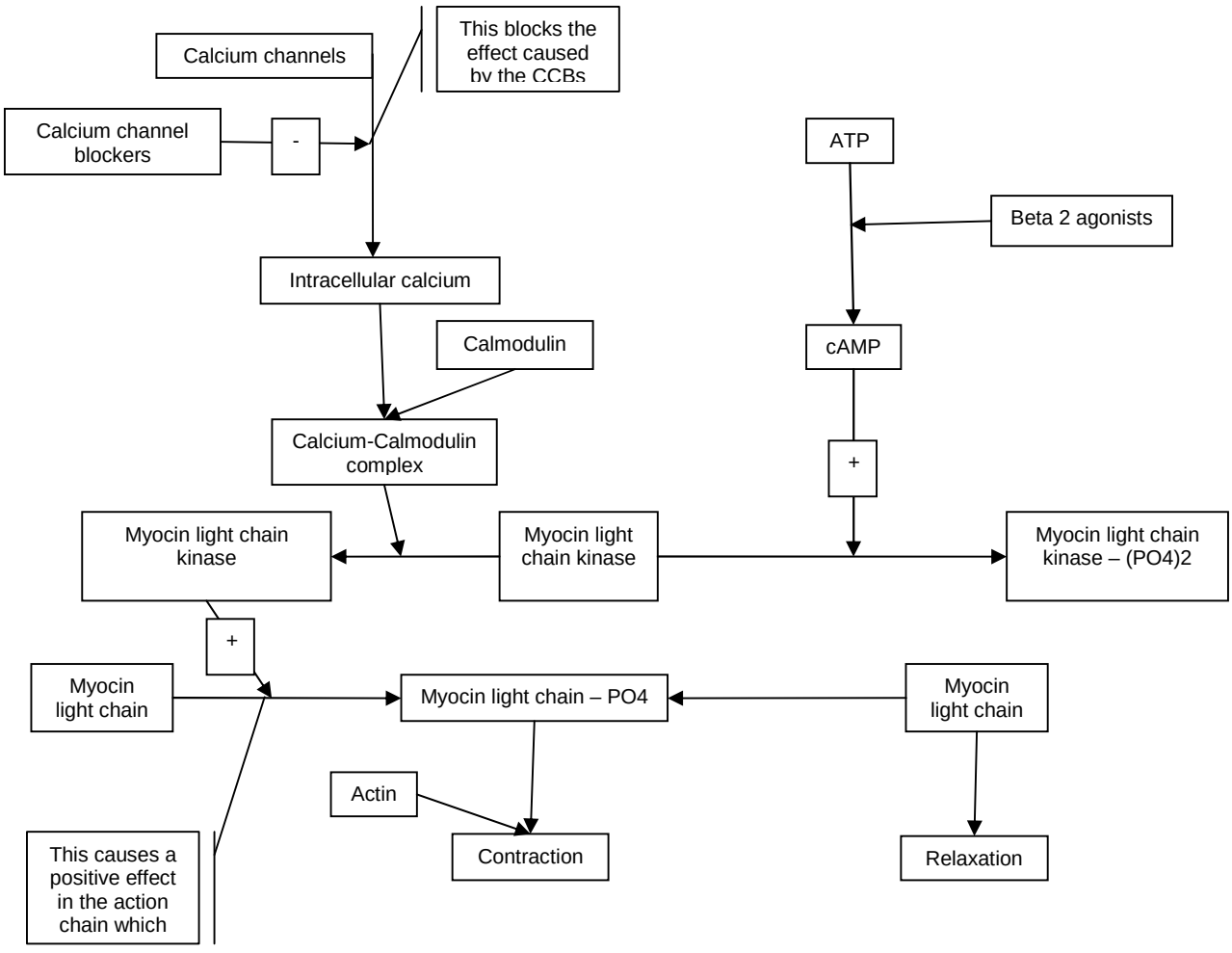


Figure 2.1: Control of smooth muscle contraction through calcium channel blocking drugs as adapted from Katzung and Chatterjee (2004:185)

From figure1.1 it can be seen that contraction of smooth muscle is triggered by calcium influx through trans-membrane calcium channels (which are blocked by CCB medicine items). Calcium combines with calmodulin, a Ca^{2+} regulated protein which converts these 2^{nd} messengers for a variety of biochemical purposes (Chin & Means, 2000:322) to form a complex that converts the enzyme myosin light chain kinase to the active form. The myosin light chain kinase is phosforilated, initiating interaction of myosin with actin and contraction follows which narrows arteries **(**Katzung & Chatterjee, 2004:185).

Two main groups of CCB medicine items are identified (Benowitz, 2009:176; Arcangelo & Peterson, 2005: 235):

- Dihydropyridine (amlodipine, felodipine, israpidine, nicarpidine, nifedipine and nisoldipine)
- Non-Dihydropyridine (verapamil and diltiazem)

The different effects obtained by the different groups are because of the different binding sites the respective groups use. Dihydropyridine CCBs bind to one site whereas the non-dihydropyridine CCBs bind to closely related but not identical receptors in another region of drug binding. The binding of drugs to a non-dihydropyridine receptor also affects dihydropyridine binding (Katzung & Chatterjee, 2004:192).

It is thus important to differentiate between the two main groups of CCBs because these two groups have different indications, contra-indications and reported side-effects (Southern African Hypertension Society, 2006).

2.3.2 Calcium channel blockers groups

The two groups of CCBs will be discussed in this section.

2.3.2.1 Dihydropyridines

The dihydropyridine group of CCBs has a potent vasodilatory effect and because of reduction in systolic BP may cause reflex tachycardia. This group does not alter conduction and does not slow the sinus rate in the heart. Nifedipine is a first generation dihydropyridine (SRS Pharmaceuticals, 2010:2). Amlodipine, felodipine, israpidine, nicarpidine and nisoldipine are second generation dihydropyridine CCBs and are better tolerated than the first generation dihydropyridines. These drugs must be administered as multiple daily doses (except for sustained formulations) because of their short biological half-life. Amlodipine has a longer half-life and is administered once daily (Arcangelo & Peterson, 2005:235).

2.3.2.1.1 The different salts of amlodipine

Amlodipine was developed by Pfizer and marketed as a besylate salt (Miginini *et al.*, 2007:2), namely Norvasc® (Pfizer, 2001). Other amlodipine salt available in South Africa is amlodipine maleate (Anon., 2005; Pharma dynamics, 2008).

These two salts have been compared to test their bio-equivalency and it has been published that the peak plasma concentration, time to attain peak concentration as well as other pharmacokinetic data of these two salts did not differ significantly and medication containing these salts were bio-equivalent (Miginini *et al.*, 2007:1). An article published by Park and his research team (2005:1) stated the following: "…the efficacy and tolerability observed with amlodipine maleate were similar to those seen with amlodipine besylate."

Figure 2.2 indicated the structural formula of amlodipine and the two salts (Pharma IP Strategy, 2007):

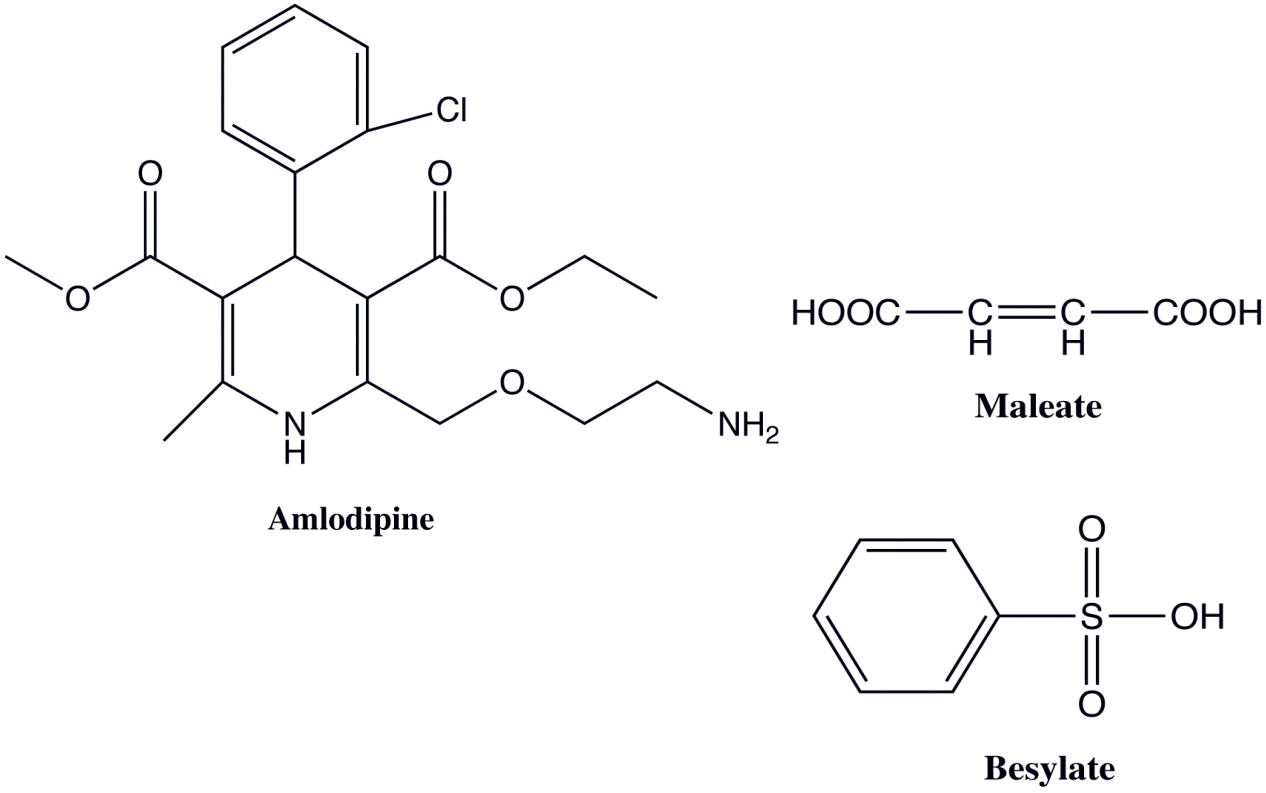


Figure 2.2: Structural formula of amlodipine and the two salts

2.3.2.2 Non-dihydropyridines

The pharmacological active ingredients, verapamil and diltiazem are both classified as non-dihydropyridines but differ slightly in their effects. Non-dihydropyridine calcium channel blockers can be sub-divided into benzothiazepines (diltiazem e.g. Tilazem®) and phenylalkylaminine (verapamil e.g. Isoptin®) (Baxter, 2008:860; Snyman, 2009:103).

Verapamil reduces the conductibility of the AV (atrioventricular) node in the heart and causes negative inotrophic and chronotropic effects on the heart, reducing contractibility and heart rate. This causes a reduction in oxygen demand (Arcangelo & Peterson, 2005:235; MedicineNet.com, 2004). Because of this effect verapamil should be used with caution in patients with depressed cardiac function and AV conduction abnormalities (Arcangelo & Peterson, 2005:235; MedicineNet.com, 2004; Southern African Hypertension Society, 2006). Verapamil is administered in divided doses with exception of the sustained formulations that are administered once daily (Arcangelo & Peterson, 2005:235).

Diltiazem also reduces heart rate but to a lesser extent. The effect that diltiazem has on conduction and contractibility is less than the effect of verapamil, but diltiazem has a more potent vasodilatory effect. The immediate release formulation is taken four times daily before meals and the sustained formulation is taken once daily on an empty stomach (Arcangelo & Peterson, 2005:235). Baxter (2008:868) on the other hand said that the absorption of israpidine, diltiazem and verapamil is not altered when taken with food.

2.3.3 Common side-effects and contra-indications

Common side-effects of using calcium channel blockers are nausea, headache, oedema (swelling of the legs), low BP, palpitations, drowsiness, dizziness, fatigue, altered sleeping patterns and abdominal or chest pain (MedicineNet.com, 2004; Snyman, 2009:103) and this has also been stated in the package inserts of CCB containing products (Pfizer, 2001; Pharmacia, 2005).

Less common side-effects were also observed e.g. alopecia (hair loss), altered bowel habits (e.g. diarrhoea and constipation), arthralgia, asthenia, back pain, dry mouth, dyspnoea, gingival hyperplasia, gynaecomastia, hyperglycemia, impotence, increased urinary frequency, leucopenia, malaise, mood changes and depression, muscle cramps and myalgia (MedicineNet.com, 2004; Pfizer, 2001; Pharmacia, 2005).

2.3.3.1 Side-effects and contra-indications of the dihydropyridine CCBs

There should be caution when using amlodipine in the elderly. Clearance is reported to decrease by 40 – 60% in elderly patients (Pfizer, 2001) and causes an increased concentration of amlodipine in these patients. It is recommended that elderly patients start the drug therapy on a lower initial dose (Pfizer, 2001; Pharmacia, 2005; Rossiter, 2010:156; Snyman, 2009:103).

A reduction in the clearance of amlodipine by the human body is also seen in patients with moderate to severe heart failure (Pfizer, 2001; Pharmacia, 2005; Snyman, 2009:103). According to the Southern African Hypertension Society (2006) long acting calcium channel blockers are a possible contra-indication for patients suffering from heart failure. They also state that it is a possible contra-indication to give these long acting CCBs (once daily medication e.g. amlodipine) to patients on ARV (antiretroviral) therapy as well as patients suffering from tachyarrhythmias (Rossiter, 2010:156). Compatibility of CCBs with ARVs and other medications will be discussed later in this chapter.

Because amlodipine is metabolised by the liver (Baxter, 2008:860) and excreted by the kidneys, it should be used with caution in patients with renal and/or hepatic impairment (Pfizer, 2001; Pharmacia, 2005; Rossiter, 2010:156; Snyman, 2009:103). Lower initial doses in these patients are strongly advised. The same caution should be taken when using nifedipine in patients with hepatic and/or renal impairment (Rossiter, 2010:156).

Nifedipine is contra-indicated in breastfeeding or pregnant patients (Snyman, 2009:103), but has been used in pregnant or breastfeeding mothers unresponsive to other antihypertensive medication (Rossiter, 2010:156). It is also contra-indicated in hypotensive patients as well as cases of patients suffering from unstable angina or acute myocardial infarctions (Rossiter, 2010:156).

2.3.3.2 Side-effects and contra-indications of the non-dihydropyridine CCBs

When diltiazem or verapamil (non-dihydropyridine CCB) are given to individuals with heart failure, symptoms of heart failure may worsen because these drugs reduce the ability of the heart to pump blood (MedicineNet.com, 2004; Southern African Hypertension Society, 2006). This happened because of their negative inotropic activity (Baxter, 2008:860) and it is suggested that this group should not be administered to patients suffering from heart failure (Rossiter, 2010:156; Snyman, 2009:103; Southern African Hypertension Society, 2006).

The Southern African Hypertension Society (2006) stated in their Hypertension Management Algorithm poster that it should be noted that verapamil causes constipation.

2.3.4 Conditions favouring the use of CCBs

The use of a CCB in some cases or conditions may be preferred if the clinical effect thereof is of greater therapeutic value to the patient and the optimal treatment for the specific condition.

2.3.4.1 Conditions favouring use of dihydropyridine CCBs

According to an article published in the Reproductive Toxicology Journal (Weber-Schoendorfen *et al*., 2008:1) it is stated that there is no major teratogenic risk when using dihydropyridine calcium channel blockers during the first trimester of pregnancy. The Southern African Hypertension Society (2006) lists pregnancy as a condition favouring the use of dihydropyridine type CCBs.

2.3.4.2 Conditions favouring use of non-dihydropyridine CCBs

This group of CCBs is the therapy preferred for the treatment of the black hypertensive patients (Southern African Hypertension Society, 2006). Because non-dihydropyridine CCBs slows the heart rate (Arcangelo & Peterson, 2005:235; MedicineNet.com, 2004) it is the CCB treatment of choice in patients suffering from tachycardia (Southern African Hypertension Society, 2006).

2.3.5 Combination therapy used with CCBs

A study done by Miranda and colleagues (2008:5) showed great success when they compared BP control of patients using an amlodipine and ramipril (ACE (angiotensin-converting enzyme) inhibitor) combination with amlodipine monotherapy. The combination therapy gave a greater reduction in BP when compared to the amlodipine monotherapy and was well tolerated (Miranda *et al*., 2008:5).

Atorvastatin in combination with amlodipine reduced coronary heart disease events by 53% if compared with placebos. Atenolol in combination with atorvastatin showed a 16% decrease in coronary heart disease events if compared to placebos (Sever *et al.,* 2006:2987). This indicates a synergestic interaction between amlodipine and atorvastatin.

Neutel (2006:3) is of the opinion that combination therapy could have fewer side-effects than monotherapy. By adding an ACE inhibitor to a dihydropyridine CCB causes less oedema and greater reduction in BP than the same dose as monotherapy (Neutel, 2006:3). Further the author is convinced that combination therapy is therapeutically more effective and safer, which are the most important criteria in hypertension management.

Neutel (2006:5) claimed that combination therapy in treating hypertension appeared to be therapeutically more effective than the stepped care approach and provides more effective and convenient therapy with fewer side-effects. Two drugs used in combination showed to have additive effects in the reduction of BP and three drugs in combination suggested to also have additive BP lowering effects (Law, 2003:3).

It was suggested that low dose combination therapy should be considered as first option in lowering BP. These low dose combinations reduced the risk of strokes by more than 60% and reduced IHD (ischemic heart disease) episodes by half, with a low prevalence of adverse effects (Law *et al.*, 2003:7).

A study done with a low dose combination of a controlled release nifedipine and candesartan found that the use of the combination was more effective from a therapeutic as well as an economic viewpoint if compared with an up-titrated monotherapy of candesartan (Fujikawa *et al.,* 2005:590).

It was stated by Abernethy & Schwartz (1999:1450) that CCBs are highly effective antihypertensive and anti-anginal agents and have a role in multidrug therapy for these conditions. It should be noted that some interactions can occur.

2.3.6 Compatibility of calcium channel blockers with other medication

CCBs are metabolised by the cytochrome P450 isoenzyme CYP3A4 and also inhibits this enzyme (Abernethy & Schwartz, 1999:1450; Baxter, 2008:860). This is the same enzyme responsible for the metabolism of a large amount of other medications. This is an important fact with regard to possible medication interactions.

CCBs should not be used in combination with other CCBs. In combination they cause an increased plasma concentration level of each other and BP would reduce accordingly. Discontinuation of the other CCB is recommended (Baxter, 2008:864).

Hypotension may be the reaction when combining CCB medicine items with medication containing nitrates (Baxter, 2008:873). The active ingredient amlodipine has been declared unsafe in combination with long-acting nitrates and sublingual glyceryl trinitrate as it could cause hypotension (Baxter, 2008:873; Pfizer, 2001; Pharmacia, 2005; Snyman, 2009:103).

It is further advised that CCBs should not be taken in conjunction with H_2-reseptor antagonists (e.g. cimetidine). This causes an increased plasma concentration of the CCB (Abernethy & Schwartz, 1999: 1450; Baxter, 2008:871). It was suggested that the dosages of the CCBs should be reduced when used with products containing cimetidine. Diltiazem

dosages should be reduced by 30% to 50% and nifedipine by 40% to 50% respectively (Piepho *et al*., 1987). It has also been suggested that the dosages of verapamil should be reduced by 50% (Baxter, 2008:870). Amlodipine plasma concentration is not altered by cimetidine containing products (Baxter, 2008:870).

It was advised that caution should be taken when verapamil or diltiazem are to be taken with carbamazepine containing medicine items. This could result in neurotoxicity as a result of increased serum carbamazepine concentration (Abernethy & Schwartz, 1999:1450).

Information regarding adverse effects when CCBs are to be taken with protease inhibitors (e.g. ritonavir, indinavir, atazanavir & nelfinavir) is limited (Abernethy & Schwartz, 1999:1450; Baxter, 2008:874) although caution is required for these combinations. Zidovidine plasma levels were increased when used with nimodipine containing products. Adverse reactions of zidovidine are dose dependent and should be kept in mind when both the drugs are used together (Baxter, 2008:877).

The interactions between CCBs and rifampicin (a tuberculostatic agent) are of clinical importance (Abernethy & Schwartz, 1999:1450; Baxter, 2008:875; Tatro; 2004:1471). Oral verapamil was found ineffective while using rifampicin, because it reduces the plasma concentration considerably (Niemi *et al*., 2003:834; Tatro; 2004:1471). Niemi and a team of researchers (2003:834) mentioned that oral nifedipine was probably ineffective in combination with rifampicin, because the plasma concentration was also reduced drastically. The dihydropyridine CCBs are all metabolised by the enzyme CYP3A4 and it is likely that rifampicin would greatly reduce their plasma concentrations. This would result in inactive CCBs when used with rifampicin (Niemi *et al*., 2003:834; Tatro; 2004:1471).

According to Baxter (2008:864) one should be cautious when taking azole antifungals (e.g. ketoconazole & itraconazole) in combination with CCBs. Azoles cause a raise in the serum levels of the CCBs and increases the adverse effects, especially ankle and leg oedema (Jalava *et al*., 1997).

Phenobarbital decreases the plasma concentration levels of felodipine (Tatro, 2004:626), nifedipine (Tatro, 2004:979) and verapamil (Baxter, 2008:874; Tatro, 2004:1463) and it is advised that the dosages of these CCBs should be increased (Baxter, 2008:874). Other CCBs are expected to behave in the same manner as they are metabolised by the same enzymes (Baxter, 2008:874).

Baxter (2008:876) documented that nimodipine and nifedipine doses should be reduced when used with valproate (anti-epileptic) because valproate raises the plasma concentration levels of these CCBs.

Verapamil is the CCB with the most drug interactions of clinical importance (Tatro, 2004:1618). β-blockers (e.g. acebutolol, atenolol, metoprolol, pindolol, timolol etc.) in combination with verapamil were reported to increase the blood concentration and thus the effect of both these drugs and could cause hypotension (Tatro, 2004:272). A severe and clinical relevant drug interaction between verapamil and digoxin should also be noted as the combination of these two drugs causes digoxin toxicity (Abernethy & Schwartz, 1999:1450; Tatro, 2004:551). It was reported that verapamil in combination with quinidine could result in hypotension, bradicardia or even AV block. This is because the verapamil interferes with the clearance of quinidine and prolongs its half-life (Tatro, 2004:1144).

2.3.7 Non-substitutable list

The guideline on generic substitution was published in the list of non-substitutable medicines in December of 2003 and stated that nifedipine in extended/delayed release formulations are not to be substituted for brand names other than prescribed by a prescriber as it is on the List of Non-substitutable Medicines (MCC, 2003:3). The list of non-substitutable medicines is periodically reviewed and altered at the discretion and recommendation of the MCC. The following trade names are classified as extended or delayed release nifedipine formulations available on the South African market:

- Adalat Retard 10 mg
- Adalat Retard 20 mg
- Adalat XL 30 mg Tab
- Adalat XL 60 mg Tab
- Cipalat Retard 20 mg
- Nifedalat 20 mg SR Tab
- Adco-Vascard 30 mg SR

Version 2 was published in April 2010 which did not contain the substituting restrictions on nifedipine or any other CCB medicine items (MCC, 2010: 2).

2.3.8 Recommended and prescribed daily dosages

In this section RDD (recommended daily dosage) and PDD (prescribed daily dosage) are discussed.

2.3.8.1 Recommended daily dosage

RDD is the specified dosage of the drug to use for a certain condition, as taken from the South African Medicine Formulary (Rossiter. 2010:155) and Martindale (Sweetman, 2010) and tabulated. The preparations on the South African market, according to the above authors, were listed in the table below.

Table 2.1: RDDs of CCBs on SA market

Drug and formulation	**RDD as per SAMF** (Rossiter, 2010:155)	**RDD as per Martindale** (Sweetman, 2010)
Nifedipine	Dose dependent on formulation as stated below	Max: 90 mg daily
Adalat® Retard (10 mg,20 mg)	10-20 mg twice daily. Max: 60 mg daily	
Adalat® XL (30 mg, 60 mg)	Initial: 30 mg daily. Max: 90 mg daily	
ADCO-Vascard® (30 mg)	Initial: 30 mg daily. Max: 90 mg daily	
Nifedalat® SR (20mg)	20-40 mg twice daily	
Fedaloc® (30 mg,60 mg)	Initial: 30 mg daily. Max: 90 mg/day	
Amlodipine	Initial: 5 mg daily. Max: 10 mg daily	Initial: 5 mg daily. Max: 10mg daily
Felodipine	Initial: 5 mg daily. Max: 20 mg daily	Initial: 5 mg daily. Max: 20 mg daily
Isradipine	Dose dependent on preparation as stated below	Initial: 2.5 mg twice daily. Max: 10 mg twice daily.
Dynacirc® 2.5 mg tablets	2.5 mg twice daily. Max: 5 mg twice daily	
Dynacirc® 5 mg SRO capsules	5 mg daily	
Lercanidipine	10 mg daily. Max: 20 mg daily	Initial: 10 mg daily. Max: 20 mg daily
Nimodipine	60 mg four hourly	60 mg four hourly
Verapamil	240 mg daily. Max: 240 mg twice daily	Max: 480 mg daily
Diltiazem	Max: 360 mg daily	Max: 540 mg daily

Sinaiko (1996:1971) indicated that 0.25 mg to 0.5 mg per kg body weight could be used of nifedipine in a hypertensive emergency in a child and the extended release nifedipine could be used for long-term therapy at a dose of 0.25 mg to 3 mg per kg body weight.

It should be noted that only the extended or slow release nifedipine formulations should be used for hypertension an ischaemic heart disease treatment as the other formulations have a short half-life and offer a poor 24-hour control of the disease. The patients then have increased risk of myocardial infarctions (Rossiter, 2010:155).

2.3.8.2 Prescribed daily dosage

PDD was defined by the WHO (2003:14) as the average daily dose prescribed of a drug or substance. This can be obtained by calculating the average dose on a representative sample of Prescriptions (WHO, 2003:14). PDD in this study was calculated from the medical aid's claim database of the specified years. This will be discussed later in Chapter 3.

2.3.9 Other effects and the possible future uses of CCBs

Calcium channel blockers are currently also used for their antimigraine effect (Donald & Warkentin, 2009:1; Ogbru, 2009), but presently this is not a registered indication.

In the future CCB medicine items may possibly be used after myocardial infarct to counter the iron overload which causes tissue damage (Oudit, 2005:73).

Nicardipine is a CCB and the expected effect it has on smooth muscle can potentially be used in asthma (Gomes *et al.*, 2007:1117). Boushey (2009:340) stated that CCBs could be used to treat asthmatic patients. An article published by Barnes (1983:3) said that experimental studies had shown that CCBs protect against bronchoconstriction and mediator release and that combination of different CCBs may be more effective. CCBs are safe to use in asthma patients and could well be the treatment of choice in patients with hypertension and/or angina who also suffer from asthma (Barnes, 1983:4).

It has also been stated that verapamil is effective in female manic patients, as shown by research done by Wisner and her team of researchers (2002:1), however more research is urgently needed in this field (Wisner *et.al.*, 2002:8).

Some added effects of CCB medicine items were also noted. It was stated (Ikeda *et al.,* 2009:52; Clunn *et al.,* 2009:4) that amlodipine has a very useful effect in patients with atherosclerosis as it reduces the intimae-media thickness of the carotid artery. Opie *et al. (*2000:9) found that verapamil, if taken for a minimum of two years, lowers blood cholesterol slightly.

2.4 Adherence to medication

Adherence to medicine items, also known as patient compliance, was defined as the extent to which a patient acts according to the prescriber's (or provider's) treatment regimen (Bester & Hammann, 2007:18). The compliance is measured over time and reported as percentage of the correct theoretical dosage intervals. It is important to know this because the clinical outcomes depend on the compliance of patients (Bester & Hammann, 2007:18).

Improved compliance according to Bester and Hammann (2007:18) may cause

- better disease control;
- satisfaction with therapy by patient as well as physician; and
- an increase in medicine expenditure with an associated decrease in overall health care costs.

Degli-Esposti *et al.* (2004:78) stated that 83.3% of patients interrupted their hypertension treatment regimen after a single Prescription. It was also stated that compliance was related to the age of the patient. For every year of treatment the risk of discontinuing the treatment decreased by 2.2%. Patients with a heart disease and on medication for it as well as on hypertension medication showed a 66.6% higher compliance than patients only on hypertensive medication (Degli-Esposti *et al.,* 2004:78). A patient who refills at least 10 prescriptions in a year (12 months) can be considered compliant with medical treatment. It refers to a compliancy ratio of more than 80% (Bester & Hammann, 2007:20). Serfontein (2010) is of the opinion that 13 refills in a year is a good indication of a patient compliance ratio.

Poor compliance in general could be attributed to the following (Bester & Hammann, 2007:18):

- Complicated medicinal regimen (i.e. multiple disease conditions with different medicines).
- Forgetfulness.
- Lack of patient knowledge (i.e. unclear purpose of treatment or not educated on the specific condition).
- Medicine cost.
- Perceived lack of effect.
- Physical difficulty complying with instructions (e.g. opening containers, handling tablets, swallowing difficulties and travelling to place of treatment).
- Side-effects (real or perceived).

- Unattractive formulation (e.g. unpleasant taste).
- Unclear administration instructions.

It has been reported that approximately a third of chronic patients had strong concerns about potential adverse effects of taking their medication and such concerns could result in lower adherence (Horne & Weinman, 1999:564). It is also important to notice that a patient would rather go without medication which causes adverse effects and live with hypertension which has no initial signs or symptoms to patients (Osterberg & Blaschke, 2005:493). This could also contribute to poor compliance.

The compliancy percentages for hypertension medication in 2007 in South Africa were 63.3% and CAD (coronary artery disease) medication was 63.7% (Bester & Hammann, 2007:21). It was documented that 54.2% of Nigerian hypertensive patients were compliant with their therapeutic regimen (Kabira *et al.,* 2004:17).

Compliance could be improved by the providers considering the following strategies (Osterberg & Blaschke, 2005:493; Osberg & Rudd, 2005:430):

- Identify poor compliance.
- Look for markers of non-compliance as missed appointments, missed refills and no response to medication.
- Ask about barriers of compliance without confrontation.
- Emphasise the importance of the regimen and the effects of compliance.
- Discuss feelings of patient about ability to follow the regimen, design support to promote compliance where necessary.
- Provide clear and simple instructions and simplify regimen as much as possible.
- Encourage the use of a medication-taking system.
- Make a connection between something done every day (e.g. brushing teeth) and taking the required medication.
- Listen to the patient and customise the regimen according to the patient's wishes.
- Obtain help from family members, friends and community services where needed.
- Reinforce desired behaviour and results when appropriate.
- Consider medications of which the efficacy will not be affected by delayed or missed doses.
    - Medication with relative long half-lives.
    - Extended release medications.
    - Transdermal medications.

A 10% increase in compliance by diabetic patients has a 9% to 29% reduction in health care cost (Bester & Hammann, 2007:19). This shows a substantial reduction in overall costs by achieving better compliance.

In an article Degli-Esposti *et al.* (2004:78) stated that of the total spent on antihypertensive medication (€ 1 238 752.37) during the studied period, € 745 328.31 (60.2%) was spent on medication continued through the study, € 253 293.08 (20.4%) was spent on items that were switched during the study and € 240 130.98 (19.4%) was spent on discontinued treatment.

2.5 The health care sector of South Africa

The total health care sector of South Africa consists of a private sector and public sector (SouthAfrica.info) and will be discussed below:

2.5.1 The public sector of South African health care

The public health care system of South Africa needs to serve more patients than the private sector. The public sector is funded by the state and offers the services for free to patients (SouthAfrica.info. 2010). It was found that 24% of the money spent in the private health care sector in 2000 was spent by the state on the public health care sector of South Africa (SouthAfrica.info. 2010), which serves more than 80% of the South African public (Ross, 2010).

An article by Ross (2010) stated that the South African health system was “pro-rich”. The richest sector of South African citizens uses most of the private outpatient services as the poor citizens of R.S.A. battle with TB, high HIV rates, crime associated incidence and conditions caused by being underfed and underweight (Ross, 2010). A free health care system could be provided to the masses, but the health care in S.A. is mostly market-driven by the private sector and avoiding the sick (SAPA, 2008). A solution was necessary.

2.5.1.1 National Health Insurance

The NHI (National Health Insurance) was introduced by Pres. Zuma in his State of the Nation address in 2009. Some feel that the NHI will help resolve the problems faced by medical aid members who are not getting value for their money. They feel that the medical aid industry failed to control health care cost and the only way to overcome the present problems in the health care system of S.A. is by pooling the health care funds, combining the public- and private health sectors (Kruger, 2007; SAPA, 2009). The proposal of the NHI was felt by some to be without doubt the most significant development in the health care sector of S.A. (I-Net Bridge, 2010) and the main aim should be to provide the most benefits to the most people with the funds available (Kruger, 2007).

It was proposed that the NHI should be funded from general taxes, a new mandatory payroll levy and some medical aid contributions all pooled together. These mandatory NHI contributions could initially be less than their current medical aid contributions but will gradually increase to the level of contributions paid to medical aids by their members. Health care services will be equally accessible by the entire population and the credibility of the NHI will rely on the visible improvement in the provision of quality services for all. Cost and

shortages of medication will be reduced by implementing a state company producing drugs (Hudson, 2009).

It was stated that S.A. had adequate resources to provide health care to everyone, but redistribution of these resources from the minority to the majority of the population would be required (SAPA, 2008). It is most likely that medical aids will be negatively affected by the implementation of NHI (I-Net Bridge, 2010). Every working citizen will have to contribute to the NHI and every South African will be registered and then assigned to specific health care facilities closest to him/her. These members will then receive a card to show when they visit a health care facility. All patient information will be electronic which will help authorities to plan according to the need (Hudson, 2009). This centralisation of data could facilitate further pharmaco-economic studies.

However, the implications of the availability of CCBs in the newly proposed health system must still be decided and it is not sure what influence the proposed system may have on the present as well as future CCB treatments. CCBs currently in the Essential Drug List are: amlodipine 5 mg and 10 mg tablets as well as nifedipine slow release 30 mg tablets (DoH, 2008:54).

Some feel that the implementation plans of the NHI are overoptimistic. The shortage of health care staff and the fourfold burden of illness in S.A. should be taken into account (Watson, 2009). It has been documented that the proposed scheme may cost up to R 216 billion and South Africa may not be able to afford this (SAPA, 2010). Finding an insurance model to suit the South African environment will be a difficult task as stated by Kruger (2007). As in other countries the benefit package might not be fully comprehensive e.g. the queues in the U.K., the need for top-up cover in France and talks of not treating smokers or obese patients for some conditions until they stop smoking or lose weight. In some developed countries these are some factors and cases in point (Kruger, 2007).

It has been stated that NHI is achievable, but not in a day. It will be a progressive phased introduction, allowing resources to be deployed economically (SAPA, 2010).

Fujikawa *et al.* (2005:590) stated that the evaluation of the economic cost of health care with regard to the NHI are becoming increasingly important, especially in cases like in Japan where there is a growing financial burden on the NHI. South Africa as a developing country will also be burdened by financial constraints. The choice of medication, including CCBs, may be crucial for the success of a national health insurance initiative (Serfontein, 2010).

2.5.2 The private sector of South African health care

Only 16% of South Africans currently have health insurance (Ross, 2010). In an article by the Council for Medical Schemes (CMS, 2008a:15) it was stated that the percentage of health insurance holders in South Africa decreased to 14% because it is not affordable to all. It was stated that the medical scheme contributions are raising faster than their income which results in an increase in member contributions (CMS, 2008a:7). It was suggested that interventions should be implemented or cost would continuously increase, having an impact on access to private health care in S.A (CMS, 2008a:8).

The number of private hospitals and other institutions are growing constantly and the private sector houses the most health care professionals (SouthAfrica.info, 2010). SouthAfrica.info (2010) stated that approximately R 800.29 was spent per patient on medication in the private sector against the R 59.36 spent per patient by the state on medication in the public health care sector of S.A.

The CMS (2008a: 9) stated that the three most important contributors to medical scheme costs are hospitals (29.7%), medicines (18.3%) and specialists (18%) and that an increase in patient contributions could largely be confined to cost increases in these three areas.

The CMS (2008a:7) stated that the health care resources are limited and the private sector, servicing a small but wealthy group of individuals, is diminishing the available resources for the rest of the population.

2.5.2.1 Council for medical schemes

The CMS is a statutory body established by the Medical Schemes Act (131 of 1998) to provide regulatory supervision of private health financing through medical schemes (CMS, 2010b).

The CMS supervises a massive and very important health industry. In 2002 there were143 (49 open and 94 restricted) registered medical schemes (CMS, 2008b:23). Currently there are about 124 (41 open and 83 restricted) medical schemes in South Africa (CMS, 2008b:23; CMS, 2010b) with around 7.1 million beneficiaries and these schemes have a total annual contribution flow of about R 57, 6 billion (CMS, 2010b). The decline in the number of medical schemes brought forward less competition and fewer options for different patients of different financial income groups (CMS, 2008b: 57).

2.5.2.1.1 Prescribed minimum benefits

PMB (Prescribed Minimum Benefits) was defined by the CMS (CMS, 2010a) as a set of defined benefits to ensure that all medical scheme members have access to certain minimum health services, regardless of the benefit option they have selected. The aim is to provide people with continuous care to improve their health and well-being and to make health care more affordable (CMS, a).

Medical schemes have to cover the costs related to the diagnosis, treatment and care of (CMS, a) the following:

- Any emergency medical condition.
- A limited set of 270 medical conditions (Diagnosis Treatment Pairs).
- 25 chronic conditions (listed as the Chronic Disease List (CDL)).

CCBs are mainly used for their antihypertensive and anti-anginal effects (Donald & Warkentin, 2009:1; Snyman, 2009:103). Angina pectoris is the pain associated with CAD. Hypertension and CAD are two conditions on the CDL and covered by medical aids (South Africa, 1998:2).

2.5.2.1.2 Price regulations on medicine prices

After the 1994 elections in South Africa the new minister of health set a goal to improve equity in the health care sector, improving access the health care facilities for all citizens in South Africa. Reducing the prices of medicine was one of those elements (Gray, 2009: 15).

The price of medicine could be reduced with the increase in the use of generic equivalents where possible. It was also recommended that free gifts and bonuses to pharmacists, medical practitioners and dentists should be prohibited. A Single Exit Pricing (SEP) structure was also implemented which replaced the retail percentage mark-up system with a fixed professional fee to be added to the cost of medicine items (Gray: 2009:16). This, however, still remains a controversial issue between the state (Department of Health) and health care providers and in 2010 the implementation thereof has been hampered by court cases. This aspect is, however, beyond the scope of this study (Serfontein, 2010)

2.6 Aspects of hypertension: prevalence and treatment

Hypertension is known as the silent killer because it does not cause symptoms for many years until vital organs are damaged (Porter, 2009).

2.6.1 Definition

- Dorland's Illustrated Medical Dictionary (1988:799) defined hypertension as persistently high arterial BP above 140 mmHg systolic over 90 mmHg diastolic pressure.
- The Department of Health of South Africa defined hypertension as follows: " A condition characterised by a BP elevated above normal measured on three separate occasions, a minimum of two days apart. A measured systolic BP equal or more than 140 mmHg and/or diastolic BP equal or more than 90 mmHg (DoH, 2008:63).
- U.S. Department of Health And Human Services (2004:11) defined hypertension as a BP above 140/90 mmHg.
- The American Heart Association (2010:17) defined hypertension as an untreated systolic BP of 140 mmHg or higher, or a diastolic BP of 90 mmHg or higher, or taking antihypertensive medication, or at least twice been told by a health professional that one has hypertension.

2.6.2 Background

Hypertension is the most common CV disease (Benowitz, 2009:167). Primary hypertension (also known as essential hypertension) is hypertension without a known cause (Benowitz, 2009:167; Porter, 2009). The Merck Manual (Porter, 2009) stated that 85% to 95% of patients with HBP have primary hypertension. Secondary hypertension is HBP with a known cause and 5% to 15% of patients have secondary hypertension. Secondary hypertension is caused by kidney disorders (e.g. renal artery stenosis, pyelonephritis, glomerulonephritis, kidney tumors, polycystic kidney disease, injury to a kidney and radiation therapy affecting the kidneys), hormonal disorders (e.g. hyperthyroidism, hyperaldosteronism, Cushing's syndrome, pheochromocytoma and acromegaly), the use of certain drugs (e.g. NSAIDS, oral contraceptives, corticosteroids, cyclosporine, erythropoietin, cocaine, alcohol abuse and excessive amounts of licorice), and other disorders (e.g. coarctation of the aorta, arteriosclerosis, preeclampsia, acute intermittent porphyria and acute lead poisoning) (Benowitz, 2009:167; Porter, 2009).

When BP rises above 140/90 mm Hg the heart enlarges because the work load (resistance of blood flow) increases as the heart needs to pump harder (Benowitz, 2009:168; Porter, 2009). The artery walls thicken as well which results in stiffening and later hardening which is

called atherosclerosis. The enlarged heart can cause abnormal heart rhythms and heart failure and the stiffened artery walls, also known as atherosclerosis (Figure 2.9), could cause an increased risk of stroke, heart attack and kidney failure (Porter, 2009).

Hypertension increases the risk of mortality and morbidity. Antihypertensive treatment can decrease both (Halpern *et al.*, 2006:1039).

2.6.3 International prevalence of hypertension

Balu and Thomas (2006:810) stated that hypertension was the most commonly diagnosed disease in the United States. It was estimated that 17.4% of the U.S. population over the age of 18 years had hypertension (Balu & Thomas, 2006: 810) and that 23% of the white population, 32% of the black population and 23% of the Mexican American population had hypertension (Porter, 2009).

The American Heart Association (2010:17) states that one in three Americans has HBP and that the estimated prevalence for hypertension in America for 2006 was 74 500 000 which included 35 700 000 male patients and 38 800 000 female patients.

The percentages of male and female patients diagnosed with hypertension were shown in Figure 2.3 below:

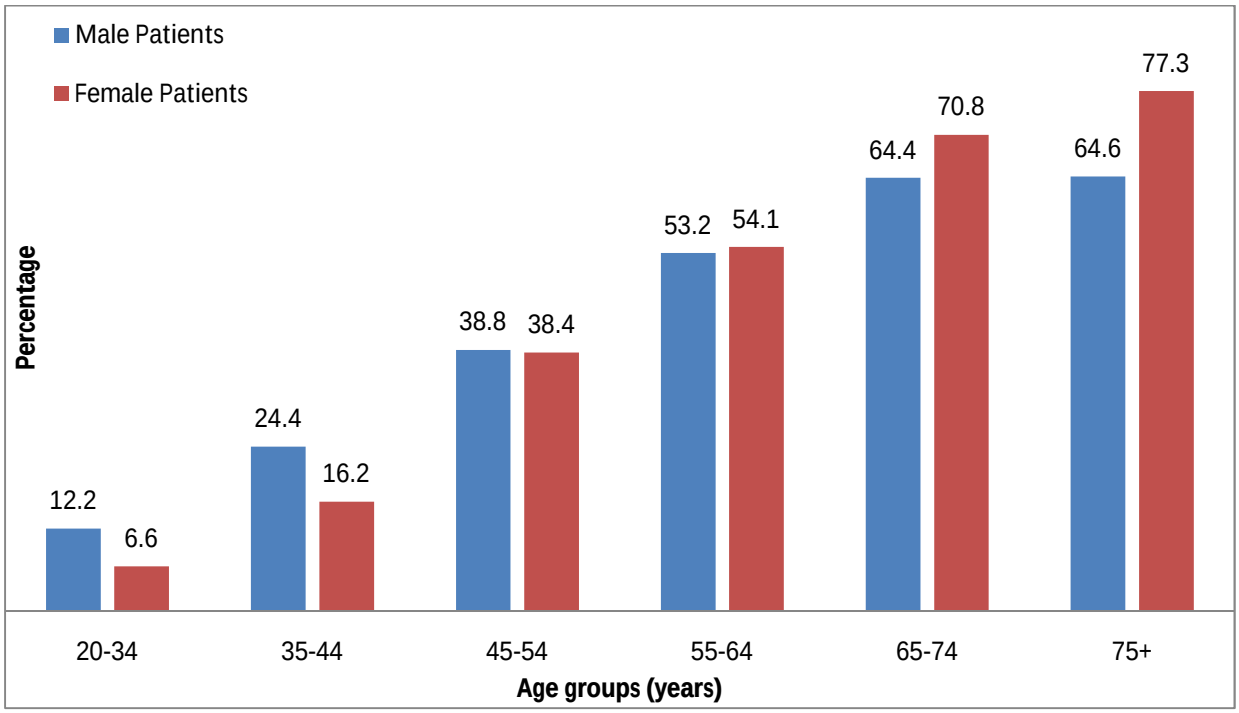


Figure 2.3: Percentages of male and female patients of different age groups in America diagnosed with hypertension

A higher percentage of men than women have HBP until age 45 (American Heart Association, 2010:17). This could be because prior to menopause, women have a better CV risk profile than men (Pilote *et al.*, 2007: 21). Following menopause the risk profile of men and women are similar (Pilote *et al.*, 2007: 21). This was reflected in Figure 2.3. From ages >45≤64 the percentages were similar, but after 64 years a much higher percentage of females have hypertension in America (American Heart Association, 2010:17).

The prevalence of hypertension in the black community in America is among the highest in the world and increased from 1988 to 2002 from 35.8% to 41.4% in adults, with a prevalence of 44% in black females. The reason for the high prevalence of hypertension in black female patients could be because of a higher prevalence of obesity (Pilote *et al.*, 2007:21). Females also tend to be less active than their male counterparts. The hypertension prevalence among the white citizens also increased from 24.3% to 28.1% in the same time (American Heart Association 2010:17).

The American Heart Association (2010:18) documented a mortality figure of 56 561 of which 24 382 were male and 31 179 were female in the year 2006. Statistics from 2003- 2006 also show that 55.9% of hypertensive adults in America aged 20 and older does not have their hypertension under control (American Heart Association 2010:18). This is a frightening figure.

It was estimated that the direct and indirect cost of HBP for 2010 will be $76.6 billion (American Heart Association 2010:18) and that hypertension would rise to a prevalence of 29% worldwide by 2025, this means an estimated number of 1.56 billion adults would have been diagnosed with HBP by the year 2025 (Kearney *et al.*, 2005: 221).

2.6.4 South African incidence of hypertension

The Preliminary Report of the South African Demographic and Health Survey (DoH, 2003a:23) stated that 8.8% of males and 18.8% of females in South Africa have hypertension.

The following graphs were drawn up from statistics in the Preliminary Report of the South African Demographic and Health Survey (DoH, 2003a:23).

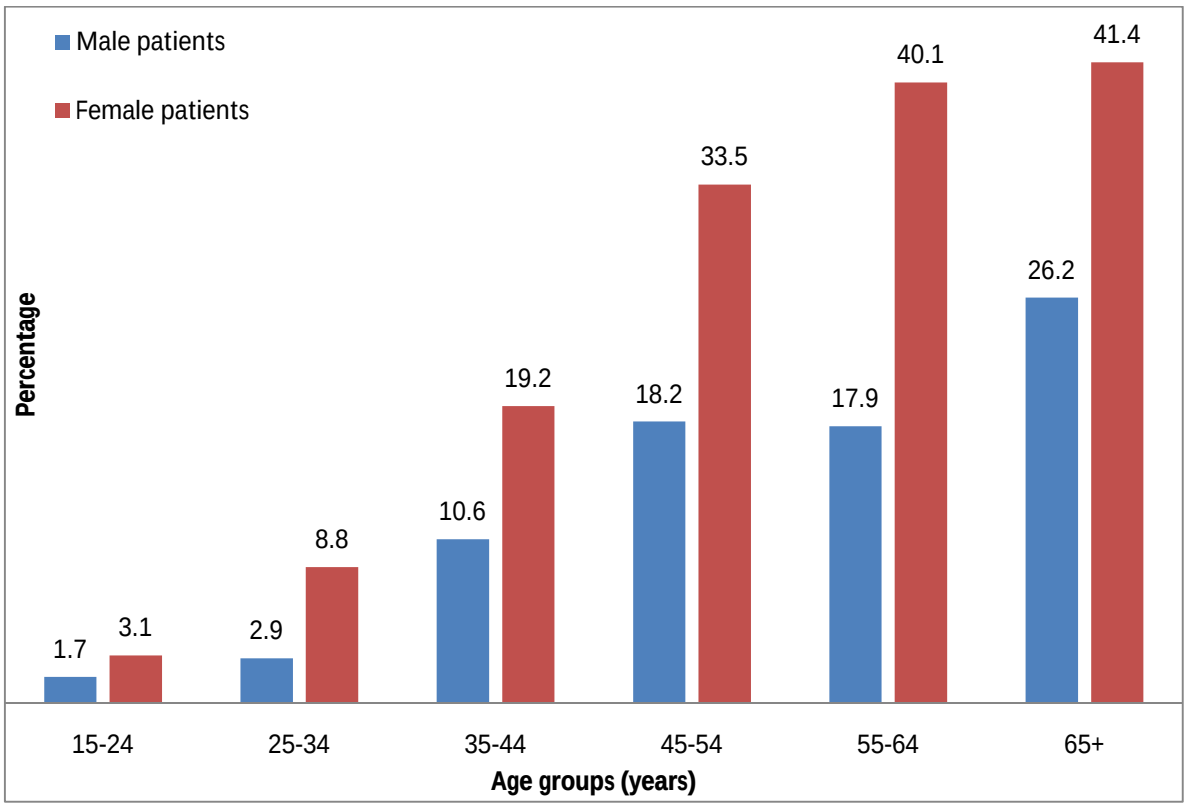


Figure 2.4: Percentages of male and female patients of different age groups in South Africa diagnosed with hypertension

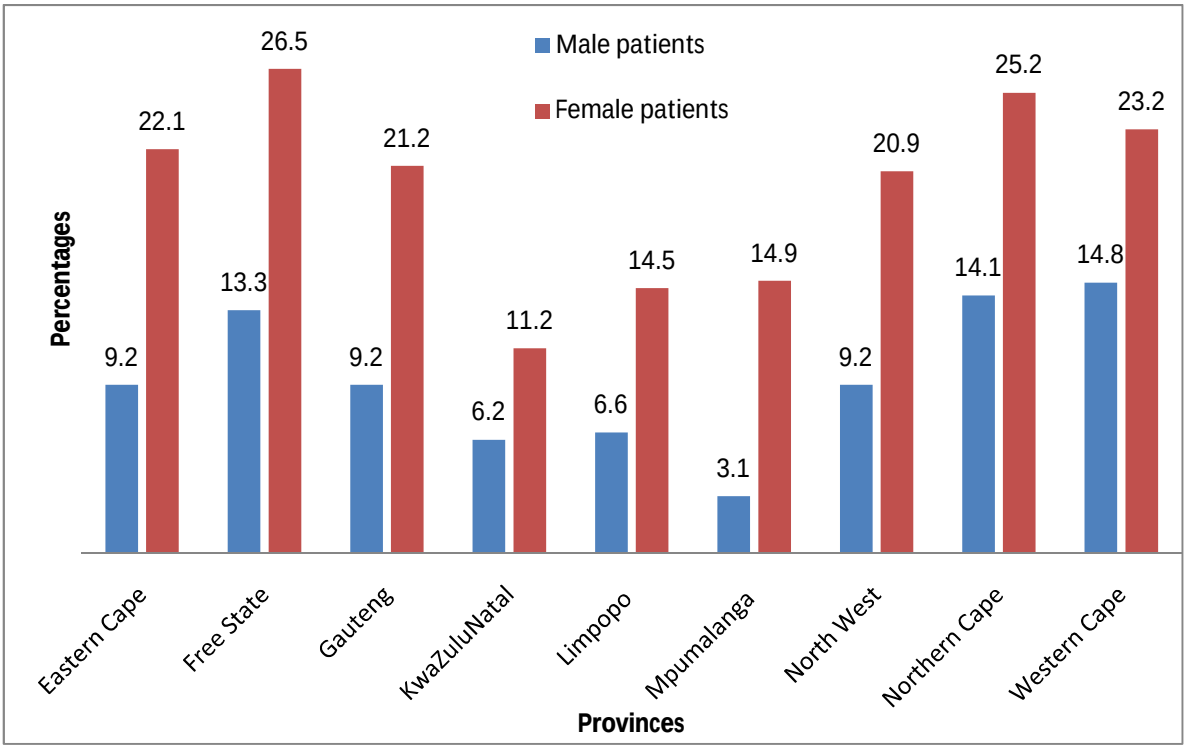


Figure 2.5: Percentages of male and female patients in South Africa diagnosed with hypertension as in the 9 provinces

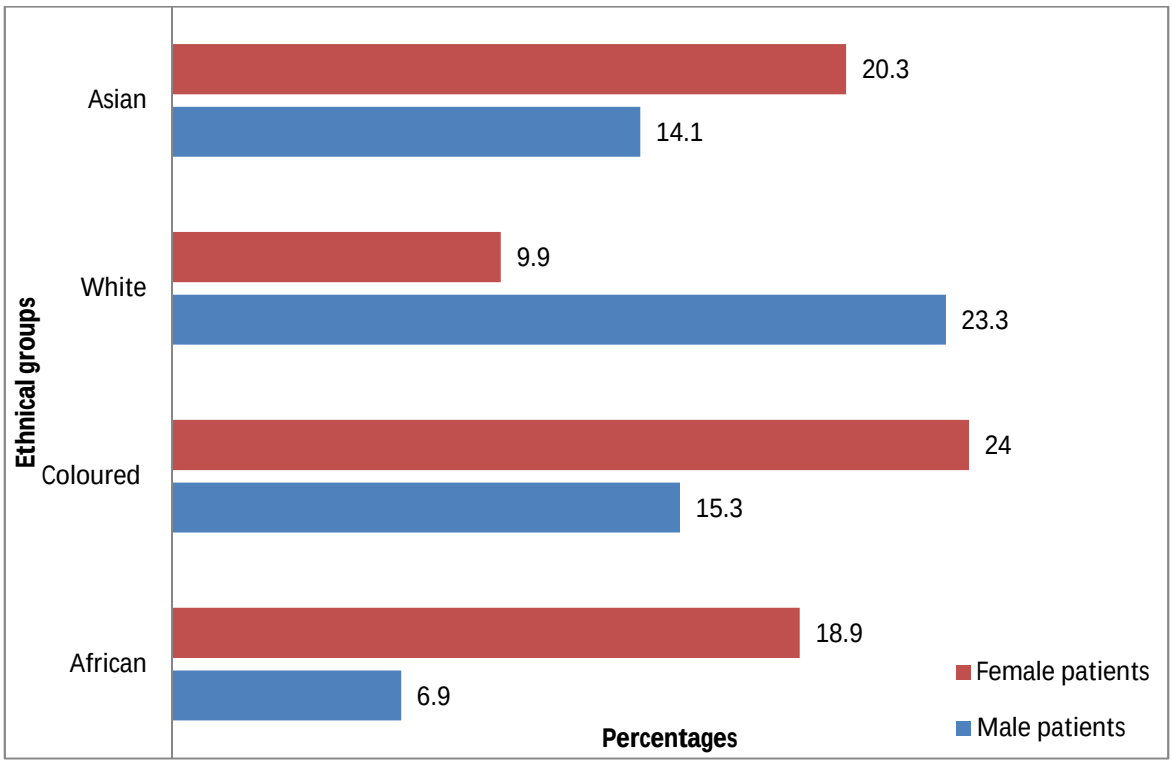


Figure2.6: Percentages of male and female patients in South Africa diagnosed with hypertension as in the four different race groups

2.6.5 Hypertension in children

Although hypertension occurs more often in adults it affects children as well (IPHA, 2008; Pilote *et al.*, 2007:5). Most of the children living with hypertension have underlying cardiorenal disease resulting in secondary hypertension. Primary hypertension (also known as essential hypertension) also occurs in childhood without an identifiable cause. Children with HBP tend to end up being hypertensive adults (IPHA, 2008; Pilote *et al.*, 2007:8).

Statistics issued by the International Pediatric Hypertension Association (IPHA, 2008) showed that 5% to 11% of children and adolescents may have essential hypertension and this could influence behavioural changes or alter school performances. More boys than girls were diagnosed with hypertension in the U.S.A. from 1995 to 2003 (Pilote *et al.*, 2007:10).

Hypertensive children tend to have other medical problems. These problems, as in adult patients, include obesity, high blood cholesterol levels and/or high blood sugar levels (IPHA, 2008; Pilote *et al.*, 2007:5). A reason for concern is that obesity increased almost threefold over the past two decades in adults as well as children in the U.S.A. (Pilote *et al.*, 2007:5). It was documented that only 31.9% of obese children between ages 2 to 19 in the U.S.A. were active (American Heart Association, 2010:13) which is a great contributing factor to hypertension in these children.

It has been suggested that the BP of children and adolescents should, like adults (South Africa, 1998:94), be tested at least once per year (IPHA, 2008; Sinaiko, 1996:1971). Children suffering from conditions like heart disease, renal disease, hepatic disease or in cases of prematurity, low birth weight, bone marrow transplant or evidence of increased intracranial pressure should have their BP measured with every visit to a medical setting (Portman *et al.,* 2005:264).

It was stated (Sinaiko, 1996:1971) that the right size cuff for the patient should be used as a too large cuff will give false low readings. Anxiety caused by the health care facility of the BP measuring procedure should be kept in mind (Sinaiko, 1996:1971). It is important to let the tested child sit still for approximately five minutes prior to testing (Portman *et al.,* 2005:264).

It was reported that there were no significant differences in the BP of whites, blacks, Hispanics or Asian patients up to adolescents. It was also reported that sex did not have the same influence on BP of children as seen in adult patients (Sinaiko, 1996:1971).

The first step in treating hypertension in children would include some lifestyle changes that include weight loss, decreased sodium intake and a diet rich in potassium in the form of fruit and vegetables (Portman *et al.,* 2005: 285). These are also some of the lifestyle changes suggested for adult hypertensive patients (DoH, 2003b:73; International Society of Hypertension, 2005; South Africa, 1998:94; U.S. Department of Health and Human Services, 2004:31).

2.6.6 Hypertension classification

Hypertension was classified into different stages of hypertension as shown in the table below (U.S. Department of Health and Human Services, 2004:11; Wells *et al.,* 1999:131).

Table 2.2: The classification of blood pressure in adults

Category	Systolic (mmHg)	Diastolic (mmHg)
Normal	≤120	≤ 80
Prehypertension	>120 ≤140	>80 ≤ 89
Hypertension Stage 1 (Mild Hypertension)	>140 ≤ 160	>90 ≤ 99
Hypertension Stage 2 (Moderate Hypertension)	>160 ≤ 180	>100 ≤ 109
Hypertension Stage 3 (Severe Hypertension)	>180	> 110

A diastolic BP above 130 mmHg is known as a hypertensive crisis and the person should be referred to a hospital immediately (DoH, 2003b:76).

It should be noted that BP should be lowered over a few days. A sudden drop in BP could be dangerous (DoH, 2003b: 73).

2.6.7 Treatment

The main objective of treating hypertension is to reduce the risk of CV complications. In this section different treatment strategies will be discussed in depth as well as compared to each other.

2.6.7.1 Lifestyle modifications

Kearney *et al.* (2005:222) stated that lifestyle changes of the general public would result in lower prevalence of hypertension worldwide. Lifestyle modifications are also the very first step in the treatment of hypertension (DoH, 2003b:73; International Society of Hypertension, 2005; South Africa, 1998:94; U.S. Department of Health and Human Services, 2004:31).

These lifestyle modifications that have been advised include the following (DoH, 2003b:73; International Society of Hypertension, 2005; South Africa, 1998:94; U.S. Department of Health And Human Services, 2004:31):

- Weight loss in overweight patients.
- Regular physical activities.
- Smoking to be stopped.
- Moderate alcohol intake (preferably no alcohol intake).
- Salt intake to be restricted.
- Fat intake to be restricted.
- Adequate dietary fibre intake e.g. fruit, vegetables and unrefined carbohydrates.

It is not certain whether these present treatment guidelines in the treatment of hypertension as showed below will remain unchanged in the implementation of the proposed NHI system (Section 2.5.1.1).

2.6.7.2 Stepwise treatment of hypertension as in the standard treatment guidelines and essential drug list

Below follows the stepwise treatment of hypertension as adapted from the Standard Treatment Guidelines and Essential Drug List (DoH, 2008:63).

Step 1

Stage and complications	Treatment	Target
Stage 1 hypertension without any disease and no major risk factors	Lifestyle modification	Control of BP within 3 months below the 140 / 90 mmHg level

Step 2

Stage and complications	Treatment	Target
Failure of Step 1 for treating hypertension or Stage 1 hypertension with a major risk factor or disease or Stage 2 hypertension at diagnosis	Lifestyle modification and 12.5 mg hydrochlorothiazide daily	Control of BP within 1 month below the 140 / 90 mmHg level

Step 3

Stage and complications	Treatment	Target
Failure of Step 2 for treating hypertension or Stage 3 hypertension	Lifestyle modification and 12.5 mg hydrochlorothiazide daily and ACE inhibitor, e.g. enalapril 10 mg daily or **Long acting CCB**, e.g. amlodipine 5 mg daily	Control of BP within 1 month below the 140 / 90 mmHg level

A β-blocker, e.g. atenolol 50 mg daily as in Standard treatment guidelines and essential drug list (DoH, 2003b:73) was replaced by an ACE inhibitor, e.g. Enalapril 10 mg daily or Long acting CCB, e.g. amlodipine 5 mg daily in the Standard treatment guidelines and essential drug list (DoH, 2008:63).

Step 4

Stage and complications	Treatment	Target
Failure of step 3 for treating hypertension	Lifestyle modification and 12.5 mg hydrochlorothiazide daily and ACE inhibitor, e.g. enalapril 10-20 mg daily and **Long acting CCB**, e.g. amlodipine 5 mg daily	Control of BP within 3 months below the 140 / 90 mmHg level without side-effects

The β-blocker, e.g. atenolol 50 mg daily as in Standard treatment guidelines and essential drug list (DoH, 2003b:73) was removed from Step 4 treatment.

Step 5

Stage and complications	Treatment	Target
Failure of Step 4 for treating hypertension	Lifestyle modification and 25 mg hydrochlorothiazide daily and ACE inhibitor, e.g. enalapril 20 mg daily and **Long acting CCB**, e.g. amlodipine 10 mg daily and add β-blocker, e.g. atenolol 50 mg daily	

An extra step in the treatment regimen for hypertension in Standard treatment guidelines and essential drug list (DoH, 2008:63) was added.

Step 6

Stage and complications	Treatment	Target
Failure of step 5 for treating hypertension	Refer patient secondary care	

2.6.7.3 Stepwise treatment of Hypertension according to the Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure

Below follows the stepwise treatment of hypertension as adapted from the Seventh report of the joint national committee on prevention, detection, evaluation and treatment of HBP (U.S. Department of Health and Human Services, 2004:31).

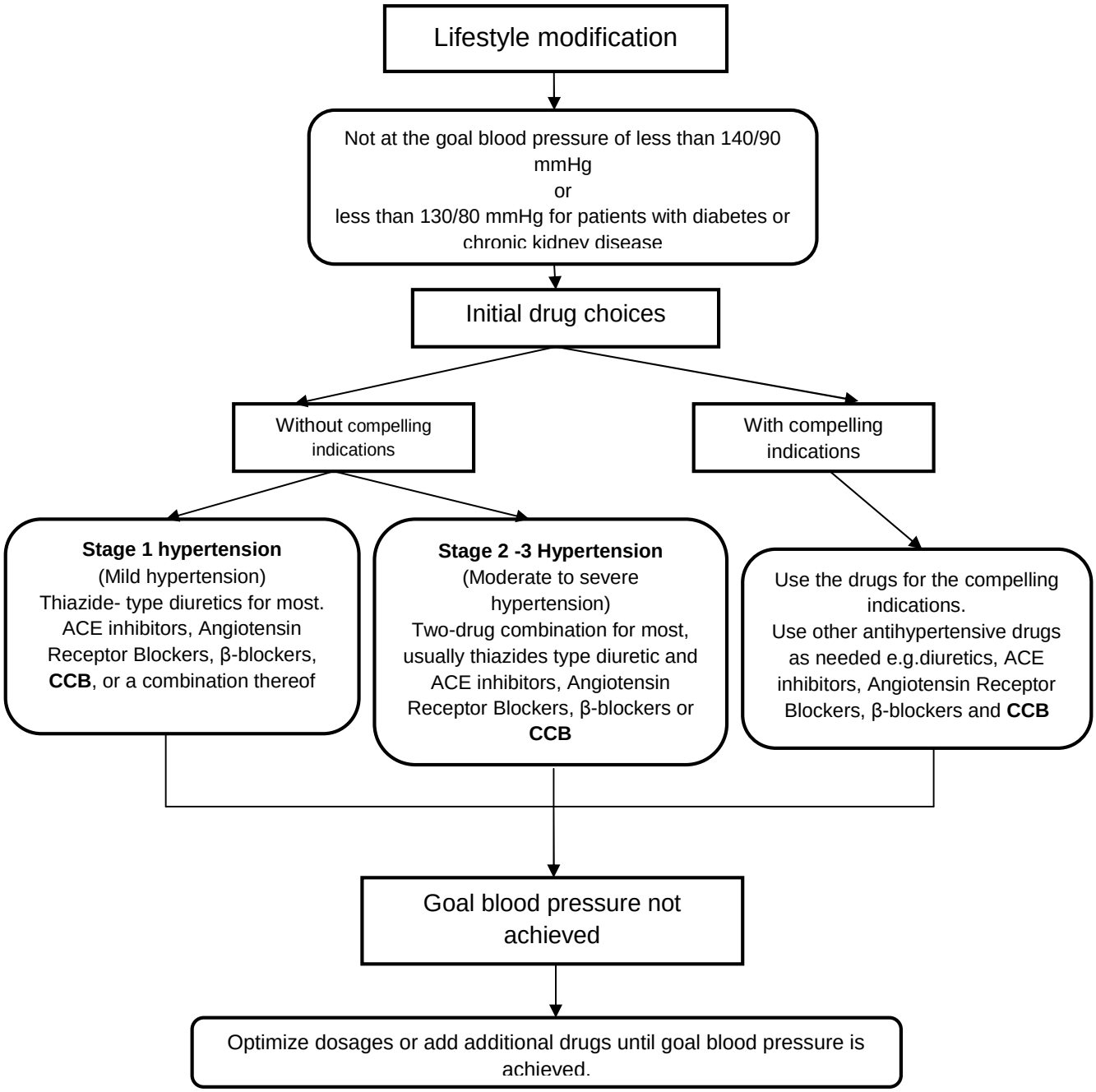


Figure 2.7: Treatment algorithm for hypertension from the Seventh report of the joint national committee on prevention, detection, evaluation and treatment of high blood pressure (U.S. Department of Health and Human Services, 2004:31)

2.6.7.4 Stepwise treatment of hypertension according to the Medical schemes act no. 131 of 1998

Below follows the stepwise treatment of hypertension as adapted from the Medical Schemes Act no. 131 of 1998 (South Africa, 1998:94).

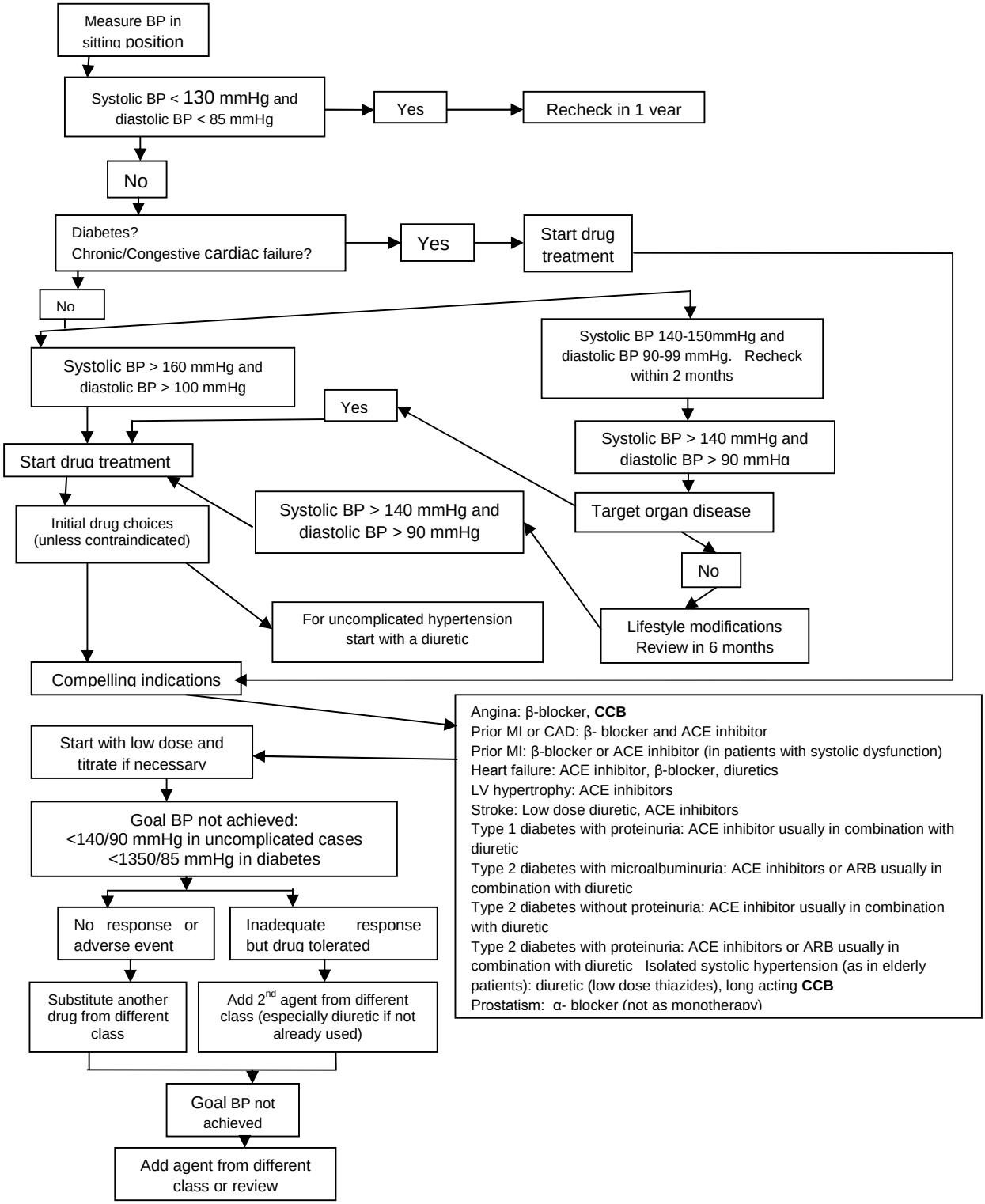


Figure 2.8: Treatment algorithm for hypertension from the Medical schemes act no. 131 of 1998 (South Africa, 1998:94)

As seen above CCBs should not be used as initiate therapy against hypertension but as an add-on. Abernethy & Schwartz (1999: 1449) stated that CCB medicine items were recommended as first-line therapy only if there exists a compelling reason not to administer a thiazide diuretic or β-blocker.

Degli-Esposti *et al.* (2004:78) reported that CCB medicine items were in 2nd position of medicine items most commonly prescribed as first-line therapy for hypertensive patients. The most commonly prescribed medicine items for hypertensive patients were ACE inhibitors, prescribed in 28% of the cases.

Table 2.3: Table of comparison between the three different treatment guidelines for hypertension

Aspects compared	**Essential Drug List 2008** (DoH, 2008:63)	**JNC 2004** (U.S. Department of Health and Human Services, 2004:31)	**The Medical Schemes Act no. 131 of 1998** (South Africa, 1998:94)
First step in reducing BP	Lifestyle modification	Lifestyle modification	Lifestyle modification
Recommended duration after lifestyle modification to repeat BP monitoring	3 months	Not specified	6 months
Specified ideal BP in patients without other complications	≤ 140/90 mmHg	≤ 140/90 mmHg	≤ 140/90 mmHg
Specified ideal BP with complications	≤ 140/90 mmHg	≤ 130/80 mmHg	≤ 130/85 mmHg
Specified intervals for BP monitoring for non hypertensive patients	Not specified	Not specified	12 monthly
Specified intervals for BP monitoring for hypertensive patients	1 to 3 monthly (as specified per step)	Not specified	6 monthly
Treatment decision process	Stepwise approach, depending on failure of upper step	Categorising BP in its different stages	Following the algorithm
First Medical treatment that follows lifestyle modifications	Diuretics	Diuretics	Diuretics
When to add-on medicine to current therapy	Specified by stepwise system	When goal BP not achieved after treatment per category	Inadequate response and/or goal BP not achieved.
Last step in treatment guidelines	Refer	Optimise dose or add additional drugs until BP achieved. Consider consultation with hypertension specialist	Add agent from different class or review
Level or step in guidelines where the usage of CCBs are advised	Step 3	As part of the initial drugs, after lifestyle modifications	After a diuretic had been added for the treatment of the compelling indication

All the different treatment guidelines consider a BP of more than 140/80 mmHg as hypertensive of HBP (DoH, 2008:63; South Africa, 1998:94; U.S. Department of Health And Human Services, 2004:31) follow a stepwise approach to achieve it. The very first step in the treatment of hypertension is considered by all three these guidelines to be lifestyle modifications followed by the addition of diuretics. All agree on repeated regular BP monitoring ranging from every 3 to 6 months (DoH, 2008:63; South Africa, 1998:94) for hypertensive patients and 12 monthly for non-hypertensive patients (U.S. Department of Health and Human Services, 2004:31). Regular BP monitoring, monthly in some cases (DoH, 2008:63), is needed until the targeted BP has been achieved (South Africa, 1998:94; U.S. Department of Health and Human Services, 2004:31). In cases where BP cannot be controlled it is advised to refer these patients to a hypertension specialist (DoH, 2008:63; South Africa, 1998:94; U.S. Department of Health and Human Services, 2004:31).

In the case of the guideline by the Medical Schemes Act (South Africa, 1998:94) the treatment differs according to the compelling indications. Treatment algorithm for hypertension from The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (U.S. Department of Health and Human Services, 2004:31) requires the categorising of hypertension (Table 2.2) prior to the treatment thereof.

It is important to use these treatment guidelines as a stepwise approach as this will result in the best possible therapeutic effect. CCBs are considered an important class of drugs in all these treatment guidelines and the use thereof is advised in all these guidelines.

2.7 Aspects of angina pectoris: prevalence and treatment

In this section angina pectoris will be explained in more depth as well as some statistics and treatment strategies.

2.7.1 Definition

- Angina pectoris was defined by the Dorland's Illustrated Medical dictionary (1988:82) as spasmodic, choking or suffocating pain in the chest area.
- Katzung and Chatterjee (2004:184) defined angina pectoris as a severe chest pain caused by inadequate coronary blood flow to supply the heart with oxygen as it is required.
- Wells and the team of researchers (1999:184) defined angina pectoris as a spasmodic chest pain caused by a lack of oxygen and a decrease or absence of blood flow in the myocardium.
- Angina is squeezing chest pain or discomfort that occurs when an area of your heart muscle does not get enough oxygen-rich blood and could occur in your shoulders, arms, neck, jaw, or back (National Heart, Lung and Blood Institute, 2007).

2.7.2 Background

Angina pectoris is caused by ischemic heart disease (IHD) also known as coronary heart disease (CHD). Atherosclerosis is the main etiology of IHD (Wells *et al*., 1999:182). Plaque causes the coronary arteries to become narrow and stiff (National Heart, Lung and Blood Institute, 2007), as shown in Figure 2.9. The flow of oxygen-rich blood to the heart muscle is reduced. This causes pain and can lead to a heart attack (National Heart, Lung and Blood Institute, 2007).

Figure 2.9 explains atherosclerosis:

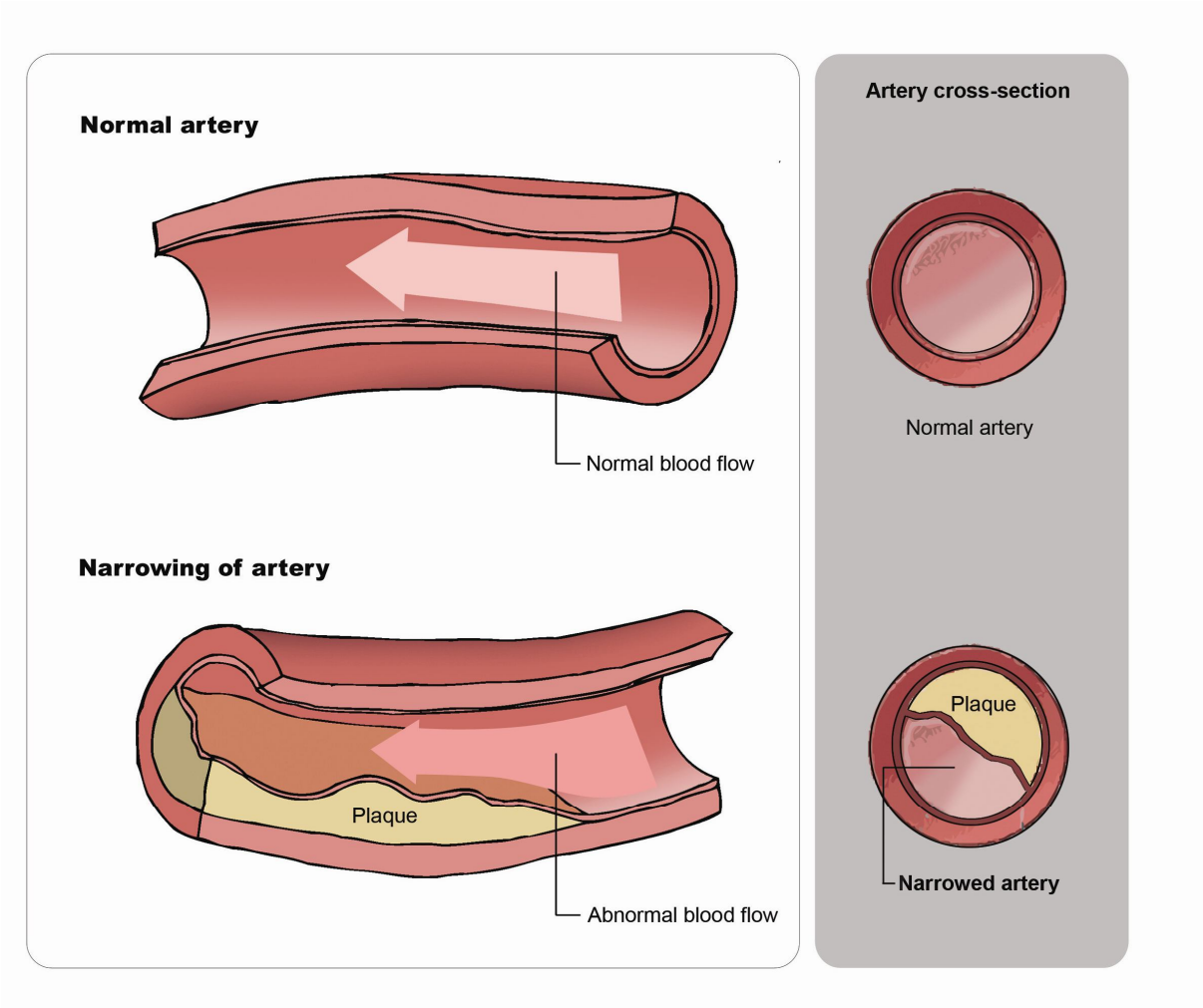


Figure 2.9: A normal artery with normal blood flow (A) and an artery containing plaque build-up (B) (adapted from National Heart, Lung and Blood Institute, 2007)

2.7.3 International prevalence of angina

The National Heart, Lung and Blood Institute (2007) stated that around 7000 000 people in the U.S.A. suffered from angina, with around four hundred thousand new reports every year.

Below the incidence of new angina episodes per 1000 population is tabulated (American Heart Association, 2010:13):

Table 2.4: Incidence of new episodes of angina per population of 1000

Age groups (years)	Non-black men (%)	Non-black women (%)	Black men (%)	Black women (%)
65-74	28.3 (2.83%)	14.1 (1.41%)	22.4 (2.24%)	15.3 (1.53%)
75-84	36.3 (3.63%)	20 (2%)	33.8 (3.38%)	23.6 (2.36%)
85+	33 (3.3%)	22.9 (2.29%)	39.5 (3.95%)	35.9 (3.59%)

The American Heart Association (2010:13) stated that an estimate of 17 600 000 American adults over the age of 20 have CHD, with a prevalence of 7.9% of U.S.A. adults (9.1% male and 7% female) established on data from 2003 to 2006. It is estimated that 785 000 would have had a coronary attack in 2010 (American Heart Association, 2010:13).

CHD was considered a major contributing factor in mortalities in the U.S.A. A total of 481 287 deaths were caused by CHD in 1995 (Wells *et al.*, 1999:183). In 2006 CHD caused 1 in every 6 deaths in the U.S.A. with 425 425 deaths in 2006 (American Heart Association, 2010:13).

It has been reported that every 25 seconds an American will suffer a coronary event and every minute someone will die of one (American Heart Association, 2010:13). The direct as well as indirect cost of CHD for 2010 was US$ 177.1 billion (American Heart Association, 2010:13).

2.7.4 South African prevalence of angina pectoris

In the South Africa Demographic and Health Survey (DoH, 2003a:24) it has been reported that 2.7% of males and 3.9% of females were diagnosed with angina with the highest percentages among Asian (males: 8.1% and females: 6.3%) and African (males: 2.8% and females: 4.1%) patients.

Below are figures 2.10, 2.11 and 2.12 according to information from the South Africa Demographic and Health Survey (DoH, 2003a:23):

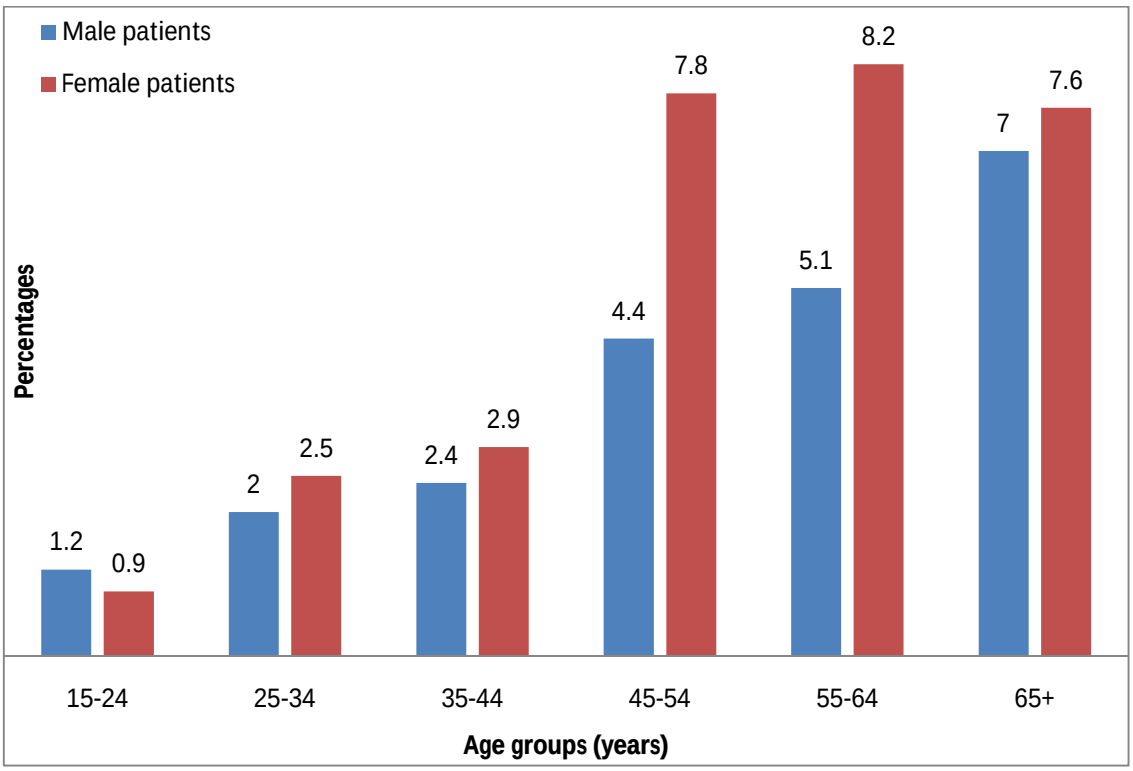


Figure 2.10: Percentages of male and female patients of different age groups in South Africa diagnosed with angina and heart attacks (adapted from DoH, 2003a:23)

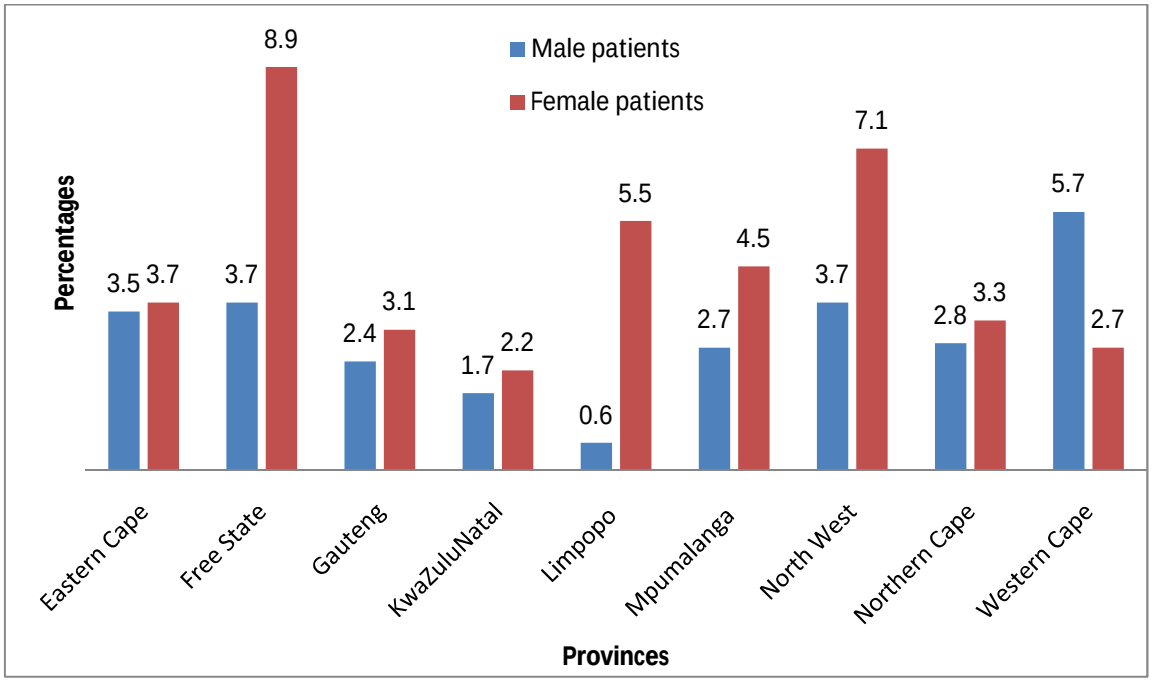


Figure 2.11: Percentages of male and female patients in South Africa diagnosed with angina and heart attacks as in the 9 provinces (adapted from DoH, 2003a:23)

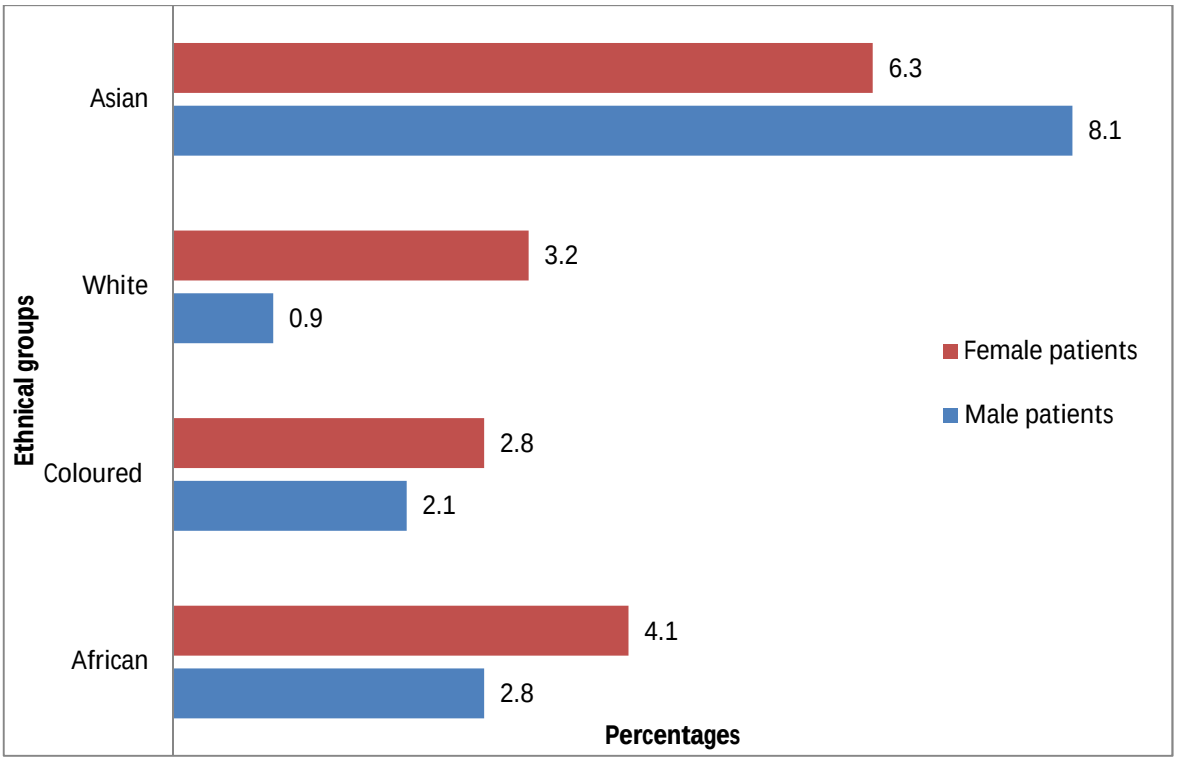


Figure 2.12: Percentages of male and female patients in South Africa diagnosed with angina and heart attacks as in the 4 different race groups (adapted from DoH, 2003a:23)

2.7.5 Types of angina pectoris

The National Heart, Lung and Blood Institute (2007) stated that there are three types of angina. This is important because of the different symptoms and ways of treatment these different types of angina require.

2.7.5.1 Stable angina

Stable angina, also known as angina of effort, is the most common type of angina and it occurs when the heart is working harder than usual. Patients with stable angina will learn to recognise the pattern and when to predict the pain. The pain will usually go away after a few minutes of rest, as the heart rate returns to normal, or when taking medication. Stable angina is not a heart attack but it is a sign that a heart attack may happen soon (National Heart, Lung and Blood Institute, 2007). Drugs used to increase the tolerance of the heart's effort include long-acting nitrates, CCBs and β-blockers. The drug choice will depend on the patient's response and if the response is inadequate another drug from another class should be added (Katzung & Chatterjee, 2004:197).

2.7.5.2 Unstable angina

Unstable angina does not follow a pattern. It may occur with or without any physical activity and is not relieved by rest or medication (National Heart, Lung and Blood Institute, 2007) such as nitrates for the acute attack (Katzung & Chatterjee, 2004:197). Chronic treatment (preventative) includes β-blockers and nitroglycerin, with CCBs added in refractory cases. Other drugs such as anticoagulant, antiplatelet and antilipid drugs should also be used on a chronic base (Katzung & Chatterjee, 2004:197). Unstable angina is very dangerous and needs emergency treatment. This is a sign that a heart attack will happen soon (National Heart, Lung and Blood Institute, 2007). Unstable angina causes about 750 000 hospitalisations a year in the U.S.A. of which approximately 70 000 develop myocardial infarctions and some die (Braunwald, 1989:410).

2.7.5.3 Variant angina (Prinzmetal's angina)

Variant angina, also known as Prinzmetal's angina, is a rare type of angina and it usually occurs while a person is at rest. It usually occurs between midnight and early morning hours in combination with severe pain. Variant angina is relieved by medicine (National Heart, Lung and Blood Institute, 2007) such as sublingual nitrates (e.g. isosorbide dinitrate and nitroglycerin) in cases of an acute attack (Katzung & Chatterjee, 2004:191). CCBs and nitrates are effective treatment for relieving and preventing episodes of variant angina (Katzung & Chatterjee, 2004:198).

2.7.6 Grading of angina of effort (stable angina)

Angina of effort was graded by the Canadian CV Society (Campeau, 1976:522) and this grading is still used today (Campeau, 2002:373). The grading is shown in the table below:

Table 2.5: Canadian CV Society grading of angina pectoris

Grade	Description
Grade 1	Ordinary physical activity does not cause angina, such as walking and stair climbing. Angina only with strenuous or rapid or prolonged exertion at work or recreation.
Grade 2	Slight limitation of ordinary activity. Walking, climbing stairs rapidly, walking uphill, walking or climbing stairs after meals, or in cold, or in windy conditions, or under emotional stress, or only during the first hours after awakening. Walking more than 2 blocks on the level and climbing more than 1 flight of stairs at a normal pace and in normal conditions.
Grade 3	Marked limitation of ordinary physical activity. Walking 1 or 2 blocks on the level and climbing more than 1 flight of stairs in normal conditions and at normal pace.
Grade 4	Inability to carry on any physical activity without discomfort, anginal syndrome may be present at rest

2.7.7 Classification

Angina pectoris is also classified by its severity (Braunwald, 1989:411).

Table 2.6: Classification of severity of angina pectoris

Classification of severity	Description
Class 1	New onset severe or accelerated angina. Patients with new onset (<2 months in duration) exertional angina pectoris that is severe or frequent (>3 episodes/day) or patients with chronic stable angina who develop accelerated angina (that is, angina distinctly more frequent, severe, longer in duration, or precipitated by distinctly less exertion than previously) but who have not experienced pain at rest during the preceding 2 months.
Class 2	Angina at rest, sub-acute. Patients with one or more episodes of angina at rest during the preceding month but not within the preceding 48 hours.
Class 3	Angina at rest, acute. Patients with one or more episodes of angina at rest within the preceding 48 hours.

In classes 2 and 3, manifestations described in class 1 may also occur. Unstable angina is no longer considered to be present when a patient has been asymptomatic or suffers angina that has been stable for more than two months.

2.7.8 Drug classes and specific drugs used in the treatment of angina pectoris

In addition to the treatment of angina, the risk factors of coronary atherosclerosis should be under control. These factors include smoking, hypertension and hyperlipidemia (Katzung & Chatterjee, 2004:197).

Angina treatment is based on the reduction in myocardial oxygen demand and an increase in coronary blood flow (Katzung & Chatterjee, 2004:197). Treatment to prevent myocardial infarction also contains antiplatelet agents (like aspirin and clopidogrel) as well as lipid-lowering agents. The treatment of unstable angina is more aggressive and contains stenting, antilipid drugs, heparin and antiplatelet agents (Katzung & Chatterjee, 2004:197).

2.7.8.1 Anti-lipid drugs

Statins (HMG-CoA structural analogs) are most effective in reducing low density lipoprotein. It has been stated that it increases the stability of atherosclerotic lesions and it could also cause a regression of anginal symptoms and possibly the prevention of further disease progression (Baller *et al.,* 1999:2877).

2.7.8.2 Heparin

Heparin interacts with antithrombin. This inhibits clotting factor protease. The conformation change of antithrombin exposes its active site for more rapid interaction with the proteases. Through a cascade of inhibition of different blood clotting factors it causes an inability of blood to clot (Hambleton, 2009:554).

2.7.8.3 Antiplatelets

Aspirin inhibits thromboxane A_2 synthesis by blocking cyclooxygenase (Denktas *et al.,* 2001:110). A dose of 81 mg aspirin produces a prolonged bleeding time, which doubles when administered for a week. This antiplatelet effect of aspirin lasts for 8 to10 days, which is the life of the platelet (Wagner *et al.,* 2009:192).

Clopidogrel and ticlopidine inhibits ADP (Adenosine diphosphate) -mediated platelet aggregation and irreversibly blocking ADP receptors on platelets. Clopidogrel and ticlopidine are used in patients hypersensitive to aspirin or patients with major gastrointestinal intolerance to aspirin. Side-effects of ticlopidine limit it's usage (Hambleton, 2009:554). Ticlopidine is not available locally (Snyman, 2009:103).

2.7.8.4 Warfarin

The data regarding the use of anti-coagulants in the treatment of angina are inconclusive (Denktas *et al.,* 2001:153; Yeghiazarians *et al*., 2000:110).

2.7.8.5 Calcium channel blockers

The use of calcium channel blockers in the treatment of stable angina is well established (Gibbons *et al.,* 1999:2843) but not used as first line therapy (Denktas *et al.,* 2001:154). Yeghiazarians and the team of researches (2000:110) reported the use of calcium channel blockers in patients with unstable angina as successful therapy. This was also stated by Opie *et al. (*2000:174). Calcium channel blockers are also accepted as effective treatment in variant angina (Opie *et al.,* 2000:174; Denktas *et al.,* 2001:153).

2.7.8.6 Angiotensin-converting enzyme inhibitors (ACE inhibitors)

It has been stated that ACE inhibitors may decrease atherosclerosis by modulating the oxidixed low-density lipoprotein receptors. ACE inhibitors can also affect the coagulation system by decreasing thrombus formation (Denktas *et al.,* 2001:153). Gasic *et al.* (1990) stated that ACE inhibitors could be used in exercise endued angina (Denktas *et al.,* 2001:153).

2.7.9 Conditions that exacerbate or provoke episodes of angina

The following are some of the conditions and/or factors that provoke or worsen an angina episode (Gibbons *et al*., 1999:2835):

Medication:

- Vasodilators
- Excessive thyroid replacement
- Vasoconstrictors

Other medical problems:

- Profound anaemia
- Uncontrolled hypertension
- Hyperthyroidism
- Hypoxia

Other cardiac problems:

- Tachyarrythmias
- Bradyarrythmias
- Vascular heart disease
- Hypertrophic cardiomyopathy

It is not sure whether these present treatment guidelines in the treatment of angina pectoris as showed in Section 2.7.8 will stay unchanged in the implementation of the proposed NHI system.

2.7.10 Treatment of angina

Below are some treatment strategies of treating angina pectoris:

2.7.10.1 Treatment strategy used in the treatment of angina pectoris as by Gibbons et al.

Here follows the treatment algorithm as adapted from Gibbons *et al*. (1999:2835).

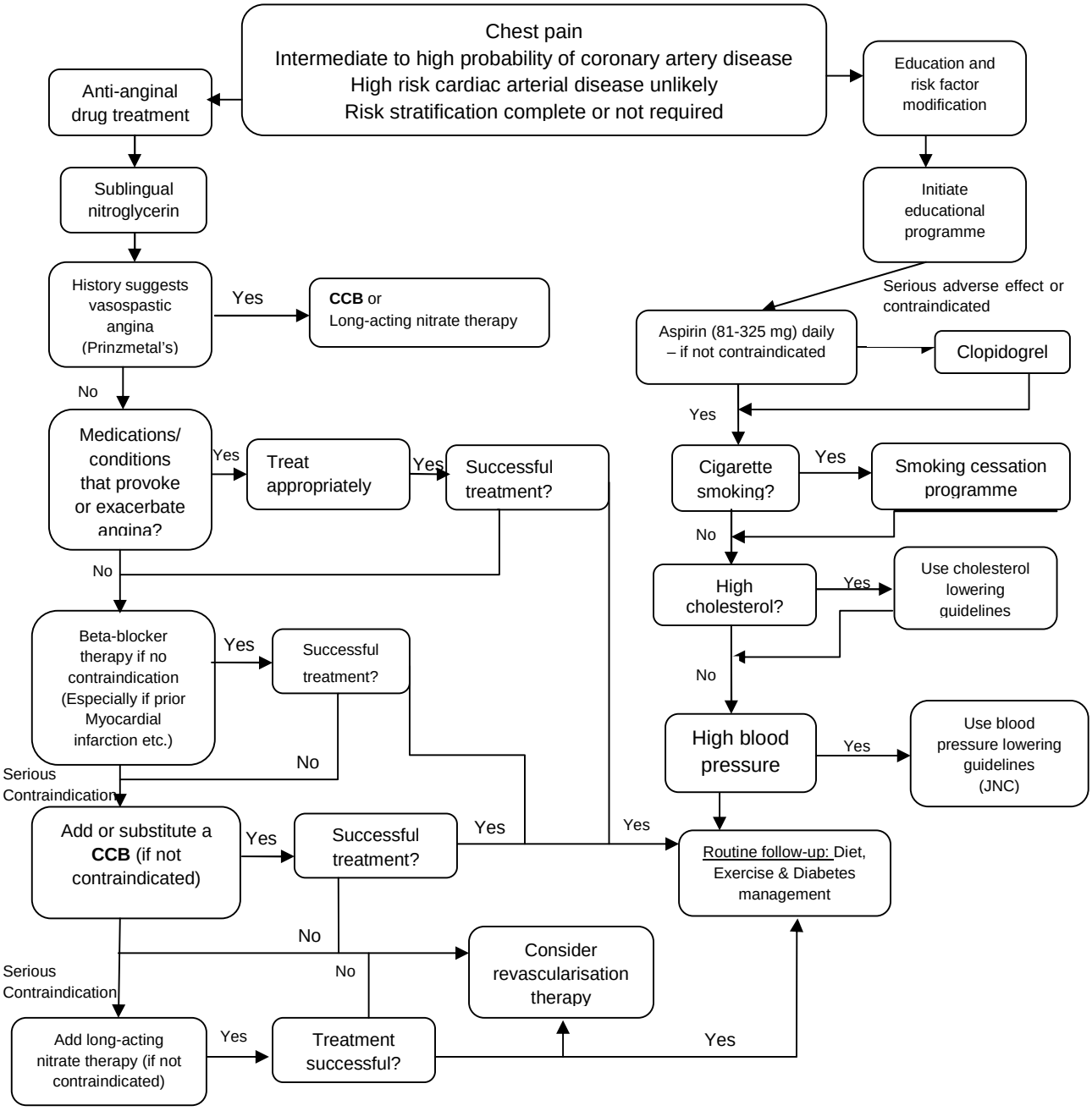


Figure 2.13: Treatment of angina (adapted from Gibbons et al., 1999:2835)

2.7.10.2 Treatment strategy used in the treatment of angina pectoris as from the Medical schemes act no. 131 of 1998

Here follows the stepwise treatment of CAD to control angina as adapted from the Medical Schemes Act no. 131 of 1998 (South Africa, 1998:69).

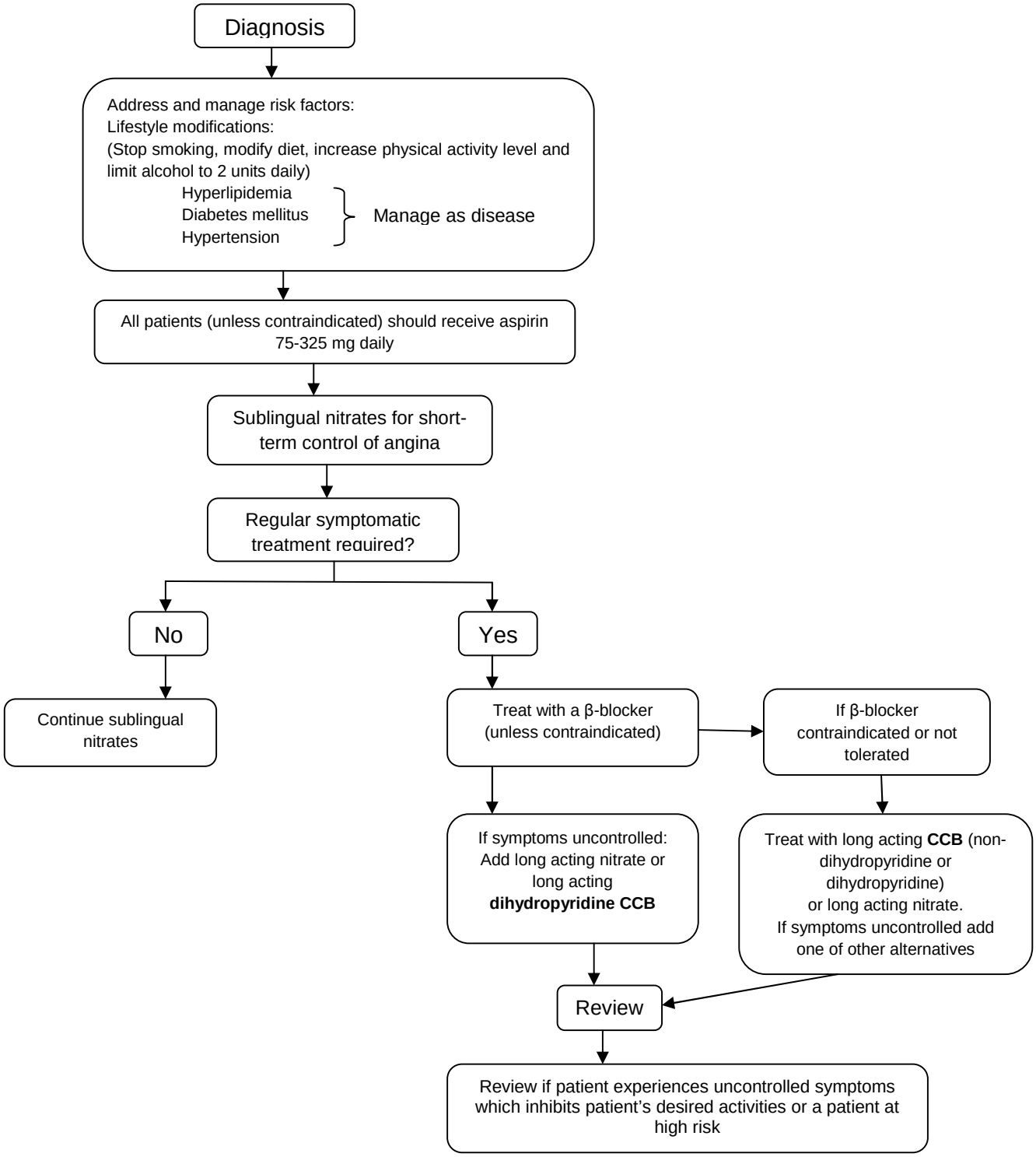


Figure 2.14: Treatment of coronary artery disease from the Medical Schemes Act no. 131 of 1998 (adapted from South Africa, 1998:69)

Table 2.7: Table of comparison between the two different treatment guidelines for angina

Aspects compared	Gibbons *et al*. (1999:2835)	Medical Schemes Act no. 131 of 1998 (South Africa, 1998:69)
Lifestyle modification as first step in treatment	Yes	Yes
First medication after the lifestyle modifications had been applied	Aspirin (81 mg to 325 mg daily)	Aspirin (75 mg to 325 mg daily)
Treatment of acute angina attack	Sublingual nitroglycerin	Sublingual nitroglycerin
When would chronic medication be supplied	Patient has history of attacks	When regular symptomatic treatment is required
First medication for chronic angina	CCB	β-blocker (if not contra-indicated)
Anticoagulant included	Yes	Yes
Treatment of hypertension included	Yes	Yes
Treatment of Diabetes included	Yes	Yes
Treatment of hyperlipidemia included	Yes	Yes
Advised to stop smoking	Yes	Yes
Level in guidelines where usage of CCBs are advised	History predicting Prinzmetal's angina and unsuccessful results with β-blocker	Unsuccessful results with β-blockers or β-blockers contraindicated

The treatment strategy for treating angina is a stepwise approach. The very first step in the treatment of angina is considered by both these guidelines to be lifestyle modifications (Gibbons *et al*., 1999:2835; South Africa, 1998:69). A step to follow is to use sublingual nitrates for acute angina attacks. These guidelines also include the treatment of hypertension, diabetes and hyperlipidemia in the treatment of angina, as these diseases

could all cause angina attacks. An anticoagulant agent is also included in these treatment guidelines (Gibbons *et al*., 1999:2835; South Africa, 1998:69).

Gibbons *et al.* (1999:2835) state that a patient with a history of previous attacks is considered for chronic angina treatment and suggest CCBs as the first group of medication to use for chronic angina. The Medical Schemes Act (South Africa, 1998:69) stated that chronic patients require regular symptomatic treatment for their angina and suggests the use of β-blockers as first-line treatment for chronic angina.

It is important to use these treatment guidelines as a stepwise approach as this will result in the best possible therapeutic effect. CCBs are considered an important class of drugs in all these treatment guidelines and the use thereof is advised in all these guidelines.

Abernethy & Schwartz (1999: 1450) stated that CCB medicine items should not be used as mono-therapy for the treatment of unstable angina, but in combinations for combination therapy has additive effects for example a dihydropyridine CCB and a β-blocker.

A study by De Portu *et al.* (2006:162) stated that amlodipine added to standard CAD treatment was highly cost-effective. The study showed a decline from 72% to 40% in patients needing revascularisation procedures while vascular events costs decline from 28% to 19% of hospitalisation expenditure.

2.8 Aspects of pharmaco-economics and appropriate examples

Pharmaco-economic research was defined by Ernst *et al.* (2007:284) as “The identification, measurement and comparison of costs (i.e. resource consumption) and consequences (clinical, economic and humanistic benefits and risks) related to pharmaceutical products and services”.

“Relative high costs (of angina pectoris) reline the importance of health economic evaluations of various diseases and medical inventions.” (Anderson & Kartman, 1995:1).

Medicine costs are of great importance as they are responsible for up to 30% to 40% of total health costs in developing countries like South Africa (WHO, 2003:26).

Pharmaco-economic studies that resulted in interventions were introduced in certain countries and reduced the financial burden of CV diseases (Fujikawa *et al.,* 2005:591; Kearney, 2005:222). An analysis of cost-effectiveness allows key decision makers to establish and implement the most appropriate interventions with the available resources (Kearney *et al.*, 2005:222; WHO, 2003:26). These in primary prevention strategies with regard to CCBs and hypertension could yield the greatest benefit, in South Africa as well (Kearney *et al.*, 2005:222).

2.8.1 Cost-benefit analysis

CBA (Cost-benefit analysis) was defined as an economic analysis that measures cost and benefits (outcomes) in monetary terms e.g. cost-benefit ratio or a net cost or benefit (Walley *et al.,* 2004:187; WHO, 2003:27). CBA represents one of the most commonly encountered pharmaco-economic applications (Bonk, 1999:29; WHO, 2003:26).

Examples of studies where CBA have been used include the following:

A study, done by Rajgopal and the team of researchers (2002:34), investigated the cost-benefit ratio for the Expanded Food and Nutrition Education Program (EFNEP) in the U.S.A., based on potential prevention of diet-related chronic diseases and conditions. This is an educational programme in assisting limited resource family members to acquire the knowledge and skills necessary to improve health and disease prevention through their daily diets. The study found a benefit-cost ratio of $10.64/$1.00 and stated that the EFNEP is a good programme to invest tax money in (Rajgopal *et al.,* 2002:36).

2.8.2 Cost-effectiveness analysis

CEA (Cost-effectiveness analysis) was defined as an economic analysis that compares health care interventions that have a common health outcome measured in natural units e.g. life years saved (Walley *et al.,* 2004:188). It could be simplified by saying that CEA measures the incremental cost of achieving incremental cost benefit (WHO, 2003:26).

Cost-effectiveness analysis measures the cost of treating an illness by using clinical measurements for the treatment outcomes e.g. number of lives saved or complications prevented (Bonk. 1999:35; WHO, 2003:26). This approach was used for example to measure the cost of achieving an extra 10 mmHg drop in BP (WHO, 2003:26). Thus, CEA could be used to show therapeutic usefulness (Bonk, 1999:35).

Examples of studies where CEA have been used include the following:

In Japan Fujikawa and the team of researchers (2005:590) stated that the recommended combination therapy with multiple agents, each at a low dose (Miranda *et al*., 2008:5; Neutel, 2006:3), was more cost-effective than up-titrating monotherapy. These results support the guidelines from both a clinical and an economic viewpoint. The use of combination therapy in hypertension could contribute to a more cost-effective treatment, decreasing the financial burden thereof as on the National Health Insurance system as functioning in Japan (Fujikawa *et al.,* 2005:591).

2.8.3 Cost-minimisation analysis

CMA (Cost-minimisation analysis) was defined as a method of cost evaluation and is used to calculate the least costly drug or treatment (WHO, 2003:26). CMA can only be used to compare products shown to have equal dose and therapeutic effects and therefore the most useful method for comparing generic equivalents. If it is impossible to prove therapeutic equivalence of a product to another, CMA is an inappropriate analysis (WHO, 2003:26).

Examples of studies where CMA have been used include:

A CMA study done by Pearce *et al.* (1998:1) involving antihypertension treatment indicated that the treatment costs to prevent major hypertensive complications are much lower with diuretics and β-blockers than with ACE Inhibitor, CCB, or α-blockers, especially in middle-aged patients (Pearce *et al.,* 1998:1).

2.8.4 Cost-utility analysis

CUA (Cost-utility analysis) was defined as an economic analysis that usually measures benefits in a unit of utility e.g. QALY (quality-adjusted life-years) (Walley *et al.,* 2004:188; WHO, 2003:27). When calculating QALY an increased quality of life is used and expressed as a utility value on a scale of zero (dead) to one (perfect quality of life) (WHO, 2003:27).

Unlike CBA, CUA is used to compare two different drugs or procedures with possibly different benefits (WHO, 2003:27) and is a specialisation of cost-effectiveness (Bonk, 1999:41).

Examples of studies where CUA have been used include the following:

A study by Raftery and a team of researchers (2005:3) found a gain of 0.124 QALY and a mean gain of life per patient of 0.11 in a group of patients subjected to nurse-led secondary prevention clinics for heart disease. An incremental cost per life year saved was £ 1 236 and per QALY was £ 1 097 (Raftery *et al.,* 2005:3).

2.8.5 Cost-of-illness evaluation

Segel (2006:2) stated that cost-of-illness studies measure the economic burden of a disease and estimate the maximum amount that could potentially be saved if a disease were cured or controlled. Cost-of-illness studies identify and evaluate direct and indirect cost of a disease (Bootman *et al.,* 1991:5).

Having knowledge of the costs of an illness could help policy makers to decide which diseases need to be addressed first by health care and prevention policy. In addition, these studies can indicate to which diseases cures would be valuable in reducing the burden of disease (Segel, 2006:2).

Examples of studies where cost-of-illness evaluations were done include the following:

It was stated by the American Heart Association (2010:18) that the estimate direct and indirect cost of HBP for 2010 was $76.6 billion. It was also estimated that the direct and indirect cost of CHD for 2010 will be US$177.1 billion (American Heart Association, 2010:13).

It was stated by Anderson and Kartman (1995:1) that the annual direct medical cost of angina pectoris in Sweden was estimated at SEK 40 052 (Swedish krona) per patient. The annual non-medical cost of angina pectoris was entimated at SEK 38 225 per patient (Anderson & Kartman (1995:1).

This study will make use of cost-minimisation analysis due to the nature of the data available.

2.9 Aspects of drug utilisation studies

"Drug utilisation studies are an important application of pharmaco-epidemiology." (Truter, 1999:68).

2.9.1 Introduction

The need for drug utilisation studies in South Africa has been identified. Drug utilisation research is a multi-disciplinary activity and results can be used for a number of purposes e.g. a component of a management initiative, an academic investigation or a review of the performance of specific medication or a group of medication.

DUR should be formally acknowledged and encouraged as it is an important component of quality assurance. Essential infrastructure should be established for South Africa as this review may be regarded as a very important tool for promoting cost-effective use of medicine in the future health care system of South Africa (Truter, 1997:339).

The Niche Area, Medicine Usage in South Africa or (MUSA) located in the School of Pharmacy of the North-West University (NWU) is doing great work for Pharmacy with its DUR studies such as the following:

- The development of a professional fee for services for which a pharmacist may levy a fee.
- The continuous evaluation of the standard of pharmaceutical services provided by registered pharmacies in both the public and private health care sectors in South Africa.

2.9.2 Definition of DUR

- Edgren (1999:119) indicated that DUR is an "authorised, structured, and continuing program [*c*] that reviews, analyses, and interprets aggregate patterns of medication use measured against predetermined standards and criteria established for specific health care delivery systems."
- According to Kreling and Mott (1993:415) DUR is the "dynamic process aimed at the consequent improvement in the quality of health care and minimising needless expenditure"
- Jones and Radloff (2007:32) defined DUR as a "process specifically formulated to improve safe, suitable and effective drug therapy by detecting widespread variations from appropriate prescribing drug utilisation".

- Serradell *et al.* (1987:994) defined DUR as the prescribing, dispensing, administering and ingesting of drugs.
- The World Health Organization (WHO) defined DUR as "the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences."(WHO, 2003:33).
- Serfontein concluded that a good DUR would look at all processes involved in the rendering of a pharmaceutical service (Serfontein *et al*., 2001:3).

2.9.3 Why drug utilisation research?

Drug utilisation research in itself does not necessarily provide answers, but it contributes to rational drug use in three important ways (Sjöqvist & Birkett, 2003:78):

2.9.3.1 Description of drug use patterns

Drug utilization research will increase our understanding of how drugs are being used, considering the following aspects (Sjöqvist & Birkett, 2003:78):

- Making estimates of the numbers of patients exposed to drugs within a given time period. These estimates may either refer to all drug users, regardless of when they started to use the drug (prevalence), or focus on patients who started to use the drug within the selected period (incidence).
- Describing the extent of use at a certain moment and/or in a certain area (e.g. country, region, community, hospital). Such descriptions are most meaningful when they are part of a continuous evaluation system (when the patterns are followed over time and trends in drug use can be described).
- Estimating (e.g. on the basis of epidemiological data on a disease) to what extent drugs are properly used, overused, or underused.

  Describing the pattern or profile of drug use (alternative drugs used for particular conditions and to what extent).
- Comparing observed patterns of drug use with current recommendations or guidelines for the treatment of a certain disease.
- Applying quality indicators to drug utilisation patterns. e.g. so-called DU90% that reflects the number of drugs that account for 90% of drug prescriptions and adherence.
- Feeding back drug utilisation data to prescribers. This is useful when the individual's drug prescribing can be compared with some form of best practice, and with the average Prescriptions in an area.

- Relating the number of adverse effects to the number of patients exposed in order to assess the potential magnitude of the problem. It could be detected that the reaction is more common in a certain age group, under certain conditions or at a special dose level, improving the information on proper use to assure a safer use. Thereby withdrawal of the drug from the market may be avoided.

2.9.3.2 Early signals of irrational use of drugs

Drug utilisation research may generate hypotheses that set the agenda for further investigations by (Sjöqvist & Birkett, 2003:78):

- Comparing drug utilisation patterns and costs between different regions or time periods. Hypotheses can be generated to form the basis for investigations of the reasons for, and health implications of, the differences found. Geographical differences and changes over time in drug use may have medical, social and economic implications and are thus important to identify, explain and sometimes correct.
- Comparing patterns of drug use with current guidelines for the treatment of a certain disease. Hypotheses can be generated about whether discrepancies represent less than optimal practice, whether education is required, or whether the guidelines need to be reviewed in the light of actual practice. These considerations include underuse and overuse of drugs.

2.9.3.3 Interventions to improve drug use follow-up

Drug utilisation research may enable us to assess whether interventions undertaken to improve drug use have had the desired impact by (Sjöqvist & Birkett, 2003:78):

- Monitoring and evaluating the effects of measures taken to improve undesirable patterns of drug use (regional or local formularies, information campaigns, regulatory policies, etc.)
- Following the impact of regulatory changes or changes in insurance or reimbursement systems.
- Assessing to which extent promotional activities of the pharmaceutical industry and educational activities of the society exercise an impact on the patterns of drug use.

2.9.4 Types of DUR

The process of DUR can be categorised into three categories:

2.9.4.1 Retrospective DUR

According to Chrischilles and colleagues (1996:172) retrospective DUR can be defined as a system that combines data of all prescribed medication into a conclusion to shorten the identification of improper prescribing patterns.

Thomas *et al* (2004:434) defined retrospective DUR as a system that examines medicine usage after medication has been dispensed and often takes place after the medication has been consumed. The core objective of retrospective DUR is to distinguish the inappropriate prescribing patterns or the sub-optimal drug use and to design interventions with providers and consumers to prevent inappropriate prescribing and unfavourable medication usage (Thomas *et al*., 2004:434).

A retrospective study involves the computerised screening of medication claims by pharmacies each month to detect the exceptions that may appear. These exceptions break the determined formula for appropriate prescribing patterns (Hennessy & Strom, 2003:1494).

2.9.4.2 On-line prospective DUR (OPDUR)

This type of DUR is also known as co-existing reviews. This study is conducted at the exact time the dispensing claim is set. This indicates that potential problems are identified while dispensing a Prescription. It is more accurate in preventing problems and therefore has a greater advantage to the client (Thomas *et al., 2*004:434). On-line prospective DUR enhances the information available to the pharmacists that will lead to better cognitive services of pharmacists (Chrischilles *et al.,* 1996:174).

2.9.4.3 Prospective reviews

Prospective reviews are based on a complete medical history to allow the practitioner to evaluate the specific condition from pre-existing therapies while the medication is dispensed to the patient.

A prospective study is ideal as it is designed to identify potential problems while dispensing e.g. therapeutic duplication, improper dosage or the incorrect duration of therapy (Thomas *et al.,* 2004:434) and correcting them before dispensing.

The objective of prospective DUR (PDUR) is to reduce problems that might occur in future as a result of the improper prescribed medication therapy (Chrischilles *et al.,* 1996:172).

This study will focus on a retrospective DUR approach due to the nature of the data available.

2.10 Chapter summary

CCBs have a broad spectrum of usages but they are mostly used for the treatment of hypertension and angina in patients (Snyman, 2009:103). Some interactions with other medication as well as some contra-indications have been reported (Baxter, 2008:873; Pfizer, 2001 & Pharmacia, 2005; Snyman, 2009:103). This is because CCBs are metabolised by the cytochrome P450 isoenzyme CYP3A4 and this is the same enzyme responsible for the metabolism of a large number of other medications (Baxter, 2008:860). Adverse effects could have a negative impact on the compliance figures of patients using CCBs as well as other antihypertensive or anti-anginal medication (Osterberg & Blaschke, 2005:493). Compliance figures locally as well as internationally do not resemble successful compliance to date (Bester & Hammann, 2007:21; Kabira *et al.,* 2004:17).

It is preferred that CCB medicine items should be used for some conditions. It is favoured that pregnant hypertensive patients use dihydropyridine type CCBs and tachycardia patients use non-dihydropyridine CCBs (Southern African Hypertension Society; 2006).

An estimate of 17.4% of the U.S.A. population over the age of 18 years suffer from hypertension (Balu & Thomas, 2006: 810). The direct and indirect cost of HBP for 2010 was $ 76.6 billion (American Heart Association 2010:18). Statistics by the International Pediatric Hypertension Association (IPHA, 2008) have showed 5% to 11% of children and adolescents may have essential hypertension. The Preliminary Report of the South African Demographic and Health Survey (DoH, 2003a:23) stated that 8.8% of males and 18.8% of females in S.A. suffer from hypertension.

Some treatment guidelines were viewed and discussed (DoH, 2008:63; South Africa, 1998:94; U.S. Department of Health and Human Services, 2004:31). It is important to use these treatment guidelines as a stepwise approach as this will result in the best possible therapeutic effect. CCBs are considered an important class of drugs in all these treatment guidelines and the use thereof is advised in all these guidelines.

Angina pectoris has a prevalence of 7.9% in the U.S.A. and it was estimated that the direct and indirect cost of CHD for 2010 was $ 177.1 billion (American Heart Association, 2010:13). In S.A. (DoH, 2003a:24) it is reported that 2.7% of males and 3.9% of females were diagnosed with angina in 2003.

Some treatment strategies were viewed and discussed (Gibbons *et al.*, 1999:2835; South Africa, 1998:69) and it was shown that it is important to treat the other conditions that could cause the angina attacks.

The importance of pharmaco-economic studies was pointed out and different types of pharmaco-economic evaluations were defined. DUR analysis was discussed and defined and the uses of DUR were brought forward. Types of DUR were analysed and differences pointed out at the end of the chapter.

As previously mentioned the study will make use of cost-benefit analysis as well as retrospective DUR in the analysis of the available data.

In the next chapter (Chapter 3) the research methodology of the empirical investigation, the measuring instruments as well as the selection criteria used in this study are going to be listed. A brief discussion of the ethical aspects of the study as well as the limitations to the study will also be given.

CHAPTER 3

Methodology

3.1 Introduction

In this chapter a discussion of the research methodology of the empirical investigation, the measuring instruments as well as the selection criteria used in this study were given. A brief discussion of the ethical aspects of the study will be given. The limitations to the study will also be listed.

3.2 Research objectives

The general and specific research objectives will be discussed for the literature review and empirical study:

3.2.1 General research objective

The general research objective was to determine the prescribing patterns of CCB medicine items during 2005 to 2008 in a section of the private health care sector of South Africa.

3.2.2 Specific research objectives

The research objectives consisted of two phases namely a literature review and an empirical investigation:

3.2.2.1 Phase 1: Literature review

The specific research objectives of the literature review included the following:

- To determine the general indications and possible future uses of CCB medicine products.
- To determine conditions for which the use of CCB medication is considered as the preferred therapy.
- To determine the possible uses of drug utilisation review (DUR), pharmaco-economic, pharmaco-epidemiology, prescribed daily dosages (PDD) and cost analysis with regard to CCB usage.

3.2.2.2 Phase 2: Empirical investigation

The specific research objectives of the empirical study included the following:

- To analyse the general prescribing patterns of CCBs and the identification of possible changes from 2005 to 2008.
- To determine the possible differences in the prescribing patterns between various age groups and genders of patients using CCBs.
- To determine the differences in the prescribing patterns of CCBs between general practitioners and specialists.
- To establish refill-adherence rates with regard to CCBs using data from a medicine claims database.
- To establish potential savings that could be generated by means of generic substitution of CCBs in the private health care sector of South Africa.

More is said about the empirical investigation in Chapter 4 of this study.

3.3 Research methodology

The research methodology will be discussed in terms of the research project and the different data sources used as set out below:

3.3.1 The research design

The research project can be classified as a retrospective quantitative DUR where the drug therapy is reviewed after the patients had received their medication. Retrospective databases serve as a rich source of information on patient medication behaviours in a real-world setting and could provide important information regarding compliance with their hypertension medication (Halpern *et al.,* 2006:1046).

A retrospective drug review may detect patterns in prescribing, dispensing or administering of medicine to prevent the recurrence of inappropriate use (Webber, 1999:3). More comprehensive retrospective data would be needed, e.g. data including blood pressure measurements. These data are important for assessing the relationships among medication choices, patient behaviour and clinical outcomes (Halpern *et al.,* 2006:1046). DUR as a research information instrument, providing information to improve medication usage, was discussed in Section 2.7.

The prescribing patterns of CCBs in a section of the private health care system will be investigated. The cost minimisations that can be achieved by generic substitution will also receive attention.

3.3.2 Data Source

The data used in this study were obtained from a medicine claims database of a PBM company for the study years 1 January 2005 to 31 December 2008 in South Africa. This company manages the benefits of a group of medical aids of South Africa by providing a real-time auditing process for patients to claim medication and services needed from pharmacies, hospitals and other health practices.

3.3.3 Study population of this study

The study population consisted of the total medicine database, cardiovascular medicine section and CCB medicine section (Snyman, 2009:103) from 1 Jan 2005 to 31 Dec 2008 as expressed in Table 3.1 below:

Table 3.1: Study population

	Year	Total number of patients	Total number of Rx	Total number of medicine items	Total cost of items (R)
Total medicine database	2005	1 509 621	8 391 836	19 500 774	1 819 865 251.63
	2006	1 558 090	8 906 348	21 113 422	1 959 738 734.09
	2007	1 178 596	7 911 096	19 075 724	1 918 284 176.66
	2008	974 497	6 775 873	16 439 253	1 785 871 013.85
Cardiovascular medicine	2005	242 264	1776415	2 635 003	355 307 457.65
	2006	250 084	1930850	2 915 092	380 646 597.78
	2007	210 720	1799149	2 766 553	368 164 055.53
	2008	198 847	1709718	2 669 759	342 565 308.41
CCB medicine	2005	49 148	315 434	318 258	44 665 330.42
	2006	54 778	367 403	370 460	49 947 392.72
	2007	50 573	362 902	366 049	51 419 051.20
	2008	50 601	364 511	367 437	48 645 226.29

3.3.4 Data analysis

Data analysis was done by using the Statistical Analysis System (SAS) and tables and graphs have been compiled by using Excel®.

3.3.5 Measuring instruments

The following measuring instruments were used in this study:

3.3.5.1 Prevalence

Prevalence according to Waning and Montagne (2001:20) was defined as the number of existing cases of a specific illness in a defined population in a specific time period. In this study, prevalence was used to indicate the number of medicine items or prescriptions claimed during a specific time period as recorded on a database of a PBM.

Prevalence was used throughout chapter 4 to indicate the study population, prescriptions issued and items dispensed.

3.3.5.2 Cost

Oxford Dictionaries (2010) defined cost as an amount that has to be paid or spent to buy or obtain something. For the purpose of this study the total cost of medicine items was divided into:

- Medical aid contribution: the part of the item's price the medical aid paid.
- Member contribution: so-called co-payment the member paid on the price of an item.

The following equations were used to evaluate cost:

3.3.5.3 Cost saving

For the purpose of this study cost saving can be seen as the cost of medicine that can potentially be saved if medicine items (e.g. innovator) are substituted for other medicine items containing the same active ingredient and the same strength (e.g. generic) as required by MCC (2003:3).

In this study cost savings were calculated for the following hypothetical scenario:

- If 100% of the innovator products were substituted for the other generic products on the database for the years available on the South African market.

The hypothetical cost was calculated as if all the innovators were substituted with all available generic equivalents, using the equation as follows:

$$Hypothetical\ cost = (number\ of\ inovator\ items) \times (average\ cost\ per\ generic\ item)$$

The hypothetical cost is then used to calculate potential cost savings. Cost savings were calculated by using the following equation:

$$Cost\ saving = (total\ cost\ of\ innovator) - (hypothetical\ cost)$$

Cost savings are also expressed as percentages of potential saving. The cost saving percentage is done by using the following equation:

$$Cost\ saving\ \% = \frac{cost\ saving}{total\ cost\ of\ innovator} \times 100$$

Cost saving of products of the same active ingredient, strength and formulation (e.g. sustained release formulations) was calculated, however, cost saving was not calculated where the innovator was less expensive than the generic, where there are no generics on the market. Generic substitution of extended/sustained release formulations containing the pharmacological active ingredient nifedipine were not allowed from December 2003 (MCC, 2003:3). In April 2010 a revised List of non-substitutable medication were released and the extended/sustained release nifedipine containing formulations were not listed anymore (MCC, 2010:2).

This study was done on data from 1 Jan 2005 to 31 Dec 2008. In that time extended/sustained release nifedipine containing formulations were on the List of non-substitutable medication (MCC, 2003:3) and generic substitution in this study was done from that viewpoint. No generic substitutions were done on extended/sustained release formulations containing the pharmacological active ingredient nifedipine.

3.3.5.4 Cost prevalence index (CPI)

The cost prevalence index shows the relationship between the cost and prevalence of specific items and the CPI is used to investigate drug utilisation patterns (Serfontein, 1989: 180).

$$CPI = \frac{cost\ \%}{prevalence\ \%}$$

Where:

CPI = cost prevalence index

Cost (%) = percentage of cost calculated by dividing the evaluated cost by the total cost in that section.

Prevalence (%) = percentage of prevalence calculated by dividing the evaluated prevalence by the total prevalence in that section.

Interpretation:

- CPI < 1: The items evaluated are relatively inexpensive.
- CPI = 1: There is a balance between the cost and prevalence of the specific item evaluated.
- CPI > 1: The items evaluated are relatively expensive (Serfontein, 1989:180).

The CPI was used in the empirical investigation section and is used to determine the expensiveness of a specific item or items relative to the number of items prescribed.

3.3.5.5 Medicine refill-adherence rate

In this study compliance was calculated by refill adherence of the patients on the database, by calculating the percentage of days for which patients received medication. The calculated refill-adherence rates assisted the researcher in this study to evaluate whether patients using CCB items were adherent to their medicinal regimens, as suggested by Bester and Hammann (2007:20) as well as Serfontein (2010).

The refill-adherence rate of an individual of a CCB medicine item (trade name) was calculated by using the following equation:

$$Refill - adherence\ rate = \frac{(total\ days\ supplied) - (days\ supplied\ of\ the\ last\ Rx)}{days\ between\ refills}$$

The data analysed for a refill-adherence rate will be divided into three groups as indicated below:

1	Unacceptable low adherence rate	< 80% refill-adherence rate
2	Acceptable adherence rate	>80% ≤ 120% refill-adherence rate
3	Unacceptable high adherence rate	>120% refill-adherence rate

Adherent patients would be those patients with refill-adherence rates of 80% ≤ 120% (Bester & Hammann, 2007:20) and will be categorised into group 2. A number of 13 prescription fills in a 365 day year could be seen as 100% complient (Serfontein, 2010).

Improved compliance according to Bester and Hammann (2007:18) may result in

- better disease control;
- satisfaction with therapy by patient as well as physician; and
- an increase in medicine expenditure with an associated decrease in overall health care costs.

The CCB medicine should have been dispensed more than once for a specific patient before it could be used in the refill-adherence rate equation. Below follows a diagram to indicate the number of medicine items that was used to calculate the refill-adherence rates from 2005 to 2008:

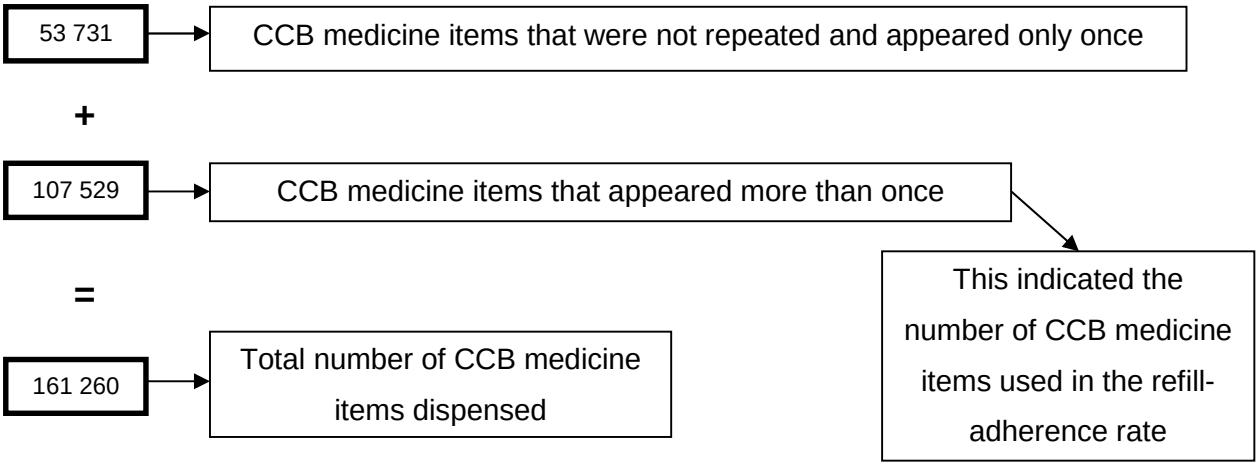


Figure 3.1: The number of medicine items used to calculate the refill-adherence rates

The cost implications of the refill-adherence rate of CCB medicine items were evaluated by means of the following equation:

$$Final\ cost = (total\ cost\ of\ CCB\ medicine\ items) - (cost\ of\ CCB\ medicine\ item\ of\ the\ last\ refill)$$

Total cost of CCB medicine items indicated the total cost of all the CCB medicine items received during the study period, calculated as follows:

Cost of CCB medicine item received + Cost of CCB medicine item received on the 1st repeat + Cost of CCB medicine item received on the 2nd repeat + Cost of CCB medicine item received on the 3rd repeat + … *n* repeat, where *n* indicates the number of repeated refills.

The total days supplied indicated the total days an individual patient had been supplied with an individual CCB medicine item. Below follows the total days supplied criteria as used during the study:

Total days supplied categories	Total days supplied of medication
1	≤ 60 days
2	> 60≤ 90 days
3	> 90≤ 120 days
4	> 120≤ 180 days
5	> 180≤ 360 days
6	> 360≤ 720 days
7	> 720≤ 1080 days
8	>1080 days

It should be noted that one should have received a CCB medicine item more than once to be included in the refill-adherence rate study. The total days supplied is a part of the refill-adherence rate.

Total days supplied category 1 was that the item had been used for more than 30 days (at least repeated once as specified above) but not yet 60 days. Those items used for 30 days longer than specified in category 1 were categorised in category 2.

A prescriber cannot write out a prescription for a medicine item for longer than six months and items used for more than 180 days (approximately six months) could be seen as items repeated on a second repeatable prescription. These items were categorised in category 5.

Items used for more than 360 days (approximately one year) but not yet two years were found in category 6, whilst category 7 presented the usage of CCB medicine items between two to three years. Category 8 included all items used for longer than 1080 days (approximately 3 years).

3.3.6 Selection criteria for the study

In this section the criteria of the data received from the pharmacy benefit management company (PBM) will be discussed.

3.3.6.1 Year division

The data used in this study ranged over four years and were divided as per year of submission. The years used in this study were specified as followed:

- 1 January to 31 December **2005**
- 1 January to 31 December **2006**
- 1 January to 31 December **2007**
- 1 January to 31 December **2008**

3.3.6.2 Age group for study purposes

In this study the age of a patient was determined from the date of birth of the specific patient whose medication had been dispensed. The age of patients was calculated on the first day of the next year of which a medicine item had been dispensed.

Age group	Patient age
Age group 1	≤ 15 years
Age group 2	>15 ≤25 years
Age group 3	>25 ≤35 years
Age group 4	>35 ≤45 years
Age group 5	>45 ≤55 years
Age group 6	>55 ≤65 years
Age group 7	>65 years

For the purpose of the study the age groups were used according to the division of the South Africa Demographic and Health Survey (2003a:23). An additional group was added of patients younger than 15 years of age.

3.3.6.3 Division of gender groups

For the purpose of the study, patients who received items or prescriptions were divided into male and female patients. In 2005, 2006 and 2007 there were patients on the database of unspecified gender. These patients were classified as unknown and were excluded from further usage and cost analysis. The three gender groups were:

- Female.
- Male.
- Unknown.

Members were divided into genders by the PBM and had not been altered in any way.

3.3.6.4 Prescribers as providers of medication

Prescribers included in this study were divided into the following:

- Cardiologists.
- General practitioners (GP).
- Paediatricians.
- Group specialists.
- Thoracic Surgery.
- Other.

Prescribers were classified into the groups specified above by the PBM and were not altered in any way.

3.3.6.5 Classification of medication used in this study

Medicine items were classified according to the following:

3.3.6.5.1 MIMS® classification

The Monthly index of medical specialities® (MIMS®) classification (Snyman, 2009:103) was used to separate all the drugs used in all cardiovascular diseases and included the MIMS® group 7 and will be referred to as the cardiovascular section throughout the study.

The CCBs were extracted from the medicine claims database for the years 2005 to 2008. As seen in Section 2.2, CCBs are used as anti-anginal as well as antihypertensive treatment regimens (Donald & Warkentin., 2009:1; Snyman, 2009:103) and both groups were included in the study. This refers to groups 7.3.7 (CCBs in hypertensive patients) and 7.4.1 (CCBs in anginal patients) of the MIMS® classification (Snyman, 2009:103). Medicines in these groups

include nifedipine, amlodipine, israpidine, felodipine, lercanidipine, verapamil and diltiazem (Snyman, 2009:103).

3.3.6.5.2 NAPPI codes

National Pharmaceutical Product Interface (NAPPI) codes of individual items were used to identify the specific item (Snyman, 2009:103). The use of specific items could be identified in usage evaluations.

3.3.6.5.3 Pharmacological active ingredients

CCB products were also classified by the pharmacological active ingredients the products contain. The CCB pharmacological active ingredients (Snyman, 2009:103) include the following:

- Nifedipine.
- Amlodipine.
- Israpidine.
- Felodipine.
- Lercanidipine.
- Verapamil.
- Diltiazem.

3.3.6.5.4 Generic status classification

The pharmacy benefit management company (PBM) divided the medicine items by the nature of the products' generic status as is shown below:

- **Rights Given:** This term was given to all the medication generics of original items of which the patents had not yet expired but rights were given to the generic company by the patent holder to produce the item.
- **No generic:** This term referred to original items still patented or where there were no generics available on the South African market.
- **Original:** This term referred to original (innovator) items of which there were generic products available on the South African market.
- **Generic:** This term referred to an equivalent of the original item, consisting of the same pharmacological active ingredient of the same strength as the original product.

The generic status classification of medicine items was used in Section 4.4 and it was used as it had been received from the PBM and was not altered in any way.

3.3.6.6 Medical scheme benefit options

The groups of CCBs were divided into the different medicine benefit options as classified on the pharmacy benefit management company's (PBM) database. The different benefit options recorded were:

- **PMB:** item indicated for a condition on the list of PMBs.
- **Chronic:** item used for a registered chronic condition.
- **Acute:** item paid out of the day to day funds, used for short-term treatments.
- **Oncology:** item used associated with cancer treatment.
- **OTC:** over the counter medication.
- **Other**

The medicine items analysed were categorised in the medicine benefit options as listed above by the PBM. This classification was used in this study and no alterations were done on the data with regard to the medicine benefit options.

3.3.7 Statistical analysis

In the empirical investigation various statistical equations and methods were used for data analysis. A short discussion of each method will follow.

3.3.7.1 Arithmetic mean

Arithmetic mean is also known as the average. It is defined as taking the sum of the observations divided by the number of observations (Banerjee, 2003:3; Bland, 2004:59).

The arithmetic mean was calculated as follows:

$$\bar{x} = \frac{\Sigma x}{n}$$

Where:

$\bar{x}$= arithmetic mean

x = value in the data set

Σ = the sum

n = number of observations

The arithmetic mean was used in the empirical chapter and referred to as average e.g. average cost and average number of items on the prescription.

3.3.7.2 Standard deviation

It is defined as the square root of all variance (Banerjee, 2003:5; Bland, 2004:62). It is a measure of the spread of data and shows how the data differ from the average. A small standard deviation shows data are clustered relatively near the mean. A larger standard of deviation shows that the data differ substantially from the average calculated (Banerjee, 2003:5).

The standard deviation was calculated as follows:

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

Where:

s = standard deviation

x = value in the data set

$\bar{x}$= arithmetic mean

n = number of observations

This equation was used wherever the average was calculated to show the spread of data from the average e.g. the distribution of data around average cost as well as around average items per prescriptions. Standard deviation will be abbreviated as SD.

3.3.7.3 Effect size

Also known as the *d*-value and Cohen's d effect size (Statistics Solution, 2009) and was defined (Cohen, 1988:3 Murphy & Myors, 2004:10) as the degree to which a certain event or phenomenon is present in a study population.

The effect size was calculated as follows:

$$d = \frac{\overline{x_a} - \overline{x_b}}{s_{max}}$$

Where:

d = effect size

$\overline{x_a}$ = average medicine treatment value of *a*

$\overline{x_b}$ = average medicine treatment value of *b*

s_{max} = highest standard deviation of *a* and *b* from the data

Interpretation

If *d* = 0.2: The phenomenon is small or unobservable.

If *d* = 0.5: The phenomenon is of medium effect and observable

If *d* = 0.8: The phenomenon is of high effect and of high practical importance (Cohen, 1988:25)

It is important to know that the terms 'small', 'medium' and 'high' effect sizes are relative and should be used in context of the data examined (Cohen, 1988:25). The effect sizes were calculated in the empirical investigation section and were used to show the relative importance in the difference of items e.g. difference between innovators and generic medications.

3.4 Validity and reliability of research instruments

The data used in this study were directly obtained from a PBM medicine claims database. The data were not changed in any way by the researcher and all research was done from the viewpoint that all data received were correct and accurate.

3.5 Study limitations

Primary or secondary hypertension or the cause thereof was not investigated in this study and neither was the external environment of the patients taking CCBs or other cardiovascular drugs.

The reasons for the use of original instead of generic products will not be possible to determine from the data source used in this study.

In 2005, 2006 and 2007 there were patients on the database of unspecified gender. These patients were classified as unknown gender and excluded from further usage and cost analysis.

It was assumed that the usage of medicine items and the classifications made by the PBM was done correctly.

The true refill adherence of a patient could not be evaluated in this study. It was only observed that the patient had received his/her medication to last him/her for a specified time period. The actual usages of these medicine items were not evaluated. A physical pill count was not done.

3.6 Ethical aspects

No specific details could be identified such as patient, exact medical practice, pharmacy or medical scheme. Confidentiality was maintained throughout the study. To ensure confidentiality each prescription record was provided with a unique number for each patient, prescription, medical aid, health provider and pharmacy. This would ensure the anonymity of patient throughout the study. To ensure the anonymity of prescribers in this study, only the type of prescriber (Section 3.3.6.4).

Approval from the PBM was given to use the database for the study. The study was approved by the North-West University Ethical Committee as a sub-project within the ‘Investigation of medicine usage patterns in a section of the private health care sector utilising data from a Pharmaceutical Benefit Management (PBM) in South Africa’ project (NWU-0046-08-S5).

The PBM's name was not reflected in this study, nor medical aids contracted by this PBM, ensuring anonymity of the source of data.

3.7 Chapter summary

This chapter focused on a discussion of the research methodology of the empirical investigation, the measuring instruments as well as the selection criteria used in this study. The limitations to the study were also listed.

In the next chapter (Chapter 4) the results and discussion of the empirical investigation of this study will be documented.

CHAPTER 4

Results and Discussion

4.1 Introduction

In this chapter the results of the empirical investigation with regard to the prescribing patterns and cost of CCB medicine items from 1 January 2005 to 31 December 2008, received from a medicine claims database were analysed and tabulated.

Prescribing patterns were evaluated according to general patient's patterns, age, gender and different prescribers. Classification according to the MIMS® (Snyman, 2009:103) was used to identify the group of medication and trade names to be analysed.

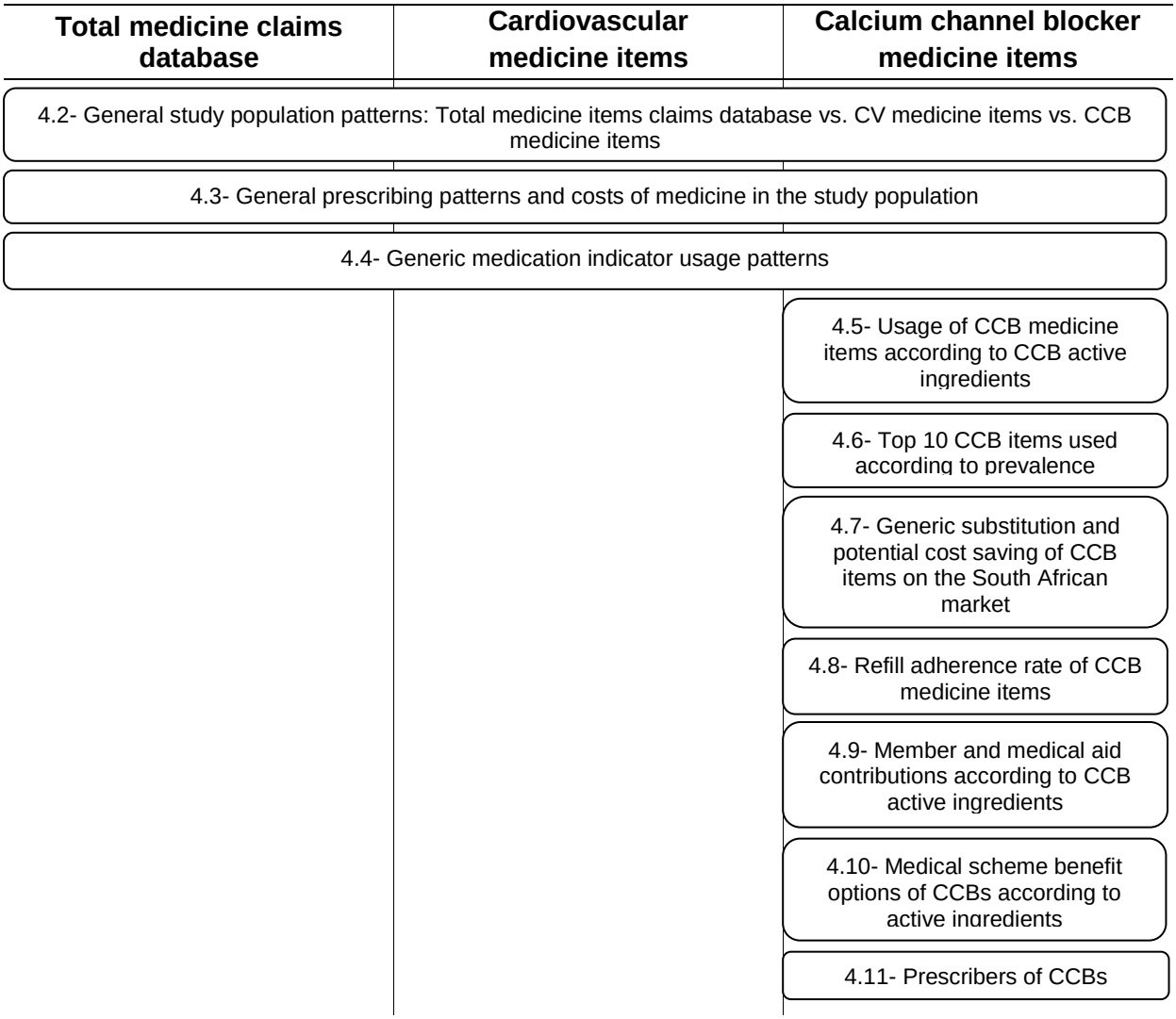
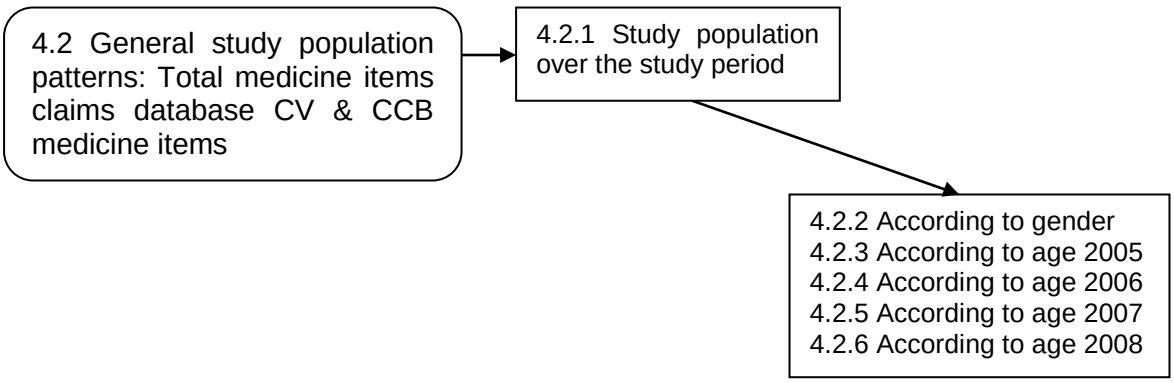


Figure 4.1: Algorithm of the research presented in the thesis

4.2 General study population patterns: Total medicine items claims database vs. CV medicine items vs. CCB medicine items

In this section the total database as received from the PBM was compared to the CV medicine group and the CCB usage according to MIMS® classification (Snyman, 2009:103) in each year from 1 January 2005 to 31 December 2008.



4.2.1 Study population over the total study period

Figure 4.2 was adapted from Table 4.6 and shows the total number of patients on the total database, the total number of patients who received CV medicine items as well as CCBs from 1 Jan 2005 to 31 Dec 2008.

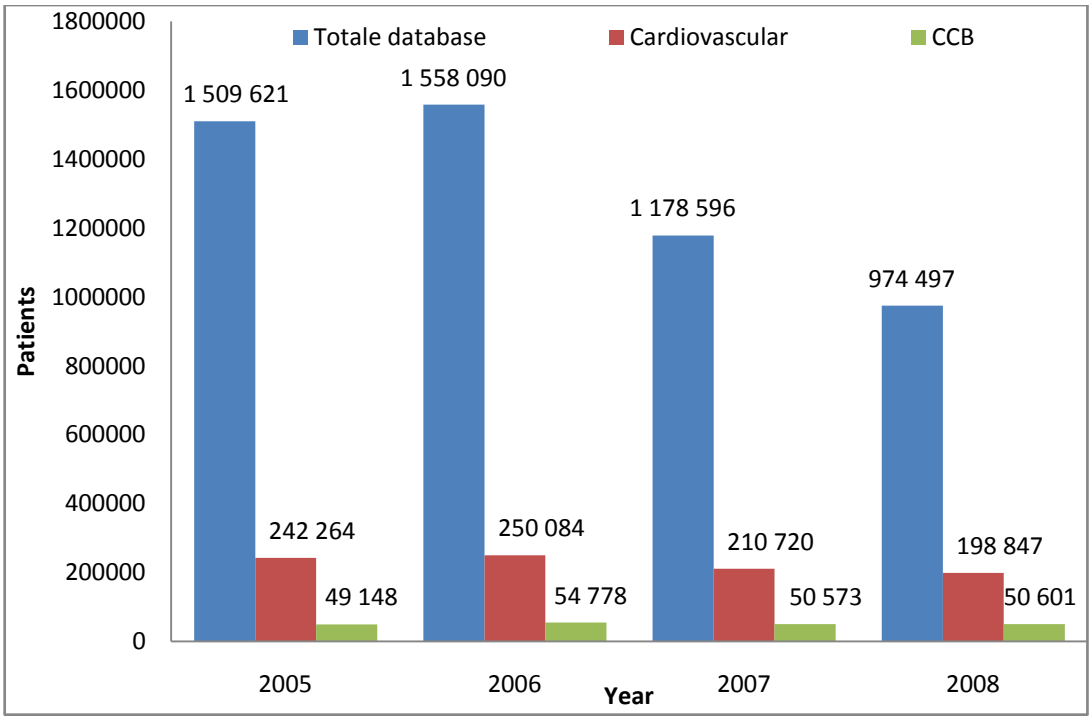


Figure 4.2: Total number of patients on the total database, those who received CV medicine items and those who received CCBs

The number of patients on the total database increased from the year 2005 to 2006 where it peaked and then decreased towards 2008. The number of patients who received CV medicine items and patients who received CCB medicine items showed the same general patterns as seen in the total database. However, the percentage of patients who received a CV item as well as the percentage of patients who received CCB medicine items increased from 2005 to 2008 as seen in Table 4.6.

During the study period the following with regard to the study population and medicine usage could be noted:

- In 2005 16.05% of all the patients on the database used a CV item and 3.26% of the total number of patients on the database used a CCB.
- In 2006 the number of patients increased and it was noted that the percentage of patients using a CV item remained unchanged while the percentage of patients using a CCB increased slightly to 3.52%.
- In 2007 17.88% of the patients on the medicine claims database used a CV item and 4.29% used a CCB.
- The percentage of patients using a CV item increased to 20.41% in 2008 and 5.19% of the patients used a CCB. From these percentages an increase in the use of CV items as well as in CCBs could be observed from 2005 to 2008. These percentages are presented in Table 4.6.

Although outside the scope of this study the decline in the total number of medical aid members was noted. Some of the reasons may have to do with some of the medical aids changing their administrators and/or members resigning from the medical aids.

4.2.2 Study population according to gender

Figure 4.3 was adapted from Table 4.8 and shows the total number of patients on the medicine claims database according to gender groups from 1 Jan 2005 to 31 Dec 2008.

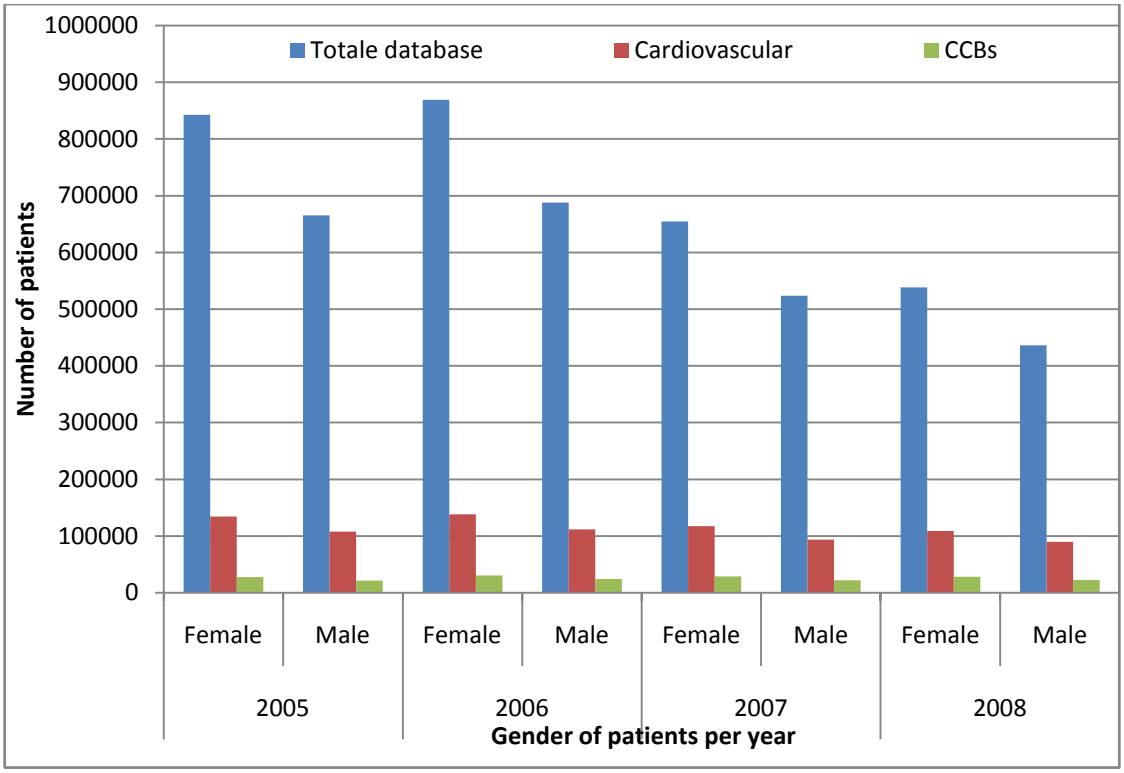


Figure 4.3: Study population patterns according to gender from 2005 to 2008

From Figure 4.3 it was seen that there were more female than male patients every year of the study period. A larger number of female patients than male patients used either a CV item or a CCB item than male patients.

- It was also noted that in 2005 15.97% (n = 134 538) of the female patients and 16.16% (n = 107 557) of the male patients on the medicine claims database used a CV item.
- In 2006 15.88% (n = 138 006) of female patients and 16.27% (n = 111 945) of male patients used a CV item.
- It was found that 17.91% (n= 117 210) of female patients and 17.84% (n = 93 444) of male patients on the medicine claims database used a CV item in 2007, and in 2008 the percentages increased to 20.24% (n = 932 970) of female patients and 20.61% (n = 89 888) of male patients.

A general increase was seen in the percentage of CCB medicine usage across the study period.

- In 2005 3.29% (n = 27 746) of female patients and 3.21% (n = 21 379) of male patients on the medicine claims database used a CCB.
- It was seen that 3.49% (n = 30 739) of female patients and 3.54% (n = 24 016) of male patients used a CCB in 2006.
- In 2007 the percentages of CCB usages increased to 4.38% (n = 28 692) of female patients and 4.17% (n = 21 865) in male patients.
- In 2008 it was recorded that 5.21% (n = 28 064) of female patients and 5.17% (n = 22 537) of male patients used a CCB.

Although the number of patients on the total database decreased from 2005 to 2008, the percentage of patients using CV items or CCB medicine items showed an increasing trend from 2005 to 2008.

4.2.3 Study population according to age groups

The study population was analysed according to the age groups, as discussed in Section 3.3.6.2, for each of the study years. The seven age groups are as follows:

Age group	Patient age
Age group 1	≤ 15 years
Age group 2	>15 ≤25 years
Age group 3	>25 ≤35 years
Age group 4	>35 ≤45 years
Age group 5	>45 ≤55 years
Age group 6	>55 ≤65 years
Age group 7	>65 years

Due to the nature of the age classification the analysis was presented and discussed per year because a graph of the seven age groups across all four of the studied years combined would be too complex, unreadable and possibly confusing. A table of summary would conclude the usage of CCB medicine items according to the classified age groups for the study period.

4.2.3.1 Study population according to age groups in 2005

Figure 4.4 and Table 4.1 were adapted from the data of Table 4.9 and show the patient distribution of the study population of 2005 across the different age groups.

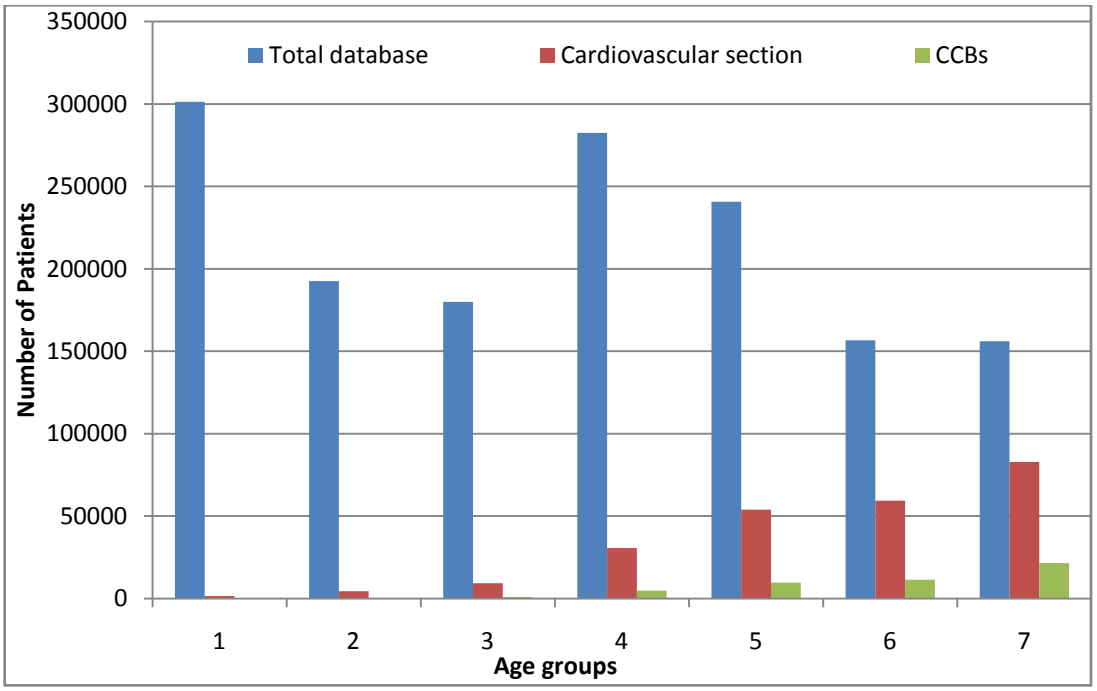


Figure 4.4: Study population according to different age groups for 2005

The total database for 2005 showed a peak in number of patients at age groups 1, 4 and 5 and the number of patients receiving CV and CCB items increased with age.

Table 4.1: Study population according to different age groups for 2005

Year	Age groups	Total database patients	Patients using CV medicine items	Patients using CCB medicine items	% Patient distribution	% Patients using a CV item	% Patients using a CCB
2005	1	301 254	1 626	106	19.96%	0.54%	0.04%
	2	192 653	4 402	251	12.76%	2.28%	0.13%
	3	179 932	9 378	1 057	11.92%	5.21%	0.59%
	4	282 378	30 678	4 871	18.71%	10.86%	1.72%
	5	240 701	53 898	9 731	15.94%	22.39%	4.04%
	6	156 636	59 321	11 557	10.38%	37.87%	7.38%
	7	156 067	82 961	21 575	10.34%	53.16%	13.82%

From the study populations of 2005 shown in Figure 4.4 and Table 4.1 the following could be gathered:

- Approximately 20% (19.96%; n = 301 254) of patients on the total database was in the ages ≤ 15 years of age.
- The number of patients decreased gradually from age group 1 to age group 2 (> 15 ≤ 25 years) (n = 192 653) and increased again in the age group of patients aged > 35 ≤ 45 years (n = 179 932).
- An increase could be seen in the age group > 45 ≤ 55 years (n = 282 378) but decreased gradually to 156 067 patients in the age group of patients older than 65 years, which represented only 10.34% of patients on the medicine claims database for 2005.
- The number of patients using any CV medication increased as their age increased.
- Analysis showed that 1 626 (0.54%) patients ≤ 15 years used at least one CV drug (0.54%).
- It was found that 30 678 (10.86%) patients used a CV item in the age group > 35 ≤ 45 years of age, 4 871 of them using CCBs.
- It should be noted that patients older than 65 represent 10% of all patients in the total database.
- Most of the patients in the CV medicine section (n = 82 961 or 53.16%) as well as in the CCB medicine section (n = 21 575 or 13.82%) could be found in the age group of patients above 65 years of age.

4.2.3.2 Study population according to age groups in 2006

Figure 4.5 and Table 4.2 were adapted from the data of Table 4.9 and show the patient distribution of the study population of 2006 across the different age groups.

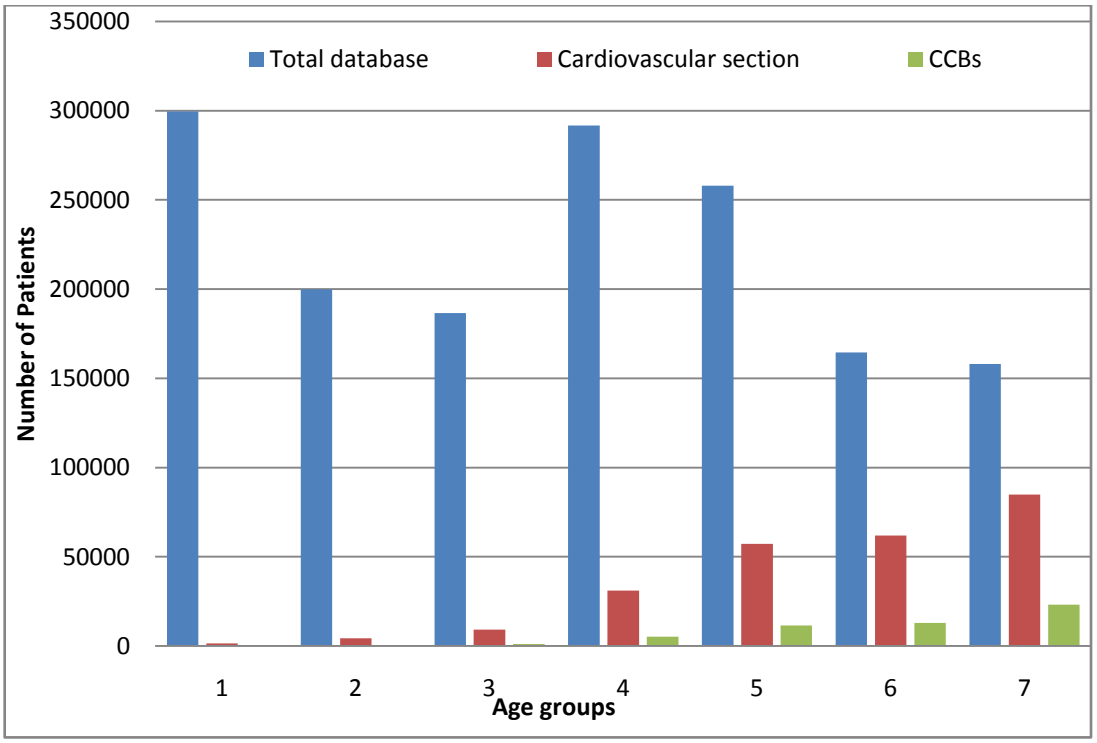


Figure 4.5: Study population patterns according to different age groups for 2006

The total database for 2006 showed the same results as seen in 2005. A peak in the number of patients at age groups 1, 4 and 5 occurred and the number of patients receiving CV and CCB patients increased with age.

Table 4.2: Study population according to different age groups for 2006

Year	Age groups	Total database patients	Patients using CV medicine items	Patients using CCB medicine items	% Patient distribution	% Patients using a CV item	% Patients using a CCB
2006	1	299 627	1 405	107	19.23%	0.47%	0.04%
	2	199 815	4 334	292	12.82%	2.17%	0.15%
	3	186 555	9 147	1 135	11.97%	4.90%	0.61%
	4	291 764	31 125	5 352	18.73%	10.67%	1.83%
	5	257 886	57 211	11 652	16.55%	22.18%	4.52%
	6	164 449	61 926	12 957	10.55%	37.66%	7.88%
	7	157 994	84 936	23 283	10.14%	53.76%	14.74%

From the study populations of 2006 shown in Figure 4.5 and Table 4.2 could be observed:

- Patients in the age group younger than 15 years of age had the highest number of patients (n = 299 627) and represented 19.23% of the total patients on the database.
- The results revealed that 1405 of those patients (0.47%) used a CV product. Of these 1 405 patients, only 107 used a CCB medicine item.
- These 106 patients represented only 0.04% of the total patients in the age group 15 years and younger on the PBM database.
- A total number of 199 815 patients > 15 ≤ 25 years of age were found on the total database. It was seen that 2.17% (n = 4 334) of them used a CV drug of which 292 (0.15%) used CCBs.
- From this point another decrease in the patients in the age group > 25 ≤ 35 years could be seen, consisting of 186 555 patients who represented an approximate 12% of the total number of patients on the PBM database of 2006.
- The age group of > 35 ≤ 45 years showed an increase in patients with 291 764 patients on the total database, 31 125 of them (10.67%) using at least one CV item.
- A number of 5 352 of patients between >35 ≤ 45 years used a CCB, accounting for 1.83% of patients in that specific age group.
- From this point the patients per age group seemed to be decreasing. There were 257 886 patients in the age group >45 ≤ 55 years, and approximate 22.2% (n = 57 211) of them used a CV product in that year and 11 652 of them (4.52%) used a CCB in 2006.
- The total patients declined once more in the age group of patients between > 55 ≤ 65 years (n = 164 449) and 61 926 of them used a CV product (37.66%) and 12 957 used a CCB (7.88%) in 2006.
- Patients over 65 years formed the smallest age group on the total medicine claims database in 2006 (n = 157 994) but presented with the largest percentage of CV medication (n = 84 936) and CCB (n = 23 283) users in 2006. It was noticed that 53.76% of patients older than 65 years used a CV item in 2006 and 14.74% of them used a CCB.

4.2.3.3 Study population according to age groups in 2007

Figure 4.6 and Table 4.3 were adapted from the data of Table 4.9 and show the patient distribution of the study population of 2007 across the different age groups.

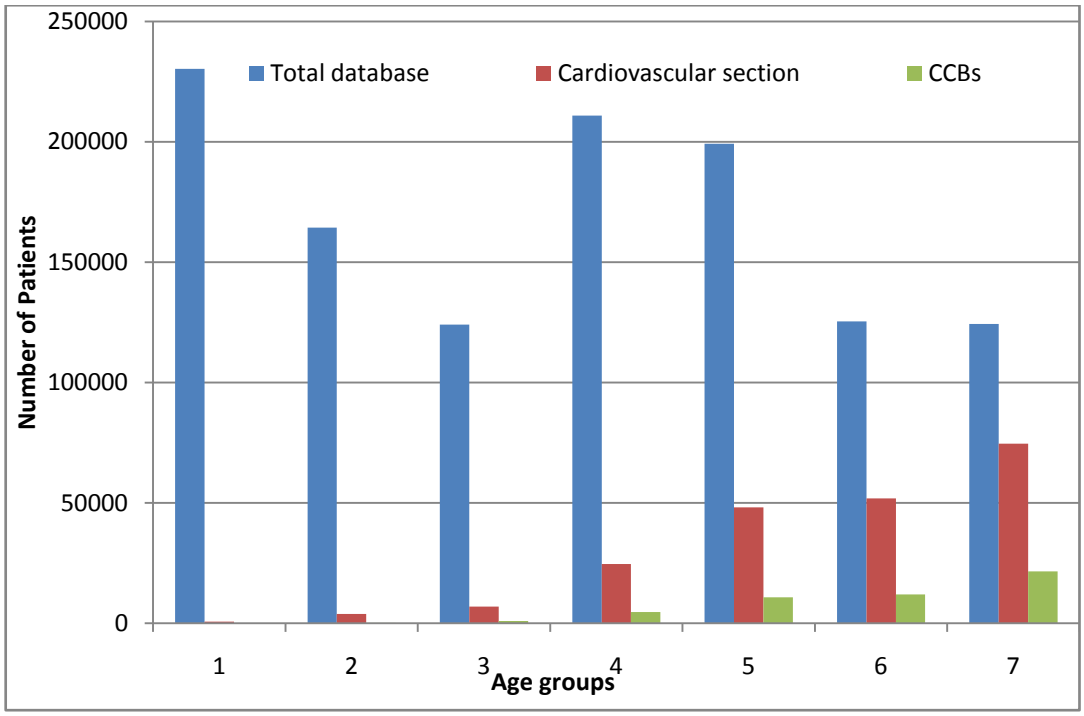


Figure 4.6: Study population patterns according to different age groups for 2007

As seen in the analyses of 2005 and 2006, the total database for 2007 showed a peak in the number of patients in age groups 1, 4 and 5 and the number of patients receiving CVs and CCBs increased with age.

Table 4.3: Study population according to different age groups for 2007

Year	Age groups	Total database patients	Patients using CV medicine items	Patients using CCB medicine items	% Patient distribution	% Patients using a CV item	% Patients using a CCB
2007	1	230 310	727	79	19.54%	0.32%	0.03%
	2	164 362	3 810	265	13.95%	2.32%	0.16%
	3	124 016	6 944	1 025	10.52%	5.60%	0.83%
	4	210 924	24 556	4 727	17.90%	11.64%	2.24%
	5	199 235	48 134	10 806	16.90%	24.16%	5.42%
	6	125 456	51 905	12 036	10.64%	41.37%	9.59%
	7	124 293	74 644	21 635	10.55%	60.05%	17.41%

The results from Table 4.6 indicated a decline of 22% in the total number of patients during 2007 in comparison with 2005. Table 4.3 showed the following:

- A number of 230 310 patients (19.54%) were found in the age group of patients below 15 years and 727 of them (0.32%) used a CV drug in 2007 and 0.03% (n = 79) of the total number of patients in this age group used a CCB.
- A decline in the number of patients > 15 ≤ 25 years (n = 164 362), as well as in patients > 25 ≤ 35 years (n = 124 016) could be noticed, but an increase in the number of CV patients (n = 3 810 and n = 6 944) and CCB patients (n = 265 and n = 1025) in this age group was seen from 2006 to 2007.
- There were 210 924 patients between ages of > 35 ≤ 45 years, representing 17.9% of the total number of patients on the medicine claims database for 2007, but decreased as the patient age groups advanced in age, with 199 235 patients between > 55 ≤ 65 years (10.64%) and 124 293 patients older than 65 years of age (10.55%).
- The number of CV and CCB patients increased as the age of patients increased. There were 48 134 patients between > 45 ≤ 55 years (24.16%) and 74 644 patients older than 65 (60.05%) who used a CV drug in 2007.
- It was noticed that an approximate 9.6% of patients (n = 12 036) > 55 ≤ 65 years used a CCB in 2007.

4.2.3.4 Study population according to age groups in 2008

Figure 4.7 and Table 4.4 were adapted from the data of Table 4.9 and show the patient distribution of the study population of 2008 across the different age groups.

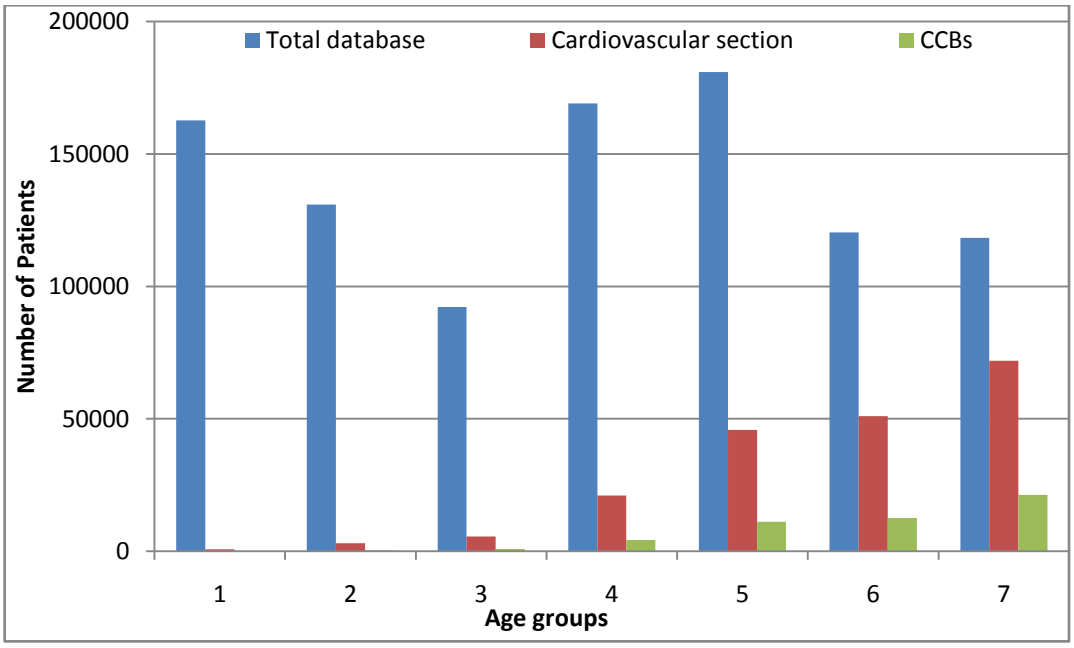


Figure 4.7: Study population patterns according to different age groups for 2008

Generally the total database for 2008 showed a peak at age groups 1, 4 and 5 and the number of patients receiving CV and CCB patients increased with age. For 2008 most of the patients on the total database were not recorded in age group 1 as in 2005, 2006 and 2007 but in age group 5 that included all patients between the ages > 45 ≤ 55 years. A decline in the number of patients over all age groups on the total database was noticed. This may indicate a change in the medical aid members' age distribution.

Table 4.4: Study population according to different age groups for 2008

Year	Age groups	Total database patients	Patients using CV medicine items	Patients using CCB medicine items	% Patient distribution	% Patients using a CV item	% Patients using a CCB
2008	1	162 675	695	59	16.69%	0.43%	0.04%
	2	130 924	2 969	256	13.44%	2.27%	0.20%
	3	92 253	5 525	892	9.47%	5.99%	0.97%
	4	169 024	21 077	4 345	17.34%	12.47%	2.57%
	5	180 878	45 787	11 210	18.56%	25.31%	6.20%
	6	120 417	50 944	12 565	12.36%	42.31%	10.43%
	7	118 326	71 850	21 274	12.14%	60.72%	17.98%

From Figure 4.7 and Table 4.4 was seen that:

- The total number of patients below the age of 15 years was 162 675 patients, representing 16.69% of the total number of patients on the medicine claims database for 2008. This was dramatically less for the same age groups for 2005, 2006 and 2007.
- It was seen that 0.43% (n = 695) of the patients below 15 years of age used a CV product and 59 patients (0.04%) used a CCB.
- The number of patients decreased in age group 2 (> 15 ≤ 25 years) and age group 3 (> 25 ≤ 35 years) but the number of patients using CV products (2.27% and 5.99% respectively) and CCBs (0.2% and 0.97% respectively) increased.
- A number of 169 024 patients (17.34%) could be seen in the age group > 35 ≤ 45 years of age and 2.57% of them used a CCB in 2007.
- The highest number of patients on the total database of 2008 was seen at the ages between > 45 ≤ 55 years (n = 180 878, 18.56%) but declined from there as the patient age increased to 118326 patients (12.14%) older than 65 years of age.
- It was observed that 25.3% of the patients in age group 5 (> 45 ≤ 55 years) used a CV item in 2008 (n = 45 787) and 11 210 of those products were CCB medicine items (6.2%).
- It was also seen that approximately 61% of patients older than 65 years used a CV item in 2008 (n = 71 850) and 21 274 of them used a CCB medicine item (17.98%).

Table 4.5 provides an overview of the prevalence of age, usage of CV and CCB medicine items across the study period. To conclude it was noted that the peak in the total database shifted from age group 1 (as in 2005, 2006 and 2007) to age group 5 and patients who used CV as well as CCBs increased as the ages of patients increased. This corresponds to a report by The American Heart Association (2010:17) which stated that the number of hypertension patients increased with increasing patient age.

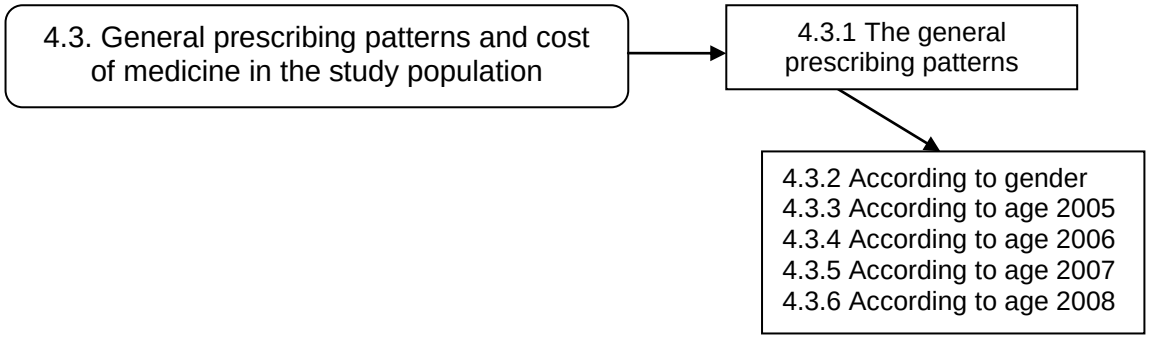
Table 4.5: Summary of the usage of CV and CCB medicine items according to age across the study period

Age groups	Year	Total database patients	Patients using CV medicine items	Patients using CCB medicine items	% Patient distribution	% Patients using a CV item	% Patients using a CCB
1	2005	301 254	1 626	106	19.96%	0.54%	0.04%
	2006	299 627	1 405	107	19.23%	0.47%	0.04%
	2007	230 310	727	79	19.54%	0.32%	0.03%
	2008	162 675	695	59	16.69%	0.43%	0.04%
2	2005	192 653	4 402	251	12.76%	2.28%	0.13%
	2006	199 815	4 334	292	12.82%	2.17%	0.15%
	2007	164 362	3 810	265	13.95%	2.32%	0.16%
	2008	130 924	2 969	256	13.44%	2.27%	0.20%
3	2005	179 932	9 378	1 057	11.92%	5.21%	0.59%
	2006	186 555	9 147	1 135	11.97%	4.90%	0.61%
	2007	124 016	6 944	1 025	10.52%	5.60%	0.83%
	2008	92 253	5 525	892	9.47%	5.99%	0.97%
4	2005	282 378	30 678	4 871	18.71%	10.86%	1.72%
	2006	291 764	31 125	5 352	18.73%	10.67%	1.83%
	2007	210 924	24 556	4 727	17.90%	11.64%	2.24%
	2008	169 024	21 077	4 345	17.34%	12.47%	2.57%
5	2005	240 701	53 898	9 731	15.94%	22.39%	4.04%
	2006	257 886	57 211	11 652	16.55%	22.18%	4.52%
	2007	199 235	48 134	10 806	16.90%	24.16%	5.42%
	2008	180 878	45 787	11 210	18.56%	25.31%	6.20%
6	2005	156 636	59 321	11 557	10.38%	37.87%	7.38%
	2006	164 449	61 926	12 957	10.55%	37.66%	7.88%
	2007	125 456	51 905	12 036	10.64%	41.37%	9.59%
	2008	120 417	50 944	12 565	12.36%	42.31%	10.43%
7	2005	156 067	82 961	21 575	10.34%	53.16%	13.82%
	2006	157 994	84 936	23 283	10.14%	53.76%	14.74%
	2007	124 293	74 644	21 635	10.55%	60.05%	17.41%
	2008	118 326	71 850	21 274	12.14%	60.72%	17.98%

A decrease in the total number of patients during the study period could be seen from Table 4.5. Table 4.5 also indicated the increase in the percentage of CV medicine items as well as CCB medicine items usage over the study period. It was observed that more than 50% of the patients older than 65 years used a cardiovascular item during the study period. This was also the age group with the largest percentage of CCB users during the study period

4.3 General prescribing patterns and costs of medicine in the study population

In this section the usage and cost of CCBs were compared to the total number of medicine items on the database as well as the total number of CV medication. This comparison was done by gender and age groups.



A number of patients, prescriptions, medicine items dispensed and associated costs were examined in the total database with regard to patients using CV medication and patients using CCBs for each year from 2005 to 2008. The average cost per prescription, the average cost per item as well as the average items per prescription were compared for each year. The cost prevalence index (CPI), as discussed in Section 3.3.5.4, was calculated for the total CV group of medication as well as for the group of CCBs for each year from 2005 to 2008.

4.3.1 General prescribing patterns

The total number of patients, prescriptions, medicine items and the cost of medication per year from 2005 to 2008 were analysed for the total database, the CV section as well as the CCB section. Percentages of CV and CCB medicine items were calculated as a percentage of the total medicine claims as presented on the database.

Table 4.6: The prevalence and cost of CVs and CCBs compared to all medication on the total database

	Year	Total patients	Total number Rx	Total number of medicine items	Total cost of medicine items (R)	Average cost per Rx* (R)	SD	Average cost per medicine item (R)	SD	Average number of medicine items per Rx*	SD	Percentage of total patients (%)	Percentage of total Rx* (%)	Percentage of total number items (%)	Percentage of total cost (%)	CPI
Total database	2005	1 509 621	8 391 836	19 500 774	1 819 865 251.63	216.86	342.30	93.32	166.36	2.32	1.52					
	2006	1 558 090	8 906 348	21 113 422	1 959 738 734.09	220.04	395.22	92.82	196.42	2.37	1.55					
	2007	1 178 596	7 911 096	19 075 724	1 918 284 176.66	242.48	600.31	100.56	324.11	2.41	1.59					
	2008	974 497	6 775 873	16 439 253	1 785 871 013.85	263.56	789.01	108.63	436.75	2.43	1.64					
Total CV section	2005	242 264	1 776 415	2 635 003	355 307 457.65	200.01	147.15	134.84	79.10	1.48	0.76	16.05%	21.17%	13.51%	19.52%	1.44
	2006	250 084	1 930 850	2 915 092	380 646 597.78	197.14	146.84	130.58	77.57	1.51	0.78	16.05%	21.68%	13.81%	19.42%	1.41
	2007	210 720	1 799 149	2 766 553	368 164 055.53	204.63	150.48	133.08	76.73	1.54	0.80	17.88%	22.74%	14.50%	19.19%	1.32
	2008	198 847	1 709 718	2 669 759	342 565 308.41	200.36	148.94	128.31	74.05	1.56	0.82	20.41%	25.23%	16.24%	19.18%	1.18
Total CCB section	2005	49 148	315 434	318 258	44 665 330.42	141.60	70.17	140.34	68.14	1.01	0.10	3.26%	3.76%	1.63%	2.45%	1.50
	2006	54 778	367 403	370 460	49 947 392.72	135.95	66.95	134.83	65.06	1.01	0.09	3.52%	4.13%	1.75%	2.55%	1.45
	2007	50 573	362 902	366 049	51 419 051.20	141.69	69.24	140.47	66.95	1.01	0.09	4.29%	4.59%	1.92%	2.68%	1.40
	2008	50 601	364 511	367 437	48 645 226.29	133.45	71.28	132.39	69.15	1.01	0.09	5.19%	5.38%	2.24%	2.72%	1.22

* Rx = prescription

The distribution of patients on the medicine claims database, patients using CV medicine items as well as patients using CCBs across the study period, were presented in Figure 4.2 of section 4.2.1. This patient distribution could also be seen from Table 4.6. From Table 4.6 the following were, *inter alia,* noted:

- The number of items dispensed and the total expenditure increased during 2006 with 8.27% and 7.69% respectively.
- From 2006 to 2008 the number of items dispensed and the total expenditure decreased to reach the lowest values of 16 439 253 items dispensed and an expenditure of nearly R 1 785.9 million in 2008.
- The average cost per prescription increased with 1.44% to R 220.04 (SD = R 395.22) from 2005 to 2006. An increase in the average cost per prescription of 9.26% to R 242.48 (SD = R 600.31) was seen from 2006 to 2007 and an increase of 8% to R 263.56 (SD = R 789.01) was seen from 2007 to 2008.
- This was in total a 17.72% increase in the average cost per prescription from 2005 to 2008. One of the reasons for the increase in the average cost per prescription could be because of a rise in the number of items per prescriptions issued.
- An increase of 4.22 % in the average number of items per prescription was seen from 2005 (2.32 SD = 1.52) to 2008 (2.43 SD = 1.64).
- The average cost per medicine item on the medicine claims database was R 93.32 (SD = R 166.36) for the year 2005. This average cost decreased slightly during 2006 to R 92.82 (SD = R 196.42) but increased by 8.34% in 2007 to R 100.56 (SD = R 324.11) and increased by another 8% in 2008 to an average of R 108.63 (SD = R 436.75) per medicine item. An average increase of 16.41% across the four-year study period had occurred.

In the CV section of Table 4.5 was seen that:

- In 2005, 21.17% (n = 1 776 415) of all prescriptions contained a CV item and 21.68% (n = 1 930 850) of prescriptions contained a CV item in 2006 and 22.74% (n = 1 799 149) of prescriptions in 2007 contained a CV item and 25.23% (n= 1 709 718) of prescriptions contained a CV item in 2008. This shows that almost a quarter of all prescriptions contained a CV medicine item during the study period.

- A number of 2 635 003 CV medicine items were issued in 2005. This accounted for 13.51% of all items dispensed in 2005.
- In 2006 the number of CV items increased to 13.81% (n = 2 915 092) of the total number of items dispensed in 2006 on the medicine claims database.
- An increase was also seen in 2007 and 2008 when 14.5% (n = 2 766 553) and 16.24% (n = 26 697 59) of all items dispensed were CV items.
- The average number of CV items per prescription was calculated at an average of 1.52 (SD = R 0.79) across the study period of 2005 to 2008.
- Even though not all CV items were used for hypertension it could be noted that an average of 1.52 (SD = R 0.79) items per prescription corresponds with Section 2.3.6 of this study which states that a combination therapy plan of treatment should be followed rather than a monotherapy approach.
- The average cost of a CV medicine item was R 134.84 (SD = R 79.10) in 2005. This was higher than the average cost of a medicine item on the total PBM database (R 93.32 SD = R 166.36). During 2006 the average cost of a CV item was R 130.58 (SD = R 77.57) which was 3.16% lower than in 2005.
- During 2007 the average cost per CV item increased with 1.91% to R 133.08 (SD = R 76.73) but from 2007 to 2008 the average cost per CV item decreased by 3.6% to R 128.31 (SD = R 74.05). Interesting enough in comparison with the total database where an increase of 16.41% in the average cost per medicine item was recorded a slight decrease of 4.84% was recorded in the average cost per CV medicine item during the four-year study period.
- The lower average cost could be because of the increased use of less expensive generic equivalents (Section 4.4.2).
- A CPI of 1.18 could be seen in the CV section of 2008, which shows a better value of medication as found in 2008 but still a result of a value more than one, indicating a relative expensive group of medication according to the definition as defined in Section 3.3.5.4. The lower CPI value could be because of an increased use of generic items in 2008 in comparison with 2005, 2006 and 2007 (Figure 4.9).

The CCB section of Table 4.5 showed the following:

- The percentage of CCB containing prescriptions increased annually from 2005 (3.76%) through to 2008 (5.38%) and the number of prescriptions containing a CCB item was the highest in 2006 (n = 367 403)
- During the study period CCBs accounted for 1.63% (n = 318 258) of the total medicine items dispensed in 2005, 1.75% (n = 370 460) of the total items dispensed in 2006, 1.92% (n = 366 049) of the total medicine items dispensed in 2007 and 2.24% (n = 367 437) of the total medicine items dispensed in 2008. This shows an increase in the usage of CCBs over time.
- The average cost per CCB item was more than the average cost of a CV item or the average cost of a medicine item on the total PBM database of any year during the study period.
- The average cost per CCB medicine item decreased by 3.93% from 2005 to 2006 (R 134.83 SD = R 65.06).
- In 2007 the average cost per CCB item was R 140.47 (SD = R 66.95) but this cost decreased by 5.75% during 2008 to R132.39 (SD = R 69.15) per item.
- Across the four-year study period a decrease of 5.66% in the average cost per CCB medicine item was recorded. This correlates well with the decrease recorded in the average cost of CV medicine items.
- The decrease in the average cost per CCB item seen in 2008 could be because of an increased use of more inexpensive generic equivalents (Figure 4.10).
- A CPI of above one as found in the CCB group of medication from 2005 to 2008 shows that this is a relatively expensive group of medication (Section 3.3.5.4). The CPI value of 1.22 in 2008 was the lowest during the study years and this could be because of an increased use of less expensive generic equivalents as seen in Figure 4.10.

Table 4.7: Aspects of cost changes in South Africa (percentages)

	General inflation rate in South Africa (Capital Professional Services, 2010)	Average change in the cost of medical items in South Africa (Healthcare Economist, 2008)	Percentage cost difference of the average cost per medicine item on the total database*	Percentage cost difference of the average cost per CV medicine item*	Percentage cost difference of the average cost per CCB medicine item*
2005	3.39%	4.3%			
2006	3.24%	3.6%	-0.54%	-3.16%	-3.93%
2007	2.85%	5.2%	8.34%	1.91%	4.19%
2008	3.85%	3.2 % (est.)	8.03%	-3.58%	-5.75%

* Values calculated from Table 4.6

The average cost per medicine item was calculated for the total PMB database, as well as the cost per medicine item of CV and CCB items and compared to the average change in costs of medical items and the general inflation of South Africa as specified by the two independent economic statistics published.

- It was seen that the average cost of a medicine item in 2006 was lower than in 2005 (Table 4.5) while the inflation was 3.24% (Capital Professional Services, 2010) and the cost of medicine should have been 3.6% more (HC Statistics, 2008).
- In 2006 the average cost of a CV item was 3.16% lower than in 2005 and the average cost of CCB items was almost 4% lower than in 2005.
- In 2007 a rise of 5.2% was recorded by HC Statistics (2008) in the average cost of medicine items. An increase of 8.34% was seen in the average cost per medicine item on the medicine claims database as well as a 1.91% increase in the average cost of CV items and a 4.19% increase in the average cost of CCB items.
- The inflation of South Africa was 3.85% during 2008 (Capital Professional Services, 2010) and an increase in the average cost of a CV item of 3.58% was seen. The average cost of a CCB item decreased by 5.75% during the year 2008. This could be because of an increased use of less expensive generic equivalents (Section 4.4). The change in CV or CCB average cost per item was less than the average change in cost of medical items for each year during the study period.

Note should be taken that the percentage change in the average cost of a medicine item from the medicine claims database was not for a specific item but the average cost of all items used

in a specific year. The patients who substituted their medicine items for a “cheaper” generic equivalent were included in the equations and these patients could have had an effect on the percentage of change in the average cost of an item.

4.3.2 General prescribing patterns according to gender

The total number of patients, prescriptions, items and the cost of medication per year from 2005 to 2008 were evaluated for the total database, the CV items as well as the CCB items according to gender (Section 3.3.6.3). Percentages were calculated for each gender as a percentage of the total database.

In the years 2005, 2006 and 2007 there were some patients whose gender were not specified on the database and these patients were indicated by the PBM database as unknown gender. This was also indicated as unknown gender in the tables of this section that follows:

Table 4.8: The prevalence and cost of CVs and CCBs compared to all medication on the total database according to gender

	Year	Gender	Total number of patients	Total number Rx*	Total number of medicine items dispensed	Total cost of medicine items dispensed (R)	Average cost per Rx* (R)	SD	Average cost per medicine item (R)	SD	Average number of medicine items per Rx*	SD	Percentage of total patients (%)	Percentage of total Rx* (%)	Percentage of total number of medicine items dispensed (%)	Percentage of total cost (%)	CPI
Total database	2005	Female	842 386	5036494	11 750 190	1 084 626 865.29	215.35	330.75	92.31	158.69	2.33	1.54					
		Male	665 505	3348219	7 734 461	733,769 633.85	219.15	358.17	94.87	176.88	2.31	1.47					
		Unknown	1 730	7123	16 123	1 468 752.49	206.20	622.31	91.10	329.67	2.26	1.37					
	2006	Female	868 891	5336202	12 699 707	1 162 254 536.29	217.81	380.43	91.52	188.12	2.38	1.58					
		Male	688 091	3565328	8 403 158	796 360 401.04	223.36	416.16	94.77	208.10	2.36	1.50					
		Unknown	1 108	4814	10 557	1 123 796.76	233.44	529.46	106.45	336.87	2.19	1.41					
	2007	Female	654 348	4754911	11 509 346	1 138 188 990.86	239.37	559.98	98.89	300.67	2.42	1.62					
		Male	523 841	3154355	7 562 466	779 508 488.81	247.12	656.34	103.08	356.74	2.40	1.55					
		Unknown	407	1818	3 912	586 696.99	322.72	697.81	149.97	445.38	2.15	1.47					
	2008	Female	538 254	4062385	9 893 928	1 057 274 453.63	260.26	752.96	106.86	416.84	2.44	1.67					
		Male	436 243	2713478	6 545 325	728 596 560.22	268.51	840.07	111.32	465.21	2.41	1.59					
Total CV section	2005	Female	134 538	978261.00	1 400 663	183 041 895.37	187.11	137.71	130.68	77.47	1.43	0.71	15.97%	19.42%	11.92%	16.88%	1.42
		Male	107 557	797077.00	1 232 903	172 102 228.60	215.92	156.55	139.59	80.66	1.55	0.80	16.16%	23.81%	15.94%	23.45%	1.47
		Unknown	169	1077.00	1 437	163 333.68	151.66	104.08	113.66	71.62	1.33	0.59	9.77%	15.12%	8.91%	11.12%	1.25
	2006	Female	138 006	1058054.00	1 539 707	194 789 701.98	184.10	136.97	126.51	75.63	1.46	0.73	15.88%	19.83%	12.12%	16.76%	1.38
		Male	111 945	871842.00	1 374 067	185 699 175.19	213.00	156.56	135.15	79.44	1.58	0.82	16.27%	24.45%	16.35%	23.32%	1.43
		Unknown	133	954.00	1 318	157 720.61	165.33	106.35	119.67	74.67	1.38	0.60	12.00%	19.82%	12.48%	14.03%	1.12
	2007	Female	117 210	990732.00	1 465 522	189 594 111.56	191.37	140.44	129.37	74.78	1.48	0.75	17.91%	20.84%	12.73%	16.66%	1.31
		Male	93 444	807998.00	1 300 463	178 489 288.29	220.90	160.47	137.25	78.67	1.61	0.85	17.84%	25.62%	17.20%	22.90%	1.33
		Unknown	66	419.00	568	80 655.68	192.50	117.72	142.00	77.39	1.36	0.57	16.22%	23.05%	14.52%	13.75%	0.95
	2008	Female	108 959	932970.00	1 400 223	175 887 779.94	188.52	138.85	125.61	72.10	1.50	0.77	20.24%	22.97%	14.15%	16.64%	1.18
		Male	89 888	776748.00	1 269 536	166 677 528.47	214.58	159.06	131.29	76.02	1.63	0.86	20.61%	28.63%	19.40%	22.88%	1.18

Table 4.8: The prevalence and cost of CVs and CCBs compared to all medication on the total database according to gender (continued)

	Year	Gender	Total number of patients	Total number Rx*	Total number of medicine items dispensed	Total cost of medicine items dispensed (R)	Average cost per Rx* (R)	SD	Average cost per medicine item (R)	SD	Average number of medicine items per Rx*	SD	Percentage of total patients (%)	Percentage of total Rx* (%)	Percentage of total number of medicine items dispensed (%)	Percentage of total cost (%)	CPI
Total CCB section	2005	Female	27 746	176 797	178 266	24 659 535.70	139.48	69.38	138.33	67.41	1.01	0.09	3.29%	3.51%	1.52%	2.27%	1.50
		Male	21 379	138 467	139 822	19 983 730.18	144.32	71.07	142.92	68.96	1.01	0.10	3.21%	4.14%	1.81%	2.72%	1.51
		Unknown	23	170	170	22 064.54	129.79	74.42	129.79	74.42	1.00	0.00	1.33%	2.39%	1.05%	1.50%	1.42
	2006	Female	30 739	204 966	206 619	27 560 062.17	134.46	66.18	133.39	64.41	1.01	0.09	3.54%	3.84%	1.63%	2.37%	1.46
		Male	24 016	162 289	163 693	22 366 310.49	137.82	67.85	136.64	65.82	1.01	0.09	3.49%	4.55%	1.95%	2.81%	1.44
		Unknown	23	148	148	21 020.06	142.03	64.09	142.03	64.09	1.00	0.00	2.08%	3.07%	1.40%	1.87%	1.33
	2007	Female	28 692	204 123	205 679	28 547 578.27	139.85	68.23	138.80	66.45	1.01	0.09	4.38%	4.29%	1.79%	2.51%	1.40
		Male	21 865	158 693	160 284	22 859 239.24	144.05	70.45	142.62	67.54	1.01	0.10	4.17%	5.03%	2.12%	2.93%	1.38
		Unknown	16	86	86	12 233.69	142.25	62.64	142.25	62.64	1.00	0.00	3.93%	4.73%	2.20%	2.09%	0.95
	2008	Female	28 064	201 124	202 485	26 803 965.72	133.27	70.19	132.38	68.66	1.01	0.08	5.21%	4.95%	2.05%	2.54%	1.24
		Male	22 537	163 387	164 952	21 841 260.57	133.68	72.61	132.41	69.74	1.01	0.10	5.17%	6.02%	2.52%	3.00%	1.19

***** Rx = prescriptions

The distributions of male and female patients on the PBM database, patients using CV items and those using CCBs across the study period were discussed in Section 4.2.2. It was noted that more female than male patients received medicine items. This resulted in more prescriptions and more medicine items for female patients.

- During 2005 there were 5 036 494 prescriptions and 11 750 190 medicine items dispensed to female patients and only 334 819 prescriptions and 7 734 461 medicine items to male patients.
- The number of prescriptions and items dispensed in 2006 increased for female and male patients, with 5 336 202 prescriptions and 12 699 707 items for female patients and 3 565 328 prescriptions and 8 403 158 medicine items for male patients.
- The number of prescriptions and medicine items decreased during 2007 by 10.89% in the number of prescriptions and 3.37% medicine items to 4 754 911 prescriptions and 11 509 346 medicine items to female patients and by 11.53% to 3 154 355 prescriptions and by 10% to 7 562 466 medicine items for male patients. The total patients, prescriptions and medicine items decreased from 2007 to 2008 for both male and female patients.

According to the studied database it was seen that the average cost per prescription for male patients was relatively more than for female patients in each year of the study period.

- In 2005 the average cost per prescription for female patients was R215.35 (SD = R 330.75) and for male patient the same year was R 219.15 (SD = R 358.17).
- In 2007 the average cost per prescription on the total PBM database was R 239.37 (SD = R 559.98) for female patients and R 247.12 (SD = R 656.34) for male patients.
- It was also noted that male patients used slightly more expensive medicine items than female patients if the average price per medicine item during the study period is taken into account.
- In 2006 the average cost per medicine item for a female patient was R 91.52 (SD = R 188.12) and the average cost per medicine item for a male patient was R 94.77 (SD = R 208.10).
- The *d*-values calculated showed no significant difference between the average cost of medicine items between male and female patients (Appendix Table A.1).

- From Table 4.8 it was noted that on average a female patient received more items per prescription than a male patient and this meant that the higher cost per prescription for a male patient could possibly not be because of a higher number of items per prescription.

A higher percentage of male patients used a CV item than female patients in 2005, 2006 and 2008 but in 2007 it was noted that 17.91% of female patients on the medicine claims database used a CV item which was0.07% more than the male patients (17.84%) of 2007.

- American Heart Association (2010:17) indicated that the incidence of hypertension was higher in male patients up to age 54 years. After that the incidence of hypertension in female patients was higher than in male patients.
- The Department of Health (2003a:23) showed in the Preliminary Report of the South African Demographic and Health Survey that more female than male patients suffered from hypertension at the time of publishing the report.

The average cost per CV item for male patients was more than for female patients during the studied period, showing that men used more expensive medicine items.

On average relatively more CV items per prescription were dispensed to male patients (2005: 1.55 SD = 0.8, 2006: 1.58 SD = 0.82, 2007: 1.61 SD = 0.85 and 2008: 1.63 SD = 0.86) than to female patients (2005: 1.43 SD = 0.71, 2006: 1.46 SD = 0.73, 2007: 1.48 SD = 0.75 and 2008: 1.5 SD = 0.77) during the study period.

- This could possibly mean that it is more difficult to control CV conditions in male patients than in female patients. As showed in Section 2.4.7 and Section 2.5.10, an item should be added to the treatment regimen if the results achieved with the current regimen were not as desired.
- The number of CV items per prescription showed that on average more than one CV item were dispensed per prescription across all genders. Combination therapy was supported in the literature study (Section 2.3.5).

Further analysis of the CV medicines usage shown in Table 4.8 showed the following:

- A higher percentage of prescriptions issued to male patients contained a CV item than the prescriptions issued to female patients.

- It was noted that 19.42% of prescriptions issued to female patients contained a CV item in 2005 and 23.81% of male prescriptions contained a CV item.
- A higher percentage of CV items was dispensed to male patients (2005: 15.94%, 2006: 16.35%, 2007: 17.2% and 2008: 22.88%) than to female patients (2005: 11.92%, 2006: 12.12%, 2007: 12.73% and 2008: 14.15%) during the study period.
- It was seen that male patients' CV expenditure was larger than that of female patients in every studied year from 2005 to 2008.
- The incline in CV items per prescription from 2005 to 2008 but at the same time decline in the expenditure towards CV medicine items from 2005 to 2008 in male and female patients could be because of an increased use of less expensive generic equivalents as seen in Figure 4.9.
- The CPI value in female patients using CV items was lower than in male patients using CV items of the same year and it could be concluded that the CV treatment of female patients was relatively less expensive compared to those of male patients, as discussed in Section 3.3.5.4.

A definite increase in the use of CV items from 2005 to 2008 was noticed in both genders.

The usage of CCBs according to Table 4.8 indicated aspects such as the following:

- There were more female patients receiving a CCB during the study period than male patients and a higher percentage of female patients (2005: 3.29%, 2006: 3.54%, 2007: 4.38% and 2008: 5.21%) used a CCB medicine item than male patients (2005: 3.21%, 2006: 3.49%, 2007: 4.17% and 2008: 5.17%) each year during the study period.
- In 2005 it was noted that a higher percentage of prescriptions containing a CCB was issued to male patients (4.14%) than female patients (3.51%).
- This was also seen in 2006 (female: 3.84%; male: 4.55%), 2007 (female: 4.29%; male: 5.03%) and 2008 (female: 4.95%; male: 6.02%) that a higher percentage of total prescriptions issued to male patients contained a CCB medicine item than for female patients.
- The average cost per CCB medicine item used by male patients was relatively higher (2005: R 142.92 SD = R 68.96, 2006: R 136.64 SD = R 65.82, 2007: R 142.62 SD = R 67.54 and 2008: R 132.41 SD = R 69.74) than those used by female patients

(2005: R 138.33 SD = R 67.41, 2006: R 133.39 SD = R 64.41, 2007: R138.80 SD = R 66.45 and 2008: R 132.41 SD = R 69.74) during the study period.

- The *d*-values calculated between the average cost per CV medicine item of female and male patients showed no significant difference (Appendix Table A.1).
- It was calculated that on average 23.14% of the total expenditure of male patients was used on CV medicine items against the 16.74% used by female patients.
- CCB items made up a bigger percentage of the total items used in male patients than in female patients during the study years of 2005 (female: 1.52%; male: 1.81%), 2006 (female: 1.63%; male: 1.95%), 2007 (female: 1.79%; male: 2.12%) and 2008 (female: 2.05%; male: 2.52%).
- A relatively larger percentage of the total expenditure was spent on CCB items in the male patients evaluated (2005: 2.72%, 20062.81%, 2007: 2.93% and 2008: 3%) than the female patients evaluated (2005: 2.27%, 2006: 2.37%, 2007: 2.51% and 2008: 2.54%) in the study period.

The percentage of patients using a CCB item, prescriptions, CCB items used and expenditure used on CCB items increased from 2005 to 2008 in both male and female patients. Increasing trends in the usage of CCBs were recorded during the study period.

The *d*-values of the average cost per medicine items in the total database were calculated against the average cost per CV and CCB medicine items (Appendix Table A.1).

- The calculated *d*-values showed no significant difference between the average cost of items on the total database and the average cost of CV or CCB medicine items of the same gender.

All CPI values calculated were above one which showed that all the groups evaluated were relatively expensive according to the definition in Section 3.3.5.4. A balance between cost and prevalence could be experienced in the unknown gender group of 2007 in the CCB as well as in the total CV groups with a CPI of 0.95 in both cases.

4.3.3 General prescribing patterns as per age groups

The total number of patients, prescriptions, medicine items and the cost of medication per year from 2005 to 2008 were evaluated for the total database, the CV section as well as the CCB section according to the seven age groups discussed in Section 3.3.6.2. Percentages were calculated of each age group as a percentage of the total database. It should be noted that Rx in Table 4.8 refers to prescriptions.

Table 4.9: The prevalence and cost of CVs and CCBs compared to all medication on the total database according to age groups

	Year	Age groups	Total patients	Total number Rx	Total number of items dispensed	Total cost of items dispensed (R)	Average cost per Rx (R)	SD	Average cost per item (R)	SD	Average number of items per prescription	SD	Percentage of total patients (%)	Percentage of total Rx (%)	Percentage of total number items dispensed (%)	Percentage of total cost (%)	CPI
Total database	2005	1	301 254	931 772	2 295 273	134 261 603.65	144.09	152.11	58.49	78.92	2.46	1.34					
		2	192 653	621 069	1 363 307	105 505 242.76	169.88	235.11	77.39	129.38	2.20	1.29					
		3	179 932	772 487	1 689 740	129 939 032.15	168.21	281.13	76.90	147.99	2.19	1.31					
		4	282 378	1 455 210	3 303 533	264 990 880.29	182.10	312.59	80.21	153.63	2.27	1.37					
		5	240 701	1 552 195	3 512 132	330 127 070.85	212.68	339.89	94.00	168.82	2.26	1.45					
		6	156 636	1 323 392	3 058 073	345 495 463.77	261.07	406.64	112.98	198.26	2.31	1.60					
		7	156 067	1 735 711	4 278 716	509 545 958.16	293.57	418.01	119.09	192.84	2.47	1.83					
	2006	1	299 627	964 999	2 411 180	140 528 793.96	145.63	170.69	58.28	88.79	2.50	1.36					
		2	199 815	668 374	1 501 519	113 612 769.66	169.98	262.45	75.67	144.83	2.25	1.33					
		3	186 555	796 624	1 761 168	132 064 266.38	165.78	301.89	74.99	163.66	2.21	1.32					
		4	291 764	1 547 801	3 576 188	284 501 421.02	183.81	330.17	79.55	173.41	2.31	1.39					
		5	257 886	1 700 802	3 943 463	366 082 849.51	215.24	388.96	92.83	199.07	2.32	1.48					
		6	164 449	1 409 568	3 341 441	376 957 727.12	267.43	502.47	112.81	243.74	2.37	1.64					
		7	157 994	1 818 180	4 578 463	545 990 906.44	300.30	489.79	119.25	231.58	2.52	1.88					
	2007	1	230 310	802 761	2 004 886	122 858 761.13	153.05	220.14	61.28	111.59	2.50	1.37					
		2	164 362	594 383	1 341 690	106 123 774.49	178.54	367.50	79.10	218.84	2.26	1.34					
		3	124 016	642 899	1 436 956	114 266 884.86	177.74	475.42	79.52	272.85	2.24	1.34					
		4	210 924	1312 833	3 081 439	265 208 222.24	202.01	467.35	86.07	262.79	2.35	1.43					
		5	199 235	1543 007	3 653 945	358 871 837.74	232.58	569.76	98.21	308.74	2.37	1.52					
		6	125 456	1283 230	3 112 733	380 191 385.20	296.28	827.49	122.14	445.41	2.43	1.69					
		7	124 293	1 731 983	4 444 075	570 763 311.00	329.54	716.59	128.43	373.23	2.57	1.92					
	2008	1	162 675	553 426	1 354 121	91 420 354.23	165.19	233.41	67.51	129.42	2.45	1.37					
		2	130 924	481 339	106 7397	91 373 939.85	189.83	473.04	85.60	281.83	2.22	1.34					
		3	92 253	475 472	1 048 633	93 173 193.45	195.96	652.49	88.85	375.48	2.21	1.34					
		4	169 024	1 048 360	2 445 362	227 525 912.83	217.03	592.52	93.04	340.10	2.33	1.43					
		5	180 878	1 379 367	3 294 559	343 010 934.35	248.67	765.61	104.11	422.96	2.39	1.55					
		6	120 417	1 209 997	299 2026	378 103 105.28	312.48	1056.07	126.37	585.20	2.47	1.73					
		7	118 326	1 627 912	4 237 155	561 263 573.86	344.78	902.35	132.46	480.01	2.60	1.95					

Table 4.9: The prevalence and cost of CVs and CCBs compared to all medication on the total database according to age groups (continued)

	Year	Age groups	Total patients	Total number Rx	Total number of items dispensed	Total cost of items dispensed (R)	Average cost per Rx (R)	SD	Average cost per item (R)	SD	Average number of items per prescription	SD	Percentage of total patients (%)	Percentage of total Rx (%)	Percentage of total number items dispensed (%)	Percentage of total cost (%)	CPI
Total CV section	2005	1	1 626	2 656	2 924	237 834.56	89.55	93.90	81.34	76.96	1.10	0.34	0.54%	0.29%	0.13%	0.18%	1.39
		2	4 402	9 574	10 527	1 269 098.77	132.56	115.15	120.56	91.99	1.10	0.37	2.28%	1.54%	0.77%	1.20%	1.56
		3	9 378	30 390	36 563	4 666 779.08	153.56	120.31	127.64	84.60	1.20	0.50	5.21%	3.93%	2.16%	3.59%	1.66
		4	30 678	144 271	185 779	24 671 116.98	171.01	127.27	132.80	80.26	1.29	0.57	10.86%	9.91%	5.62%	9.31%	1.66
		5	53 898	340 114	472 999	64 432 108.21	189.44	138.31	136.22	79.10	1.39	0.67	22.39%	21.91%	13.47%	19.52%	1.45
		6	59 321	471 878	702 930	97 514 191.63	206.65	147.96	138.73	78.24	1.49	0.75	37.87%	35.66%	22.99%	28.22%	1.23
		7	82 961	777 532	1 223 281	162 516 328.42	209.02	153.48	132.85	78.98	1.57	0.82	53.16%	44.80%	28.59%	31.89%	1.12
	2006	1	1 405	2 468	2 793	237 022.15	96.04	106.26	84.86	83.95	1.13	0.38	0.47%	0.26%	0.12%	0.17%	1.46
		2	4 334	9 899	11 078	1 315 020.77	132.84	120.66	118.71	95.35	1.12	0.38	2.17%	1.48%	0.74%	1.16%	1.57
		3	9 147	30 605	37 173	4 664 759.99	152.42	122.54	125.49	84.12	1.21	0.51	4.90%	3.84%	2.11%	3.53%	1.67
		4	31 125	155 178	203 693	26 145 163.41	168.48	129.35	128.36	78.53	1.31	0.60	10.67%	10.03%	5.70%	9.19%	1.61
		5	57 211	380 898	540 304	71 515 267.23	187.75	140.17	132.36	78.19	1.42	0.70	22.18%	22.40%	13.70%	19.54%	1.43
		6	61 926	516 284	781 906	104 706 161.24	202.81	148.12	133.91	77.24	1.51	0.77	37.66%	36.63%	23.40%	27.78%	1.19
		7	84 936	835 518	1 338 145	172 063 202.99	205.94	151.68	128.58	76.87	1.60	0.84	53.76%	45.95%	29.23%	31.51%	1.08
	2007	1	727	1 548	1 762	174 686.37	112.85	117.83	99.14	96.74	1.14	0.37	0.32%	0.19%	0.09%	0.14%	1.62
		2	3 810	8 927	9 919	1 177 398.88	131.89	127.02	118.70	98.00	1.11	0.38	2.32%	1.50%	0.74%	1.11%	1.50
		3	6 944	25 999	32 316	4 021 309.85	154.67	126.00	124.44	84.51	1.24	0.54	5.60%	4.04%	2.25%	3.52%	1.56
		4	24 556	134 921	181 612	23 674 769.80	175.47	132.35	130.36	77.38	1.35	0.63	11.64%	10.28%	5.89%	8.93%	1.51
		5	48 134	349 270	503 100	67 248 173.09	192.54	142.00	133.67	76.63	1.44	0.72	24.16%	22.64%	13.77%	18.74%	1.36
		6	51 905	475 462	734 587	100 133 990.27	210.60	152.30	136.31	76.27	1.54	0.80	41.37%	37.05%	23.60%	26.34%	1.12
		7	74 644	803 022	1 303 257	171 733 727.27	213.86	155.24	131.77	76.44	1.62	0.85	60.05%	46.36%	29.33%	30.09%	1.03
	2008	1	695	1 321	1 447	122 824.64	92.98	86.20	84.88	77.78	1.10	0.32	0.43%	0.24%	0.11%	0.13%	1.26
		2	2 969	7 277	8 202	952 929.25	130.95	113.58	116.18	92.42	1.13	0.40	2.27%	1.51%	0.77%	1.04%	1.36
		3	5 525	21 773	27 289	3 345 896.56	153.67	124.66	122.61	82.56	1.25	0.56	5.99%	4.58%	2.60%	3.59%	1.38
		4	21 077	118 310	161 403	20 174 169.68	170.52	132.27	124.99	74.78	1.36	0.66	12.47%	11.29%	6.60%	8.87%	1.34
		5	45 787	332 664	486 342	61 635 112.97	185.28	138.83	126.73	73.30	1.46	0.74	25.31%	24.12%	14.76%	17.97%	1.22
		6	50 944	462 028	724 187	94 566 055.05	204.68	151.08	130.58	73.85	1.57	0.82	42.31%	38.18%	24.20%	25.01%	1.03
		7	71 850	766 345	1 260 889	161 768 320.26	211.09	153.60	128.30	73.96	1.65	0.87	60.72%	47.08%	29.76%	28.82%	0.97

Table 4.9: The prevalence and cost of CVs and CCBs compared to all medication on the total database according to age groups (continued)

	Year	Age groups	Total patients	Total number Rx	Total number of items dispensed	Total cost of items dispensed (R)	Average cost per Rx (R)	SD	Average cost per item (R)	SD	Average number of items per prescription	SD	Percentage of total patients (%)	Percentage of total Rx (%)	Percentage of total number items dispensed (%)	Percentage of total cost (%)	CPI
Total CCB section	2005	1	106	191	192	25 219.23	132.04	83.86	131.35	84.16	1.01	0.07	0.04%	0.02%	0.01%	0.02%	2.25
		2	251	585	588	79 485.07	135.87	76.99	135.18	75.55	1.01	0.07	0.13%	0.09%	0.04%	0.08%	1.75
		3	1057	3 138	3 157	442 360.64	140.97	78.41	140.12	77.46	1.01	0.08	0.59%	0.41%	0.19%	0.34%	1.82
		4	4 871	19 207	19 380	2 751 437.70	143.25	76.24	141.97	73.52	1.01	0.10	1.72%	1.32%	0.59%	1.04%	1.77
		5	9 731	50 653	51 146	7 187 587.73	141.90	74.55	140.53	71.97	1.01	0.10	4.04%	3.26%	1.46%	2.18%	1.50
		6	11 557	76 361	77 000	10 942 615.51	143.30	69.17	142.11	67.28	1.01	0.09	7.38%	5.77%	2.52%	3.17%	1.26
		7	21 575	165 299	166 795	23 236 624.54	140.57	68.25	139.31	66.39	1.01	0.10	13.82%	9.52%	3.90%	4.56%	1.17
	2006	1	107	254	256	31 897.26	125.58	71.58	124.60	70.98	1.01	0.09	0.04%	0.03%	0.01%	0.02%	2.14
		2	292	682	691	87 260.71	127.95	70.97	126.28	69.25	1.01	0.11	0.15%	0.10%	0.05%	0.08%	1.67
		3	1 135	3 548	3 587	491 984.57	138.67	76.35	137.16	73.41	1.01	0.10	0.61%	0.45%	0.20%	0.37%	1.83
		4	5 352	23 040	23 325	3 208 951.44	139.28	73.31	137.58	69.81	1.01	0.11	1.83%	1.49%	0.65%	1.13%	1.73
		5	11 652	64 417	64 992	8 914 699.10	138.39	72.57	137.17	70.06	1.01	0.09	4.52%	3.79%	1.65%	2.44%	1.48
		6	12 957	89 710	90 309	12 245 601.57	136.50	65.14	135.60	63.93	1.01	0.08	7.88%	6.36%	2.70%	3.25%	1.20
		7	23 283	185 752	187 300	24 966 998.07	134.41	64.65	133.30	62.91	1.01	0.09	14.74%	10.22%	4.09%	4.57%	1.12
	2007	1	79	195	199	28 764.38	147.51	101.05	144.54	99.38	1.02	0.14	0.03%	0.02%	0.01%	0.02%	2.36
		2	265	595	601	75 439.02	126.79	75.61	125.52	72.25	1.01	0.10	0.16%	0.10%	0.04%	0.07%	1.59
		3	1 025	3 524	3 556	485 717.36	137.83	82.59	136.59	80.99	1.01	0.09	0.83%	0.55%	0.25%	0.43%	1.72
		4	4 727	22 219	22 482	3 139 039.06	141.28	75.60	139.62	71.73	1.01	0.11	2.24%	1.69%	0.73%	1.18%	1.62
		5	10 806	63 479	64 154	9 078 849.91	143.02	73.89	141.52	70.73	1.01	0.10	5.42%	4.11%	1.76%	2.53%	1.44
		6	12 036	89 102	89 868	12 730 074.40	142.87	67.83	141.65	65.54	1.01	0.09	9.59%	6.94%	2.89%	3.35%	1.16
		7	21 635	183 788	185 189	25 881 167.07	140.82	67.06	139.76	65.29	1.01	0.09	17.41%	10.61%	4.17%	4.53%	1.09
	2008	1	59	173	181	22 109.18	127.80	75.61	122.15	77.75	1.05	0.21	0.04%	0.03%	0.01%	0.02%	1.81
		2	256	543	548	60 984.17	112.31	82.38	111.28	74.81	1.01	0.11	0.20%	0.11%	0.05%	0.07%	1.30
		3	892	3 395	3 427	427 951.27	126.05	81.77	124.88	79.32	1.01	0.10	0.97%	0.71%	0.33%	0.46%	1.41
		4	4 345	21 101	21 315	2 703 158.62	128.11	75.81	126.82	72.86	1.01	0.10	2.57%	2.01%	0.87%	1.19%	1.36
		5	11 210	66 896	67 472	8 636 417.20	129.10	73.71	128.00	71.33	1.01	0.09	6.20%	4.85%	2.05%	2.52%	1.23
		6	12 565	91 732	92 556	12 230 176.08	133.33	71.29	132.14	68.62	1.01	0.10	10.43%	7.58%	3.09%	3.23%	1.05
		7	21 274	180 671	181 938	24 564 429.77	135.96	69.41	135.02	67.75	1.01	0.09	17.98%	11.10%	4.29%	4.38%	1.02

The distribution of patients on the total PBM database, patients using CV items and patients using CCB were discussed according to age groups (Section 4.2) for the studied period. Furthermore the total database as indicated in Table 4.9 indicated aspects such as the following:

- The total cost of medication on the total PBM database for patients younger than 15 years was more (R 134 261 603.65) than the medication for patients >15 ≤ 25 years old (R 105 505 242.76) in 2005. This was also seen in 2006, 2007 and 2008.
- More items per prescription were issued to patients in age group one compared to age group 2 during the study period.
- In 2006 there were 1 558 090 patients on the total database, 12.8% (n = 199 815) of patients were aged >15 ≤ 25 years old. These patients were responsible for 668 374 prescriptions between them, 7.5% of the total number of prescriptions issued in 2006.
- The highest average cost per prescription and average cost per medicine item on the total medicine claims database were seen in patients older than 65 years of age for the studied years.
- A CPI of 1.29 as found in the age group >15 ≤ 25 years old showed that the treatment in that group was being relatively expensive, but less expensive than that of patients older than 65 years (CPI = 1.83) in 2005 according to the definition in Section 3.3.5.4.
- The 199235 patients on the total database of 2007 aged > 45 ≤ 55 years received 3 653 945 medicine items, at an average of 2.37 items per prescription. It was seen that 13.77% (n = 503 100) of those items were CV items and 64154 medicine items were CCBs.
- Patients older than 65 years received 4 444 075 medicine items at an average cost of R 128.43 (SD = R 373.23) per medicine item.
- Table 4.9 showed that 60% (n = 74 644) of the patients older than 65 got a prescription for a CV item. There were 185 189 CCB items dispensed to patients older than 65 years during 2007.
- In 2008, 120 417 (12.36%) patients on the PBM database were aged >55 ≤ 65 and were responsible for the usage of medication at a cost of R 378 103 105.28. Of these patients 12 565 (10.43%) used a CCB item in 2008. The CCBs dispensed to them accounted for 3.23% (R 24 564 429.77) of the medical cost in that specific group.

Table 4.9 indicated that the average cost of a prescription containing a CV item increased as the age increased during the studied period.

- It was noted that the cost per CV item increased from age group 1 to age group 6 and then decreased in age group 7 for the period 2005 to 2008.
- In 2005 a total of 0.54% patients younger than 15 years used a CV item (n = 1 626). In the same year 10.86% of patients > 35 ≤ 45 years (n = 30 678) as well as 53.16% (n = 82 961) of patients older than 65 years used a CV item.
- In 2006 it was seen that 9 899 of prescriptions, issued to patients >15 ≤ 25 years of age, were for a CV item (1.48% of total prescriptions), 682 were for prescriptions containing a CCB item (0.1% of total prescriptions).
- Patients in age group 7 received on average more CV items per prescription than patients in age groups 1 to 6 during the period 2005 to 2008.

More CV items per patient could show a bigger difficulty to control the CV condition in older patients or that these patients may be diagnosed with more than one CV condition.

- As showed in Section 2.4.7 and Section 2.5.10, an item should be added to the treatment regimen if the results achieved with the current regimen were not as desired.
- The number of CV items per prescription showed that on average more than one CV item were dispensed per prescription across all age groups.
- Combination therapy of hypertension was supported in the literature study (Section 2.3.6).

A CPI value of 0.97 was calculated for the group of CV patients older than 65 year in 2008. This shows a lower cost prevalence ratio than seen in age groups 3 and age group 4 (CPI = 1.66 for age group 3 and age group 4) of 2005. From Table 4.9 it could also be seen that the CPI values of CV items as well as CCB medicine items decreased with increased patient age.

From Table 4.9 it could be observed that the cost of CCB medicine items increased with patient age as more patients used CCBs the older they got, e.g. in 2005 there were 251 patients >15 ≤ 25 years of age and R 79 485.07 was spent on CCBs against the 21 575 patients older than 65 years using CCBs at a cost of R 23 236 624.54 for that age group.

- In 2005 0.04% of the patients below 15 years (n = 106) used a CCB, while 4.04% (n = 9 731) of patients aged > 45 ≤ 55 years as well as 13.82% of patients older than 65 years used a CCB.
- Across all studied years it was revealed that the percentage CCB users on the total PMB database increased with increased patient age.
- More prescriptions in a year contained a CCB medicine item in older patients compared to younger patients.
- It was further noticed that 11.1% (n = 180 671) of all prescriptions of patients older than 65 years contained a CCB medicine item.
- An increased percentage of the total medication items dispensed during the study period could be attached to CCB items in older patients in comparison to younger patients.
- More of the money spent on medicine items were spent on CCB items from 2005 to 2008. The use of CCBs increased from 2005 (4.04% of patients in age group 5 used at least one CCB item in 2005) to 2008 (6.2% of patients in age group 5 used at least one CCB item in 2008) and so did the percentage of money spent on it.
- It was seen that 2.18% (R 7 187 587.73) of the total expenditure of patients in age group 5 went to CCB items in 2005 compared to 2.52% (R 8 636 417.20) in 2008.

It was also noted that the average of CCB items per prescription was 1.01 across all the age groups across the study period. This is a “good indication” because the use of more than one CCB at a time by a patient is contraindicated (Section 2.3.5).

- A CPI value of 1.02 was calculated for the group of patients older than 65 year in 2008. This shows a lower cost prevalence ratio than seen in age groups 3 (CPI =1.82) and age group 4 (CPI = 1.77) of 2005.
- From this Table 4.9 could also be seen that the CPI values decreased with increased patient age. The increased use of generic items as noticed from 2005 to 2008 (Section 4.4) could also contribute to less expensive treatment.

It was observed that as patients grew older they used more items and a large percentage of medicine items they used were of CV importance. It was seen that the use of CV as well as CCB items increased as the patients grew older.

Table 4.10 was drawn up to summarise the usage of CV as well as CCB medicine items per age groups during the study period.

Table 4.10: The percentage distribution of patients using CV and CCB medicine items per age group

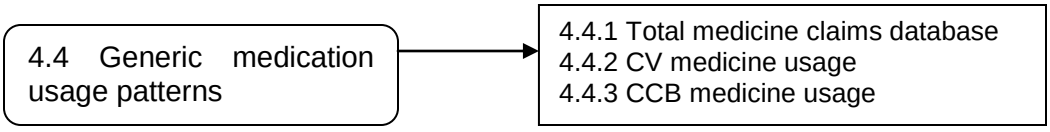
Medicine groups	Patient age group	Year			
		2005	2006	2007	2007
Patients using CV medicine	1	0.54%	0.47%	0.32%	0.43%
	2	2.28%	2.17%	2.32%	2.27%
	3	5.21%	4.90%	5.60%	5.99%
	4	10.86%	10.67%	11.64%	12.47%
	5	22.39%	22.18%	24.16%	25.31%
	6	37.87%	37.66%	41.37%	42.31%
	7	53.16%	53.76%	60.05%	60.72%
Patients using CCB medicine	1	0.04%	0.04%	0.03%	0.04%
	2	0.13%	0.15%	0.16%	0.20%
	3	0.59%	0.61%	0.83%	0.97%
	4	1.72%	1.83%	2.24%	2.57%
	5	4.04%	4.52%	5.42%	6.20%
	6	7.38%	7.88%	9.59%	10.43%
	7	13.82%	14.74%	17.41%	17.98%

From Table 4.10 it could be concluded that the usage of CV medicine items as well as CCB medicine items increased with patient age. It was also noted that CCBs grew in popularity over the study period and patients using CCBs increased from 2005 to 2008.

4.4 Generic medication indicator usage patterns

In this section the generic indicator patterns of the medicine items dispensed will be evaluated annually from 2005 to 2008 in the three main database sections (Section 3.3.3). The three sections referred to are the total medicines claims database (Section 4.4.1), the CV section (Section 4.4.2) and the CCBs (Section 4.4.3). The prevalence of each group will be calculated as a percentage of the total medicine claims database.

The diagram presents the strategies of presenting the results according to generic medication usage.



The true reasons for a patient using an original product instead of a generic could not be determined from the medical claims database and probable reasons could be that the use thereof was preferred by the prescriber or the patient, or that the specific product was unavailable for some unspecified reason, or the fact that the payment of a specific medicine item was decided by a referral price list compiled by the third party medical aid administrator. For classification of medication according to generic use see Section 3.3.6.5.4.

4.4.1 Generic medication indicator patterns of the usage of total database

Figure 4.8 shows the generic indicator patterns of all items dispensed on the total PBM database (calculated from Table 4.11).

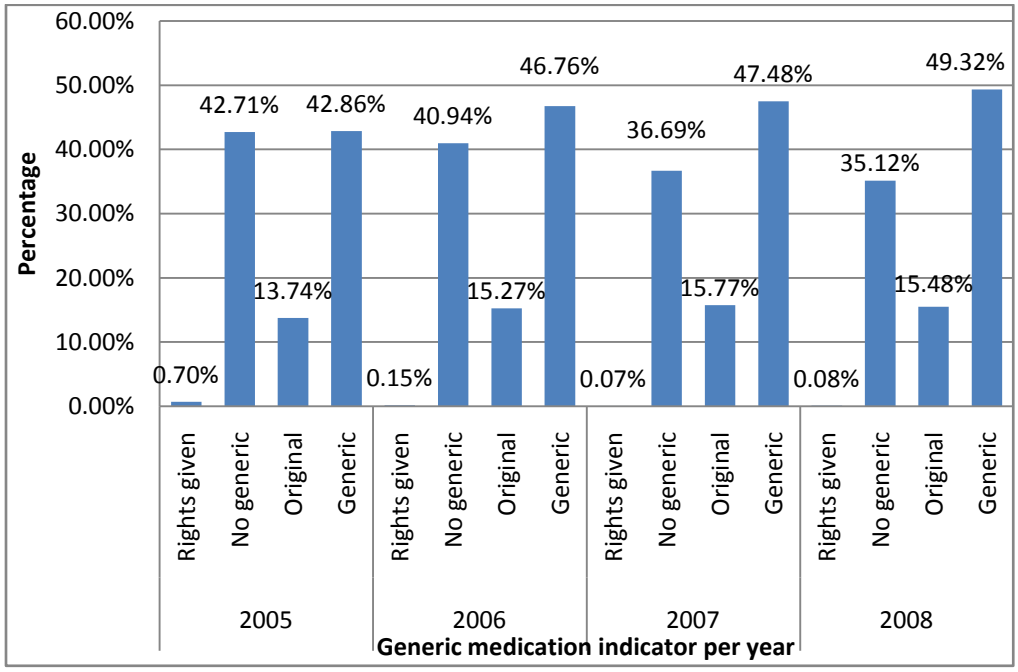


Figure 4.8: Percentages of generic usage indicator distribution of the total medicine data base

From Figure 4.8 the following could be noted:

- The percentage of the 'No generics' group decreased per annum from 42.71% (n = 8 328 268) in 2005 to 35.12% (n = 5 773 344) in 2008.
- The percentage of the usage of original products increased from 13.74% in 2005 to 15.27% in 2006 to 15.77% in 2007 and decreased in 2008 to 15.48%. This accounts for a total increase of 1.74% across the study period.
- The use of generic products increased from 42.86% (n = 8 357 250) in 2005 to 46.76% in 2006 to 47.48% in 2007 and 49.32% (n = 8 108 339) in 2008 which is a total increase of 6.61% across the study period.

Table 4.11: Generic medication usage indicator of the total medicine database for the study period

Year	Generic indicator	Number of medicine items	Cost per medicine item (R)	SD	Total cost (R)	CPI
2005	Rights given	136 529	86.62	86.36	11 825 895.65	0.93
	No generic	8 328 268	136.26	227.00	1 134 806 272.48	1.46
	Original	2 678 727	99.45	132.89	266 399 728.78	1.07
	Generic	8 357 250	48.68	60.00	406 833 354.71	0.52
2006	Rights given	32 387	95.50	38.19	3 093 081.05	1.03
	No generic	7 983 562	139.88	287.68	1 116 715 653.50	1.39
	Original	3 224 378	101.92	152.09	328 623 621.75	1.10
	Generic	9 873 095	51.79	67.28	511 306 377.79	0.56
2007	Rights given	12 811	59.49	69.29	762 063.88	0.59
	No generic	6 998 781	153.53	509.44	1 074 554 517.96	1.53
	Original	3 007 375	102.26	177.95	307 532 420.50	1.02
	Generic	9 056 757	59.12	79.26	535 435 174.32	0.59
2008	Rights given	13 318	65.45	47.64	871 710.14	0.60
	No generic	5 773 344	170.42	712.01	983 898 369.62	1.57
	Original	2 544 252	103.66	208.77	263 742 507.88	0.95
	Generic	8 108 339	66.27	86.98	537 358 426.21	0.61

From Table 4.11 the following aspects were noted:

- The average cost per medicine item of the items without possible generic equivalents was the highest from 2005 through to 2008.
- The average cost per medicine item in the mentioned group amounted to R 136.26 (SD = R 227.00) in 2005, R 36.81 more than the average cost of the group of original products (R 99.45 SD = R 132.89).
- The average cost per generic items amounted to R 48.68 (SD = R 60.00) in 2005, which was

  R 50.77 less than the average cost per original medicine items.
- In 2006 it was seen that the average cost per generic medicine item (R 51.79 SD = R 67.28) was R 50.13 less than the average cost per original medicine item (R 101.92 SD = R 152.09).

- On the total medicine claims database the average cost per generic medicine item (R 66.27 SD = R 86.98) was only R 37.39 less than the average cost per original medicine item (R 103.66 SD = R 208.77) for 2008.
- The CPI value of generic medicine items on the PBM database was smaller than one during the study period from 2005 to 2008.
- From Figure 4.11 was noted that the group of medication without generic equivalents had the highest CPI value during the study period. This indicated that they were relatively more expensive than the other groups of medicine items stated in section 3.3.6.5.4.

4.4.2 Generic medication indicator patterns of the usage of CV items

The generic indicator patterns of the items dispensed in the CV section of the PBM database were shown in a chart form (calculated from Table 4.12).

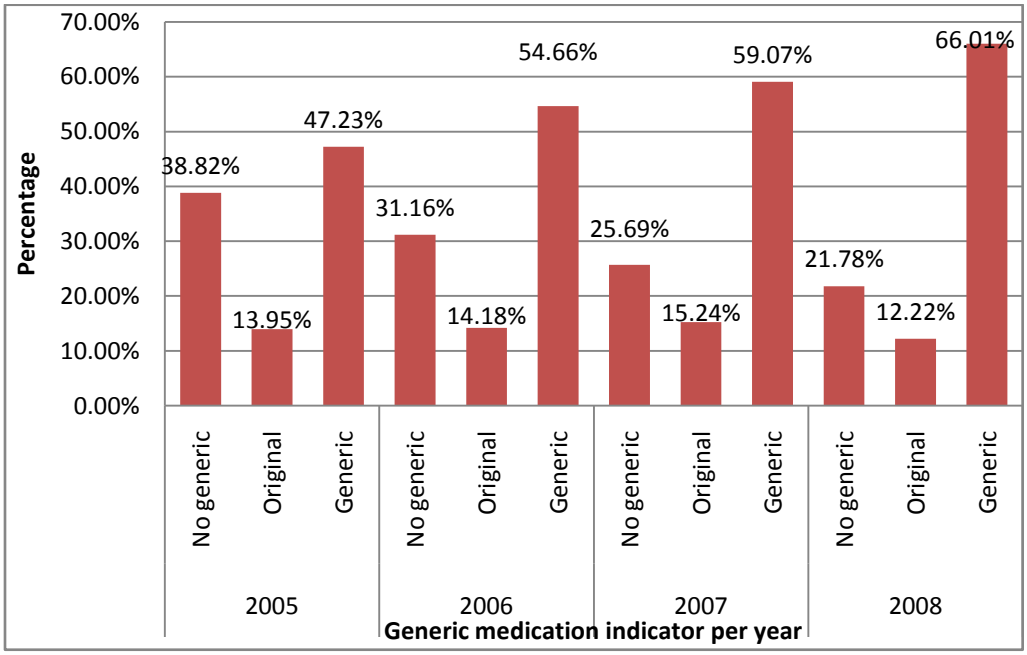


Figure 4.9: Percentages of generic usage indicator distribution of the CV medicine items

In the CV section there was no medication recorded in the 'Rights given' group as noted in the total PBM database. From Figure 4.9 was noted that:

- The percentage of the items without generics on the market decreased annually from 39% (n = 1 022 941) in 2005 to 22% (n = 581 373) in 2008. This is a total decrease of 17% across the study period.
- The original products in the CV section of the medicine claims database did not follow a distinct pattern in the study years.
- In 2005 the original items dispensed accounted for around 14% (n = 367 631) of all CV items dispensed. This percentage increased to 14.2% (n = 413 416) in 2006 and increased again in 2007 to 15.2% (n = 421 682) of all CV items dispensed.
- In 2008 the original items accounted for 12.2% (n = 326 208) of CV items dispensed.
- The usage of generic items increased annually from 47% (n = 1 244 431) in 2005 to a percentage of 66% (n = 1 762 178) in 2008, a growth of 19% over 4 years, nearly 5% per year over the study period.

Table 4.12: Generic medication usage indicator of CV medicine items for the study period

Year	Generic indicator	Number of medicine items	Cost per medicine item (R)	SD	Total cost (R)	CPI
2005	No generic	1 022 941	193.61	62.89	198 048 311.71	1.44
	Original	367 631	136.75	84.15	50 274 297.81	1.01
	Generic	1 244 431	85.97	51.74	106 984 848.13	0.64
2006	No generic	908 353	197.10	66.90	179 038 521.75	1.51
	Original	413 416	142.86	79.28	59 061 349.93	1.09
	Generic	1 593 323	89.47	50.73	142 546 726.10	0.69
2007	No generic	710 788	197.25	73.25	140 203 291.42	1.48
	Original	421 682	155.09	82.19	65 398 250.53	1.17
	Generic	1 634 083	99.48	53.35	162 562 513.58	0.75
2008	No generic	581 373	193.45	76.91	112 467 506.54	1.51
	Original	326 208	150.46	85.06	49 082 419.25	1.17
	Generic	1 762 178	102.72	53.57	181 015 382.62	0.80

The average cost per CV medicine item without a generic equivalent on the SA market was more than that of the original medicine items as well as the generic medicine items during the study period.

- It was noted that in 2005 the average cost per original CV medicine item was R 136.75 (SD = R 84.15), R50.78 more costly than the average cost per generic medicine item (R 85.97 SD = R 51.74) available on the market of 2005.
- In 2008 it was observed that the average cost per generic medicine item was R 102.72 (SD = R 53.57) and the average cost per original medicine item was R 150.06 (SD = R 85.60).
- This cost difference as seen in Table 4.12 (2005: 37.13%, 2006: 36.37%, 2007: 35.86% and 2008: 31.73%) could be the reason for the increase in the usage of generic equivalents instead of original medicine items.

The average cost per item without generic equivalents on the South African market indicated the most costly CV items on the South African market.

- The CPI values calculated for generic items (2005: 0.64, 2006: 0.69, 2007: 0.75 and 2008: 0.8) showed that these items were relatively inexpensive according to the definition in Section 3.3.5.4.
- The highest CPI values per year in the CV section were seen with medicine items without generic equivalents on the market and showed that these CV items were relatively expensive.
- In 2005 it was noted that generic items showed a balance between cost and prevalence (Section 3.3.5.4), but the CPI values increased each study year from 2005 to the value 1.17 as calculated in 2007 and 2008.

4.4.3 Generic medication indicator patterns of the usage of CCB items

The generic indicator patterns of all the CCB items dispensed in the study period are depicted in Figure 4.10 (calculated from Table 4.13).

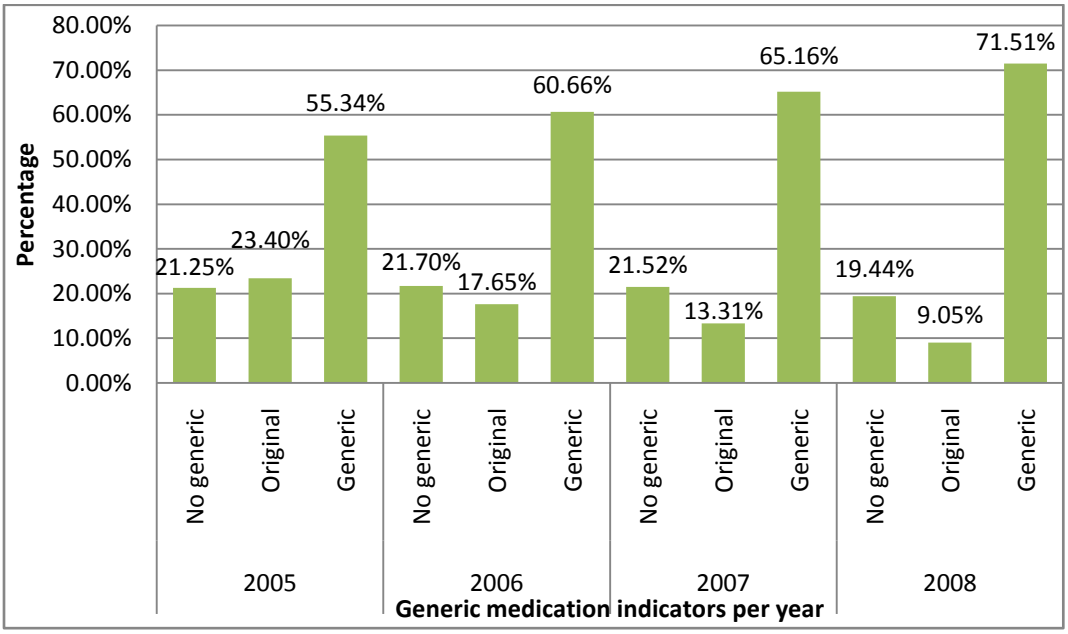


Figure 4.10: Percentages of generic usage indicator distribution of the CCB medicine items

- The CCB items without a generic substitute on the South African market accounted for 21.25% of the total CCBs dispensed on the medicine claims database in 2005.
- This figure did not change dramatically in 2006 where the CCBs without generics accounted for 21.71% dispensed through this medical claims database, as in 2007 where it accounted for 21.5%.
- A decline in the percentage of CCBs without generic substitutes on the market was seen in 2008 with 19.44% of all CCBs.

Table 4.13: Generic medication usage indicator of the CCB medicine items for the study period

Year	Generic indicator	Number of medicine items	Cost per medicine item (R)	SD	Total cost (R)	CPI
2005	No generic	67 644	206.83	53.74	13 990,998.91	1.47
	Original	74 484	162.86	52.84	12 130 665.39	1.16
	Generic	176 130	105.28	54.39	18 543 666.12	0.75
2006	No generic	80 376	203.75	54.95	16 376 324.38	1.51
	Original	65 369	153.77	49.76	10 051 824.72	1.14
	Generic	224 715	104.66	49.64	23 519 243.62	0.78
2007	No generic	78 780	213.84	61.71	16 846 120.31	1.52
	Original	48 735	159.04	53.13	7 750 879.06	1.13
	Generic	238 534	112.45	49.10	26 822 051.83	0.80
2008	No generic	71 434	219.29	64.94	15 665 100.12	1.66
	Original	33 263	159.41	60.56	5 302 515.86	1.20
	Generic	262 740	105.34	46.89	27 677 610.31	0.80

From Table 4.13 the following could be noted:

- According to the average cost per medicine item, CCB medicine items were on average calculated relatively more expensive than CV medicine items, as well as items on the total PBM database.
- In 2006 it was noticed that generic items on the total PBM database had an average cost of R 51.79 (SD = R 67.28) and the average cost of a generic CV item was R 89.47 (SD = R 50.73). The average cost of a generic CCB medicine item was R 104.66 (SD = R 49.64) in 2006.
- This relatively large price differences between the total medicine claims database, CV items and CCBs were observed during the study period.
- The average cost per generic CCB medicine item was R 112.45 (SD = R 49.10) in 2007 which was the highest average cost of a generic medicine item during the study years.
- The average cost per original CCB medicine item was 35.36% more expensive than the average cost of a generic item in 2005.

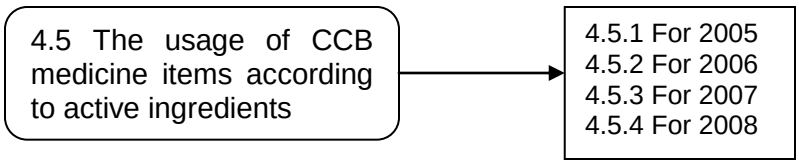
- The average cost difference between generic CCB medicine items and original medicine items decreased to 29.29% during 2007.
- In 2008 the average cost of an original CCB medicine item was R 159.41 (SD = R 60.56) and the average cost per generic CCB medicine item was R 105.34 (SD = R 46.89).
- The potential cost savings if the original CCB items were to be substituted for generic equivalent medicine items were discussed in Section 4.7.

The CPI values calculated showed that the CCB items without generic equivalents on the market were relatively expensive as by CPI definition (Section 3.3.5.4) from 2005 to 2008. The CPI value increased per annum from 1.47 in 2005 to 1.66 in 2008. The CPI values calculated for generic CCB medicine items were 0.75 in 2005, 0.78 in 2006 and 0.8 in 2007 and 2008. These values indicated that generic CCB medicine items were relatively inexpensive, as defined in Section 3.3.5.4, in comparison with other CCB items during the study period. These trends would be expected due to the perception that generic medicine items are supposed to be "cheaper".

4.5 Usage of CCB medicine items according to CCB active ingredients

In this section the usage of the pharmacological active ingredients of the medicine items in the group CCBs will be examined and displayed per year from 2005 to 2008.

As previously stated in other sections the diagram paved the way for the presentation of the results.



4.5.1 Usage of CCB active ingredients in 2005

Figure 4.11 shows that nifedipine (30%) was the active ingredient most frequently prescribed in 2005. Amlodipine (28%) and verapamil (21%) were recorded as 2nd and 3rd most used active ingredients respectively in 2005.

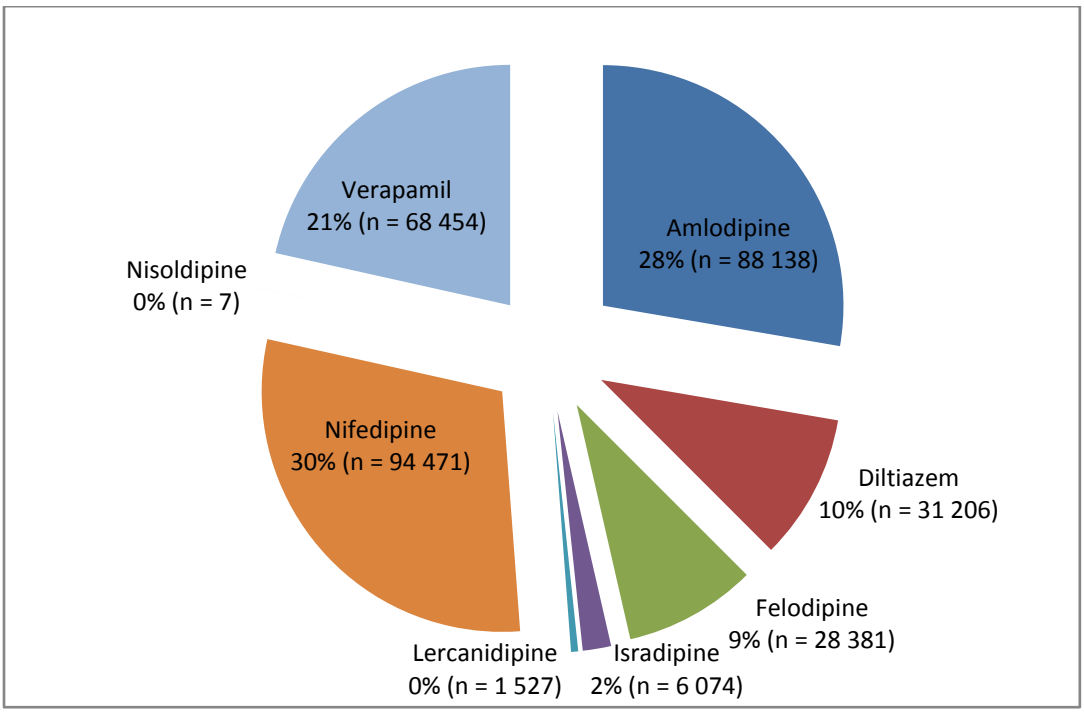


Figure 4.11: Usage of CCB active ingredients in 2005

4.5.2 Usage of CCB active ingredients in 2006

The usage of amlodipine increased from 28% in 2005 to 33% in 2006 and was the active ingredient mostly used. The usage of verapamil decreased by 1% and the usage of verapamil decreased by 2% during 2006 if compared to 2005. Diltiazem and felodipine both recorded 8% usage (Figure 4.12).

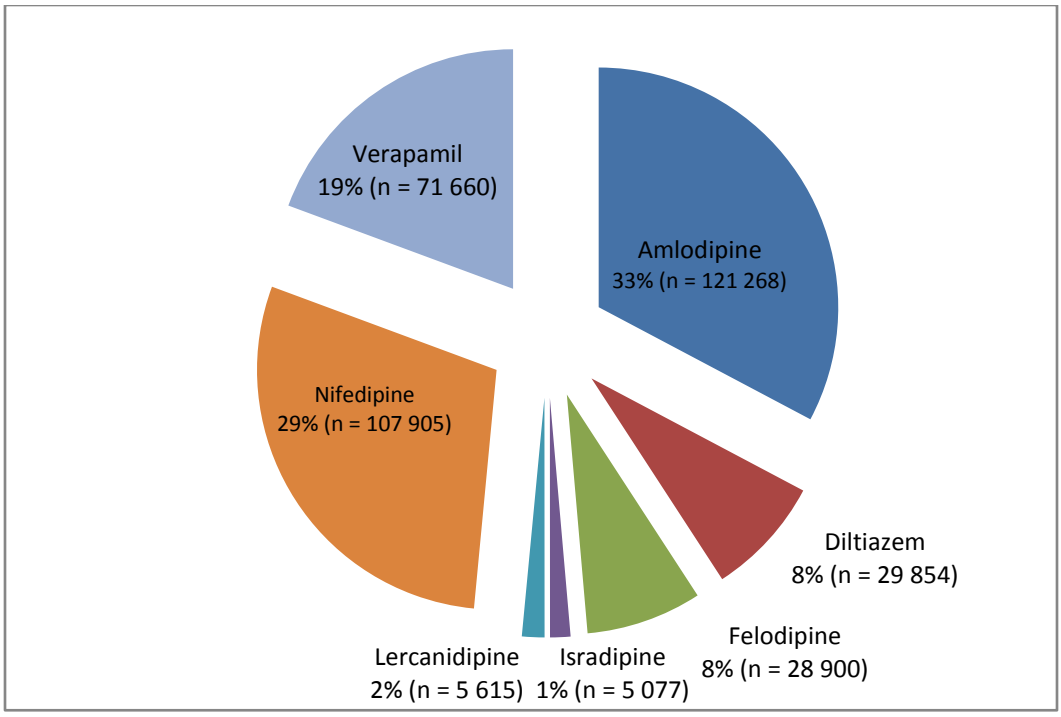


Figure 4.12: Usage of CCB active ingredients in 2006

4.5.3 Usage of CCB active ingredients in 2007

According to the results presented in Figure 4.13, more than a third of all CCB containing products dispensed in 2007 contained amlodipine. The percentage of usage by nifedipine active ingredients decreased from 30% in 2005 to 26% in 2007as the usage of amlodipine increased. A decrease in the usage of verapamil containing items from 21% in 2005 to 17% in 2007 was also noted.

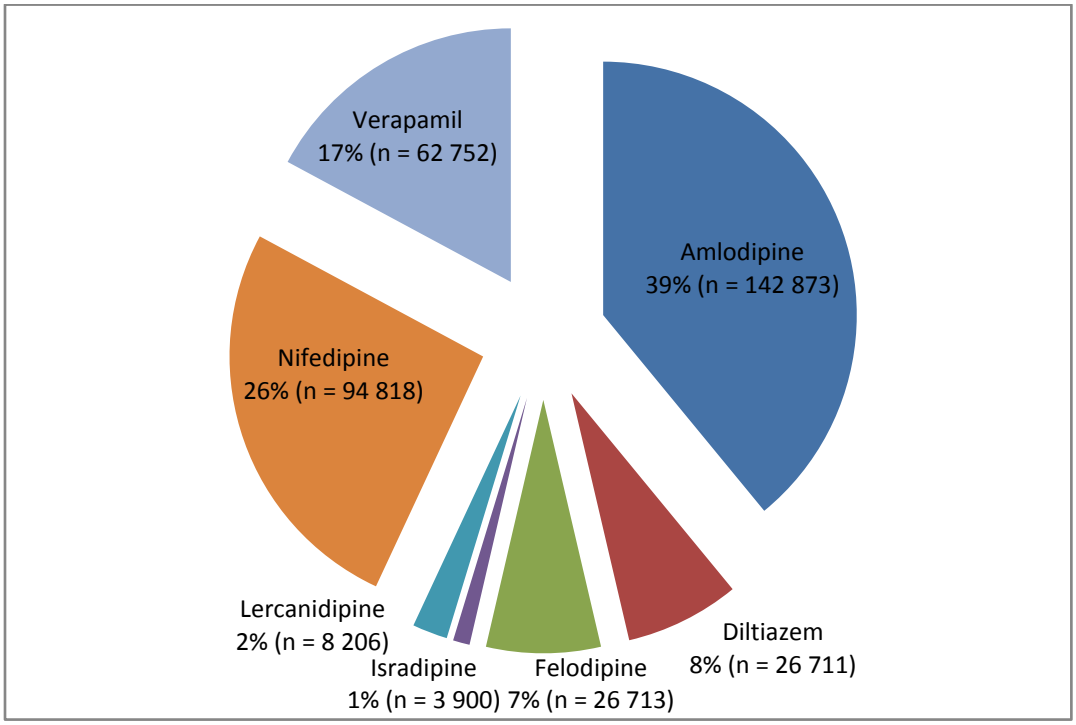


Figure 4.13: Usage of CCB active ingredients in 2007

4.5.4 Usage of CCB active ingredients in 2008

The results presented in Figure 4.14 reveal that the usage of amlodipine containing items as well as items containing the pharmacological active ingredient lercanidipine increased from 2005 to 2008. It was seen that 42% of all CCB products dispensed in 2008 contained amlodipine. The usage of nifedipine (26%) remained unchanged from 2007 to 2008.

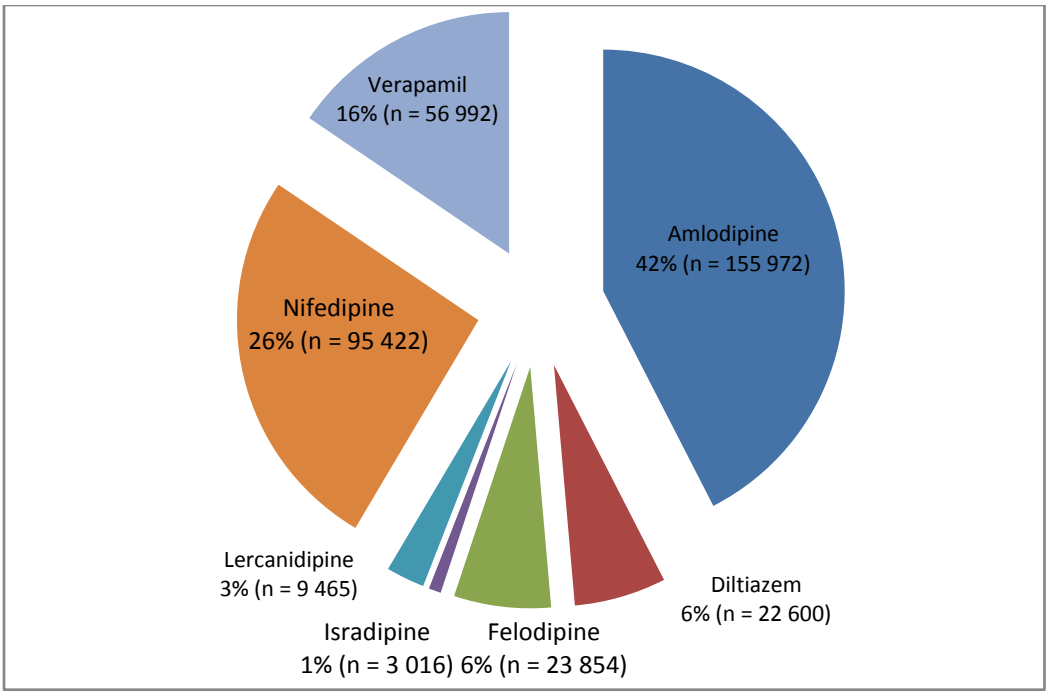


Figure 4.14: Usage of CCB active ingredients in 2008

To conclude section 4.5 of this study Table 4.14 was compiled to illustrate the usage patterns of some CCB pharmacological active ingredients during the study period. Amlodipine, nifedipine and verapamil were chosen as they represented 79% of all CCB pharmacological active ingredients contained in medicine items dispensed in 2005, 81% in 2006, 82% in 2007 and 84% in 2008.

Table 4.14: The percentage usage of the most frequently prescribed CCB pharmacological active ingredients across the study period

CCB pharmacological active ingredients	Year			
	2005	2006	2007	2008
Amlodipine	28%*	33%*	39%*	42%*
Nifedipine	30%*	29%*	26%*	26%*
Verapamil	21%*	19%*	17%*	16%*

* Percentage usage was taken from Figures 4.11 to Figure 4.14

From Table 4.14 it was seen that the use of amlodipine increased from 2005 to 2008. This could be the reason for the increased amlodipine containing medicine items that entered the South African market in 2007 and 2008 (Table 4.31 and Table 4.37).

The percentage of usage of nifedipine containing medicine items decreased by 4% from 2005 (30%) to 2008 (26%). The percentage of usage of verapamil decreased from 21% in 2005 to 16% in 2008, which was a total of 5% decrease across four years.

4.6 Top 10 CCB items used according to prevalence

A complete list of CCB trade names dispensed during the study period (2005 to 2008) is indicated as Appendix Tables A.2, A.3, A.4 and A.5.

In Section 4.6 the top 10 CCB items dispensed to patients will be evaluated. Firstly the top 10 CCB medicine items of the total CCB medicine group will be tabulated per year (Section 4.6.1). Secondly the top CCB medicine items will be evaluated per gender across the four study years (Section 4.6.2). The top 10 CCB medicine items will not be evaluated per age group as some of the age groups using CCB medicine items were relatively small, as noted in Table 4.9, and thus the data were not extracted for doing so.

A medicine item must have been on the top 10 CCB items dispensed at least one of the study years before it could be presented as part of the top 10 CCB table.

4.6.1 Top 10 CCB items used according to prevalence

In this section the top 10 CCB items dispensed to patients in a year will be tabulated separately, showing the average cost per item dispensed as well as the total items dispensed in the study years. A total of 12 CCB medicine items were listed in Table 4.15. The percentage prevalence and cost of all the CCB trade names during the study period were shown in Appendix Table A.2 to Appendix Table A.5.

Table 4.15: Top 10 CCB items dispensed according to study years

Year	2005					2006				2007				2008			
Registered trade name	Active ingredient	Position	Medicine items dispensed	Average cost per medicine item	SD	Position	Medicine items dispensed	Average cost per medicine item	SD	Position	Medicine items dispensed	Average cost per medicine item	SD	Position	Medicine items dispensed	Average cost per medicine item	SD
Amloc 5 mg	Amlodipine	5	20 418	103.73	19.15	1	45 129	99.42	16.64	1	59 987	105.10	19.73	1	57 156	97.27	20.19
Cipalat Retard 20 mg	Nifedipine	3	27 409	42.93	13.91	4	30 835	42.72	14.12	6	23 636	41.50	14.30	2	32 695	46.50	15.40
Amloc 10 mg	Amlodipine	13	9 879	140.47	17.67	6	22 797	136.30	14.70	3	31 500	143.15	19.17	3	32 574	133.12	19.08
Adalat XL 30 mg	Nifedipine	2	30 814	206.06	38.42	2	35 687	206.32	41.58	2	35 359	216.74	49.82	4	31 231	223.24	53.72
Verahexal 240 SR	Verapamil	4	24 815	101.47	23.35	5	27 131	102.02	23.14	4	25 414	110.06	25.33	5	27 289	113.35	26.37
Norvasc 5 mg	Amlodipine	1	39 825	138.62	26.97	3	35 076	131.75	24.23	5	25 396	135.94	30.49	6	16 012	132.80	36.22
Ciplavasc 5 mg	Amlodipine									18	3 999	68.1197	11.57	7	13 663	70.84	12.67
Adalat Xl 60 mg	Nifedipine	8	12 313	269.24	32.05	9	14 458	267.35	29.28	8	14 778	280.83	36.35	8	13 398	290.65	37.62
Felodipine-Hexal 5 mg	Felodipine	10	10 967	103.26	16.51	11	13 200	102.69	18.23	9	13 239	108.76	22.09	9	12 602	111.69	22.96
Calcicard SR 240 mg	Verapamil	6	19 264	134.48	33.46	7	20 013	136.00	33.20	7	15 426	142.74	35.21	10	11 119	149.06	36.16
Vascard 30 SR	Nifedipine	9	11 126	152.01	31.57	10	14 343	154.95	36.67	11	11 981	161.97	41.08	11	10 866	166.22	43.13
Norvasc 10 mg	Amlodipine	7	17 127	182.36	26.65	8	16 476	173.52	21.52	10	12 556	178.33	28.67	15	8 273	175.13	38.87

Table 4.15 illustrated, *inter alia,* the following:

- Norvasc® 5 mg was ranked the number one CCB medicine item in 2005 with 39 825 medicine items dispensed.
- Amloc® 5 mg was the top CCB medicine item dispensed in 2006 (n = 45 129), 2007 (n = 59 987), 2008 (n = 57 156).
- Norvasc® 10 mg was 7th best CCB seller in 2005, 9th in 2006, 10th in 2007 and in 15th position in 2008.
- Adalat® XL 30 mg was in the 2nd position of the top CCB medicine items prescribed from 2005 to 2007 before dropping to 4th position in 2008.
- Cipalat Retard® 20 mg was in 6th positions with 23 636 medicine items dispensed in 2007 but this number increased by 9 059 medicine items during 2008 and moved into 2nd position with 32 695 medicine items dispensed.
- Adalat® XL 60 mg was the most expensive by average cost of the medicine items listed.
- Cipalat® Retard was the least costly medicine item ranked in the top 10 list of CCB medicine items sold, with an average cost of R 42.93 (SD = R 13.91) in 2005, R 42.72 (SD = R 14.12) in 2006, R 41.50 (SD = R 14.50) and R 46.50 (SD = R 15.40) in 2008.
- Verahexal® 240 SR was a verapamil containing product and was in 4th position in 2005 (n = 24 815) and 2007 (n = 25 414) and 5th in 2006 (n = 27 131) and 2008 (n = 27 289). On average cost per medicine item it was less costly than Calcicard® SR 240 mg, the other verapamil containing product among the top 10 CCB medicine items dispensed from 2005 to 2008.
- Felodipine-Hexal® 5 mg was the only felodipine containing product among the top 10 CCB medicine items dispensed during the study period.
- The use of original items decreased as the use of generic items increased (Section 4.4.3) from 2005 to 2008.

4.6.2 Top 10 CCB items used according to prevalence according to patient gender

In this section the top 10 CCB items dispensed to female (Table 4.16) and male patients (Table 4.17) in a year will be tabulated separately, showing the average cost per item dispensed as well as the total number of items dispensed in the study years.

Table 4.16: Top 10 CCB items dispensed to female patients according to study years

Female																	
Year		2005				2006				2007				2008			
Registered trade name	Active ingredient	Position	Medicine items dispensed	Average cost per medicine item	SD	Position	Medicine items dispensed	Average cost per medicine item	SD	Position	Medicine items dispensed	Average cost per medicine item	SD	Position	Medicine items dispensed	Average cost per medicine item	SD
Amloc 5 mg	Amlodipine	5	11 683	102.98	18.93	1	26 272	98.74	15.44	1	34 863	104.89	19.36	1	33 060	97.52	19.78
Adalat XL 30 mg	Nifedipine	2	18 366	204.98	37.56	2	21 245	205.30	42.63	2	20 715	216.53	52.13	2	18 323	223.59	55.29
Verahexal 240 SR	Verapamil	3	14 846	100.87	24.28	4	16 185	101.46	23.18	4	15 394	109.81	25.73	3	16 543	113.15	26.49
Amloc 10 mg	Amlodipine	13	4 721	139.61	16.99	7	11 007	135.62	14.09	3	15 509	142.82	16.90	4	15 777	133.47	18.33
Cipalat Retard 20 mg	Nifedipine	4	14 315	42.36	13.60	5	15 483	42.02	13.92	6	12 372	41.37	14.20	5	15 278	45.44	14.93
Norvasc 5 mg	Amlodipine	1	23 331	138.13	26.89	3	20 509	130.97	23.79	5	14 798	135.43	29.85	6	9 243	132.96	36.32
Ciplavasc 5 mg	Amlodipine									18	2 254	102.89	12.47	7	7 766	70.78	13.03
Felodipine-Hexal 5 mg	Felodipine	9	6 134	102.99	17.26	10	7 360	102.64	18.13	8	7 758	108.97	20.91	8	7 458	112.27	22.72
Calcicard SR 240 mg	Verapamil	6	11 586	135.10	33.08	6	12 141	135.51	33.18	7	9 322	142.57	35.17	9	6 682	149.95	34.42
Adalat XL 60 mg	Nifedipine	10	6 107	267.71	30.18	11	7 019	266.27	30.20	9	7 265	280.98	37.23	10	6 482	291.37	38.02
Vascard 30 SR	Nifedipine	11	5 759	150.68	29.71	9	7 473	154.34	35.68	11	6 519	160.24	38.72	11	5 716	165.69	42.27
Ravamil SR 240 mg	Verapamil	8	6 507	136.05	34.81	12	6 690	135.29	39.43	10	6 980	142.64	37.28	12	5 588	147.63	37.69
Norvasc 10 mg	Amlodipine	7	7 686	180.89	26.72	8	7 508	172.30	21.76	12	5 631	178.37	28.84	16	3 655	176.32	38.04

With reference to Table 4.16 the following can be mentioned:

- Norvasc® the original amlodipine on the South African market and the 5 mg tablet was seen in the top position of most often dispensed CCBs in 2005 according to the PBM database used in this study. The 10 mg tablet was seen in 7th position in the same year.
- Amloc® 5 mg, the generic of Norvasc® 5 mg was ranked in the 5th place in 2005.
- Adalat® XL 30 mg was in 2nd position in 2005 but with the highest total cost of all CCBs dispensed to female patients in 2005 (Appendix Table A.2).
- Adalat® XL 60 mg was in the 10th position in 2005.
- The highest ranked verapamil containing product was Verahexal® 240 mg SR and was found in the 3rd position of total CCBs dispensed to female patients in 2005.
- In 2006 it was noted that Amloc® 5 mg replaced Norvasc® 5 mg, the original amlodipine containing product, from the 1st position and into 3rd.
- Adalat® XL 30 mg was still in the 2nd position in 2006, as seen in Table 4.16 of 2005. It is also the most expensive item on this top 10 list of CCB medicine items dispensed.
- Verahexal® moved to 4th from 3rd in 2006.
- Amloc® 10 mg, the generic of Norvasc® 10 mg, was seen one position afloat the original product in 7th position in 2006.
- Vascard® 30 SR, nifedipine containing item, made its debut on the list of top 10 items dispensed to female patients in 2006.
- Amloc® 5 mg reclaimed the 1st position in 2007 but the average cost per item increased from R 98.74 (SD = R 15.55) in 2006 to R 104.89 (SD = R 19.36) in 2007 for female patients.
- Adalat® XL 30 mg also kept the 2nd position in 2007 but the average cost per item increased by 5.2% from 2006 to 2007.
- An amlodipine generic called Amloc® 10 mg was found in 3rd position in 2007 which is higher on the top 10 items list than in 2006.
- The top selling item of 2005, Norvasc® 5 mg, dropped to 5th position in 2007 while Norvasc® 10 mg could not be seen on the top 10 list in 2007.
- Adalat® XL 60 mg made reappearance to the top 10 in 2007, costing 4.7% more than in 2005.
- Felodipine-Hexal® 5 mg moved from 10th in 2006 to 8th in 2007.
- In 2008 another amlodipine generic called Ciplavasc® 5 mg appeared the top 10 items dispensed to female patients in 7th position.

- Amloc® 10 mg moved down as Verahexal® 240 SR moved into the 3rd position in 2008, average cost increasing to R 113.15 (SD = R 25.73) per item.
- Cipalat Retard® 20 mg was in the 5th position in 2008 from the previous 6th in 2007 as the cost increased to R 44.44 (SD = R 14.93).
- Adalat® XL 60 mg was seen in 10th position in 2008.

Table 4.17: Top 10 CCB items dispensed to male patients according to study years

Male																	
Year		2005				2006				2007				2008			
Registered trade name	Active ingredient	Position	Medicine items dispensed	Average cost per medicine item	SD	Position	Medicine items dispensed	Average cost per medicine item	SD	Position	Medicine items dispensed	Average cost per medicine item	SD	Position	Medicine items dispensed	Average cost per medicine item	SD
Amloc 5 mg	Amlodipine	6	8 731	104.73	19.41	1	18 849	100.37	18.13	1	25 111	105.41	20.22	1	24 096	96.93	20.74
Cipalat Retard 20 mg	Nifedipine	2	13 091	43.55	14.22	2	15 352	43.43	14.28	4	11 264	41.65	14.42	2	17 417	47.44	15.74
Amloc 10 mg	Amlodipine	11	5 158	141.26	18.24	5	11 790	136.94	15.23	2	15 991	143.47	21.13	3	16 797	132.79	19.75
Adalat XL 30 mg	Nifedipine	3	12 425	207.68	39.64	4	14 427	207.83	39.96	3	14 636	217.03	46.39	4	12 908	222.74	51.41
Verahexal 240 SR	Verapamil	4	9 969	102.36	21.85	6	10 946	102.84	23.07	6	10 020	110.46	24.69	5	10 746	113.66	26.18
Adalat XL 60 mg	Nifedipine	8	6 196	270.78	33.74	9	7 427	268.39	28.36	7	7 509	280.69	35.49	6	6 916	289.97	37.24
Norvasc 5 mg	Amlodipine	1	16 470	139.31	27.08	3	14 546	132.85	24.81	5	10 591	136.64	31.37	7	6 769	132.59	36.08
Ciplavasc 5 mg	Amlodipine									19	1 745	103.43	10.81	8	5 897	70.90	12.18
Vascard 30 SR	Nifedipine	10	5 367	153.43	33.40	10	6 870	155.61	37.72	11	5 462	164.03	43.65	9	5 150	166.81	44.06
Felodipine-Hexal 5 mg	Felodipine	12	4 833	103.59	15.50	11	5 840	102.75	18.35	10	5 481	108.45	23.65	10	5 144	110.85	23.28
Norvasc 10 mg	Amlodipine	5	9 418	183.59	26.52	7	8 953	174.54	21.27	8	6 917	178.30	28.55	11	4 618	174.18	39.49
Zildem 180 mg SR	Diltiazem	9	5 651	181.99	25.63	12	5 347	182.23	26.50	12	5 171	192.12	31.17	12	4 440	200.01	34.93
Calcicard SR 240 mg	Verapamil	7	7 669	133.55	34.02	8	7 862	136.72	33.22	9	6 098	143.03	35.25	13	4 437	147.71	38.60

Table 4.17revealed, *inter alia*, the following:

- It was seen that 29.85% of all CCB items dispensed in 2005 were among the top 10 dispensed items for male patients (Appendix Table A.2).
- Norvasc® 5 mg was in 1st position of the top dispensed CCB for 2005 for male patients (Table 4.17) and female patients (Table 4.16)
- Cipalat® retard and Adalat® XL 30 mg are both nifedipine containing items and were in 2nd and 3rd positions respectively for male patients in 2005.
- Adalat® XL 60 mg was in the 8th position.
- Amloc® 5 mg, an amlodipine generic, was in 6th position, one position behind Norvasc® 10 mg.
- Verahexal® 240 SR was seen in 4th and Calcicard® SR 240, another verapamil containing item, was seen in 6th position.
- Vascard® 30 SR was a product not noticed on the equivalent female list for 2005 and was 10th on the list of top 10 most dispensed items to male patients.
- Amloc® 5 mg usage escalated to above those of Norvasc® 5mg to take the 1st position in 2006.
- According to the usage from 2006, it was noted that Adalat® XL 30 mg was seen in 4th while Cipalat retard® 20 mg was 2nd.
- Adalat® XL 60 mg, in 9th position in 2006, was the most expensive product, according to its average cost, on the top 10 listing with R 268.39 (SD = R 28.36) per item dispensed or R 9.22 (SD = R 0.67) per tablet (Appendix Table A.3).
- In 2006 Amloc® 10 mg was in the 5th position while Norvasc® 10mg was in 7th position. These are both amlodipine containing products.
- Two verapamil containing items could be found on the top 10 list in 2006 namely Verahexal® 240 mg SR in 6th position and Calcicard® 240 mg SR in the 8th position.

Table 4.18 also indicated that:

- Amloc® 5 mg and 10 mg were seen in 1st and 2nd positions respectively on the list of top 10 items dispensed for male patients in 2007 (Table 4.17).
- The original amlodipine containing products (Norvasc®) ranked in the 5th (5 mg) and 8th (10 mg) positions.
- Adalat® XL 30 mg moved up from 4th in 2006 to 3rd, the average cost increasing with approximately R 10 per item dispensed.

- The average cost of Cipalat Retard® 20 mg went down from R 0.82 (SD = R 0.17) per tablet in 2006 to R 0.80 (SD = R 0.13) in 2007 (Appendix Table A.4), so did the usage decline by 4 088 medicine items dispensed in 2007.
- Two verapamil containing items were found among the top 10, Verahexal® 240 mg SR in 6th position (2006 and 2007) and Calcicard® SR 240 mg in 9th position (2007). From this it was gathered that the least expensive verapamil product, according to average cost per medicine item, was dispensed relatively more often than the more expensive Calcicard®.
- Fewer Adalat® XL 30 mg items were dispensed in 2007 than in the previous year (2006) or in 2005 and could be noticed in the 4th position.
- Amloc® 10 mg had to move into 3rd to make the 2nd position available to Cipalat Retard® 20 mg in 2008.
- Adalat® XL 60 mg moved up to 6th position in 2008, costing an approximate R 9 more per item than the previous year.
- In 2008 Adco-Vascard® was back on the top 10 chart after being absent from it in 2007, positioned at 9th.
- Felodipine-Hexal® 5 mg was still in the 10th position as also seen in 2007 but the cost per item increased by 2.2% from 2007 to 2008.

Table 4.18 was drawn up from Table 4.16 and Table 4.17 to conclude the difference within the top dispensed medicine items for male and female patients during the study period. The top three CCB containing trade names were tabulated for each of the study years.

Table 4.18: Difference in the top dispensed medicine items for male and female patients during the study period

Year	Female	Position*	Male
2005	Norvasc® 5 mg	1	Norvasc® 5 mg
	Adalat® XL 30 mg	2	Cipalat® Retard 20 mg
	Verahexal® 240 SR	3	Adalat® XL 30 mg
2006	Amloc® 5 mg	1	Amloc® 5mg
	Adalat® XL 30 mg	2	Cipalat® Retard 20 mg
	Norvasc® 5mg	3	Norvasc® 5 mg
2007	Amloc® 5 mg	1	Amloc® 5 mg
	Adalat® XL 30 mg	2	Amloc® 10 mg
	Amloc® 10 mg	3	Adalat® XL 30 mg
2008	Amloc® 5 mg	1	Amloc® 5 mg
	Adalat® XL 30 mg	2	Cipalat ®Retard 20 mg
	Verahexal ®240 mg SR	3	Amloc ®10 mg

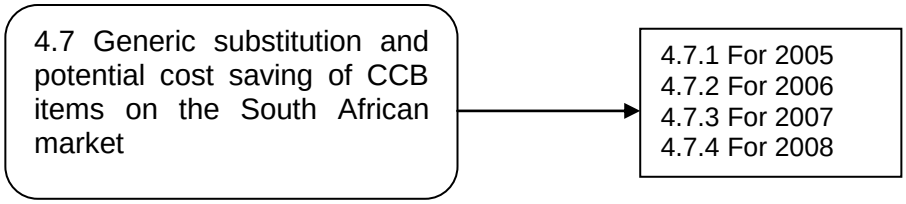
* Positions stated in Table 4.18 were taken from Table 4.16 and Table 4.17

According to Table 4.18 the top CCB items dispensed for female and male patients during the study period were the same for each of the study years although some of the items in 2nd and 3rd positions did differ. Cipalat Retard® 20 mg was more dominantly seen among the top three CCBs dispensed to male patients and Adalat® XL 60 mg as well as Verahexal® 240 mg SR were among those for the female section of Table 4.18. The differences encountered in some of the usages of the products were not further investigated in this study.

4.7 Generic substitution and potential cost saving of CCB items on the South African market

In this section the potential cost saving will be evaluated when 100% of all the original CCB items evaluated were to be substituted for different applicable generic equivalents. These scenarios should be seen in context of the year of examination. Original items were substituted for items of same strength and formulation where available as required by the MCC (2003:3). The potential cost saving by changing dosage strength e.g. by replacing a 5 mg dosage by a half of a 10 mg dosage was not considered as part of the possible cost savings evaluated in this study.

As set out in the diagram a yearly analysis of the generic substitution would be followed for analysis purposes in this study.



4.7.1 Potential cost saving of CCB items in 2005

In this section the potential cost saving as a result of generic substitution of CCB items from 1 January to 31 December 2005 will be evaluated.

Table 4.19: Potential cost saving of amlodipine containing items in 2005

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
AMLODIPINE	Norvasc 5 mg Tab	39 825	138.62	26.97	5 520 457.90	Innovator		
	Norvasc 10 mg Tab	17 127	182.36	26.65	3 123 337.31			
	Amloc 5 mg Tab	20 418	103.73	19.15	2 117 962.12	4 131 053.06	1 389 404.84	25.17%
	Amloc 10 mg Tab	9 879	140.47	17.67	1 387 717.41	2 405 854.45	717 482.86	22.97%
	Amlosyn 5 mg Tab	119	98.24	13.67	11 690.10	3 912 254.05	1 608 203.85	29.13%
	Amlosyn 10 mg Tab	49	135.42	16.82	6 635.34	2 319 254.45	804 082.86	25.74%
	Nortwin 5 mg	503	90.07	51.11	45 306.77	3 587 161.26	1 933 296.64	35.02%
	Nortwin 10 mg	218	111.61	59.81	24 331.02	1 911 547.61	1 211 789.70	38.80%

In 2005 it was noticed that Norvasc® 5 mg (the innovator amlodipine containing tablet on the market) was the CCB with the most items dispensed (Table 4.15 and Appendix Table A.2.). Norvasc® 10 mg was the item containing 10 mg amlodipine that was dispensed more often than any other 10 mg amlodipine tablet in 2005. This meant that more original amlodipine containing items were dispensed in 2005 than any of their generic equivalents. Different potential cost saving scenarios were created e.g.:

- Nortwin® 5 mg tablets posed as the least expensive 5mg amlodipine item (R 90.07 SD = R 51.11) and if all Norvasc® 5 mg items had been substituted for Nortwin® of the same strength a possible 35% (R1 933 296.64) could be saved of the total cost of Norvasc® 5 mg.
- Amloc® 5 mg feature as the amlodipine 5 mg containing item with the most items dispensed (n = 20 418) after Norvasc® 5 mg and a possible R 1 389 404.84 could potentially have been saved of total cost of Norvasc® 5 mg (R 5 520 457.90) if Amloc® 5 mg substituted Norvasc® 5 mg.
- Nortwin® 10 mg tablets featured as the least expensive 10 mg amlodipine item and if all Norvasc® 10 mg items had been substituted for Nortwin® of the same strength a possible 38.8% could have been saved of the total cost of Norvasc® 10 mg.

Table 4.20: Potential cost saving of diltiazem containing items in 2005

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
DILTIAZEM	Tilazem 60 mg Tab	689	204.95	100.84	141 212.32	Innovator		
	Tilazem 90 mg	639	257.19	87.89	164 341.55			
	Tilazem 180 CR	760	228.83	44.33	173 907.86			
	Tilazem 240 CR	194	238.14	24.85	46 199.35			
	Dilatam 60 mg Tab	1 725	84.38	28.98	145 554.33	58 137.35	83 074.97	58.83%
	Sandoz diltiazem 60 mg	2 899	71.81	25.52	208 181.80	49 478.19	91 734.13	64.96%
	Zildem 60 mg Tab	3 473	109.18	40.49	379 166.12	75 221.84	65 990.48	46.73%
	Zildem 90 mg Tab	5 233	232.38	59.65	1 216 030.01	148 489.05	15 852.50	9.65%
	Zildem 180 mg SR	10 934	181.40	25.07	1 983 379.68	137 860.67	36 047.19	20.73%
	Zildem 240 mg SR	4 660	179.70	14.45	837 413.58	34 862.28	11 337.07	24.54%

More generic equivalents of items containing diltiazem were dispensed than the original products in 2005. Possible cost saving scenarios were created to show potential savings e.g.:

- A potential saving of approximately 65% (R 91 734.13) off the total cost of Tilazem® 60 mg could be saved if Tilazem® 60 mg could be substituted for Sandoz® diltiazem 60 mg.
- If all Tilazem® 60 mg items were substituted with a generic item called Dilatam® 60 mg, more than half of the total cost of Tilazem® 60 mg (58.8%) could be saved.
- Zildem® is the only generic on the market containing 90 mg, 180 mg and 240 mg diltiazem and potential R 15 852.50, R 36 047.19 and R 11 337.07 could be saved respectively off the cost of Tilazem® if the original could be substituted for the corresponding strength of the generic item Zildem®.

Table 4.21: Potential cost saving of felodipine containing items in 2005

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
FELODIPINE	Plendil 2.5 mg Tab	5 160	172.62	28.98	890 712.04	No generic available		
	Plendil 5 mg Tab	7 100	204.73	33.28	1 453 591.74	Innovator		
	Plendil 10 mg Tab	2 410	249.00	31.11	600 085.53			
	Felodipine-Hexal 5 mg Tab	10 967	103.26	16.51	1 132 403.19	733 114.13	720 477.61	49.57%
	Felodipine-Hexal 10 mg Tab	2 744	140.31	17.96	384 997.51	338 135.57	261 949.96	43.65%

Felodipine-Hexal® 5 mg was responsible for selling 10 967 items in 2005, the highest quantity of items dispensed any felodipine containing product and was seen in the 10th position on the list of top CCB medicine items mostly dispensed in 2005 (Table 4.15). Some potential cost saving scenarios were created to illustrate the cost saving potential of felodipine generic substitution e.g.:

- A potential 49.6% off the cost of Plendil® 5 mg could be saved if it had been substituted for Felodipine-Hexal® 5 mg.
- A potential R 261 949.96 could be saved on the cost of Plendil® 10 mg if it should be substituted for Felodipine-Hexal® 10 mg.
- There was no generic for Plendil® containing 2.5 mg felodipine.

Table 4.22: Potential cost saving of nifedipine containing items in 2005

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
NIFEDIPINE	Adalat 5 mg Cap	301	113.65	95.85	34 208.74	Innovator		
	Adalat 10 mg Cap	533	154.93	175.39	82 576.04			
	Adalat Retard 10 mg	623	184.76	78.34	115 103.48	No generic substitution on extended or sustained release nifedipine formulations (MCC 2003:3)		
	Adalat Retard 20 mg	917	325.98	105.60	298 919.22			
	Adalat XL 30 mg Tab	30 814	206.06	38.42	6 349 524.99			
	Adalat XL 60 mg Tab	12 313	269.24	32.05	3 315 190.96			
	A-Lennon nifedipine 5 mg	1	16.69		16.69	5 023.69	29 185.05	85.31%
	Cardifen TM 5 mg Cap	1 437	54.16	28.60	77 825.03	16 301.55	17 907.19	52.35%
	Cardifen TM 10 mg Cap	1 940	84.73	42.19	164 380.30	45 162.22	37 413.82	45.31%
	Cipalat Retard 20 mg	27 409	42.93	13.91	1 176 686.07			
	Nifedalat 10 mg Cap	975	41.73	21.64	40 686.98	22 242.22	60 333.82	73.06%
	Nifedalat 20 mg SR Tab	5 501	33.15	12.56	182 363.79			
	Sandoz nifedipine 10 mg	581	86.96	40.47	50 525.47	46 351.25	36 224.79	43.87%
	Vascard 30 mg SR	11 126	152.01	31.57	1 691 219.93			

Extended or sustained release nifedipine containing products are not allowed to be substituted according to the Medicines Control Council of South Africa (MCC, 2003:3). Adalat® XL 30 mg was the nifedipine containing product with the most units dispensed in 2005 (Appendix Table A.2). Some cost saving scenarios were created to show potential savings e.g.:

- According to the data 85.3% (R 29 185.05) could be saved off the total cost of Adalat® 5 mg (R 34 208.74) by substituting it for A-Lennon® nifedipine 5 mg. Only 1 item was dispensed in 2005 and it was not repeated in the data of 2006 onwards.
- A possible R 17 907.19 could be saved off the total cost of Adalat® 5 mg if all the Adalat® 5 mg tablets dispensed in 2005 had been substituted for Cardifen® 5 mg.
- If all Adalat® 10 mg items were substituted for Nifedalat® 10 mg, a saving of 73% (R 60 333.82) could be generated off the cost of Adalat® 10 mg (R 82 576.04).
- The smallest potential saving (43.87%) was seen with Adalat® 10 mg substituted for Sandoz® nifedipine 10 mg.

Table 4.23: Potential cost saving of verapamil containing items in 2005

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
VERAPAMIL	Isoptin 40 mg Tab	785	53.53	31.08	42 024.95	Innovator		
	Isoptin 80 mg Tab	14	147.91	78.72	2 070.74			
	Isoptin SR 240 mg Tab	3 182	140.62	40.00	447 460.44			
	Isoptin 5 mg/2 ml Inj	8	33.96	23.17	271.70			
	Calcicard SR 240 mg	19 264	134.48	33.46	2 590 537.72	427 901.32	19 559.12	4.37%
	Ravamil SR 240 mg	10 864	135.00	35.45	1 466 680.92	429 581.99	17 878.45	4.00%
	Sandoz verapamil HCl 40 mg	1 280	31.02	14.43	39 709.56	24 353.13	17 671.82	42.05%
	Sandoz verapamil HCl 80 mg	1 014	57.86	18.11	58 671.40	810.06	1 260.68	60.88%
	Sandoz verapamil HCl 120 mg	575	77.14	29.96	44 355.68			
	Vasomil 40 mg Tab	3 765	25.00	10.20	94 130.28	19 626.10	22 398.85	53.30%
	Vasomil 80 mg Tab	2 888	54.82	19.86	158 324.90	767.50	1 303.24	62.94%
	Verahexal 240 mg SR	24 815	101.47	23.35	2 518 002.35	322 880.66	124 579.78	27.84%

More generic equivalents than original verapamil containing items were dispensed in 2005. Verahexal® 240 mg SR and Calcicard® SR 240 mg are both generic products of Isoptin® SR 240 mg and were among the top verapamil containing products dispensed in 2005 and could be found at 4th and 6th position among the top 10 CCBs dispensed in 2005 (Table 4.17). There was no Isoptin® 120 mg found on the medicines claims database in 2005. Different potential cost saving scenarios were created e.g.:

- A relatively small saving of 4% could be made off the cost of Isoptin® SR 240 mg when substituting all the Isoptin® SR 240 items for Ravamil® SR 240 mg.
- The biggest saving with a 240 mg slow release verapamil product could be achieved by substituting with Verahexal® 240 mg SR (27.8%).
- A 63% (R 1 303.24) potential saving off the cost of Isoptin 80 mg could be achieved when substituting it for Vasomil® 80 mg.
- A potential R 22 398.85 saving could be achieved when substituting Isoptin® 40 mg for the Vasomil® product of the same strength.
- Sandoz® verapamil HCl 40 mg and 80 mg could also result in relatively high savings (42.05% and 60.9% respectively) when used for substituting originals.

Table 4.24: CCB items of 2005 without generic equivalents on the market

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)
ISRAPIDINE	Dynacirc 2.5 mg Tab	974	164.18	53.15	159 910.64
	Dynacirc SRO 5 mg Cap	5 100	243.13	49.95	1 239 959.94
LERCANIDIPINE	Zanidip 10 mg Tab	1 527	148.85	26.81	227 292.82
NISOLDIPINE	Syscor-CC 20 mg	7	297.73	0.00	2 084.11

Every year items without generics could be listed. There were four such items in 2005.

- The most expensive one of them was Syscor-CC® 20 mg at R 297.73 per item.
- The highest total cost of a product without an equivalent on the market in 2005 could be seen for an isradipine containing product called Dynacirc® SRO 5 mg with R 1 239 959.94.

4.7.2 Potential cost saving of CCB items in 2006

In this section the potential cost saving with generic substitution of CCB items from 1 January to 31 December 2006 will be evaluated.

Table 4.25: Potential cost saving of amlodipine containing items in 2006

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
AMLODIPINE	Norvasc 5 mg Tab	35 076	131.75	24.23	4 621 227.02	Innovator		
	Norvasc 10 mg Tab	16 476	173.52	21.52	2 858 890.03			
	Amlate 5 mg Tab	3	93.69	1.53	281.06	3 286 153.52	1 335 073.50	28.89%
	Amlate 10 mg Tab	3	118.95	14.99	356.84	1 959 765.28	899 124.75	31.45%
	Amloc 5 mg Tab	45 129	99.42	16.64	4 486 700.61	3 487 236.82	1 133 990.20	24.54%
	Amloc 10 mg Tab	22 797	136.30	14.70	3 107 299.00	2 245 727.87	613 162.16	21.45%
	Amlosyn 5 mg Tab	1 213	99.78	18.43	121 031.73	3 499 842.51	1 121 384.51	24.27%
	Amlosyn 10 mg Tab	620	137.00	11.78	84 940.92	2 257 236.45	601 653.58	21.05%
	Nortwin 5 mg	5	0.01	0.00	0.05			
	Nortwin 10 mg	5	0.01	0.00	0.05			
	Sandoz-amlodipine 10 mg	2	144.04	0.00	288.08	2 373 203.04	485 686.99	16.99%

Amloc® 5 mg was the amlodipine containing product dispensed the most often in 2006. Amloc® 5 mg was also part of the top list of CCBs dispensed in 2006. Possible cost saving scenarios were created to show potential savings e.g.:

- Nortwin® 5 mg and 10 mg were left out of the potential percentage saving equations as R 0.05 for an item sounds impossible as they cost R 90.07 (SD = R 51.55) for the 5 mg per item and R 111.61 (SD = R 59.81) for the 10 mg item in 2005.
- A potential saving of 29% (R 1 335 073.50) could be achieved off the total cost of Norvasc® 5 mg if it had been substituted for Amlate® 5 mg.
- A 31.5% (R 899 124.75) potential saving could occur if all the Norvasc® 10 mg should be substituted for the Amlate® of the same strength.
- Sandoz® amlodipine 10 mg shows the smallest saving of 17% (R 485 686.99) if it were to be used for substituting Norvasc® 10 mg.

Table 4.26: Potential cost saving of diltiazem containing items in 2006

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
DILTIAZEM	Tilazem 60 mg	629	200.74	96.13	126 265.55	Innovator		
	Tilazem 90 mg	492	254.77	87.47	125 347.03			
	Tilazem 180 CR	622	225.64	47.51	140 346.60			
	Tilazem 240 CR	147	226.90	47.73	33 354.07			
	Dilatam 60 mg Tab	1 770	83.57	30.44	147 919.51	52 565.75	73 699.80	58.37%
	Sandoz diltiazem 60 mg	3 300	71.38	25.88	235 551.73	44 897.59	81 367.96	64.44%
	Zildem 60 mg Tab	3 274	104.63	39.75	342 547.17	65 810.07	60 455.48	47.88%
	Zildem 90 mg Tab	4 884	231.84	59.35	1 132 315.31	114 066.16	11 280.87	9.00%
	Zildem 180 mg SR	10 464	181.03	23.78	1 894 249.21	112 597.76	27 748.84	19.77%
	Zildem 240 mg SR	4 291	179.20	20.04	768 939.93	26 342.15	7 011.92	21.02%

Zildem® 180 mg SR was the diltiazem containing product with the most items dispensed in 2006 (Appendix Table A.3). Scenarios were created to show some cost saving potential of generic substitution e.g.:

- If all the Tilazem® 180 CR items had been substituted for Zildem® 180 mg SR a potential saving of R 27 748.84 could be generated.
- The highest potential saving (64.44%) could be generated when substituting all Tilazem® 60 mg items for Sandoz® diltiazem 60 mg.
- Substituting Tilazem® 90 mg for Zildem® 90 mg could generate a saving of R 11 280.87 off the original total cost of R 125 347.03 of Tilazem® 90 mg.

Table 4.27: Potential cost saving of felodipine containing items in 2006

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
FELODIPINE	Plendil 2.5 mg Tab	4 682	174.14	32.52	815 308.68	No generic available		
	Plendil 5 mg Tab	4 948	202.73	36.49	1 003 105.15	Innovator		
	Plendil 10 mg Tab	1 558	246.92	34.56	384 696.49			
	Felodipine-Hexal 5 mg Tab	13 200	102.69	18.23	1 355 480.75	508 099.91	495 005.24	49.35%
	Felodipine-Hexal 10 mg Tab	4 526	140.69	19.08	636 768.35	219 196.88	165 499.61	43.02%

Felodipine-Hexal® 5 mg was the felodipine containing item with the most items dispensed in 2006 and could be seen in the 11th position on the top list of CCB dispensed list for 2006. Some potential cost saving scenarios were created to illustrate the cost saving potential of felodipine generic substitution e.g.:

- Felodipine-Hexal® 5 mg and 10 mg are the only generics on the South African market. A potential saving of 49.35% off the Plendil® 5 mg could be generated through generic substitution.
- A potential R 165 499.61 could be saved off the total cost of Plendil® 10 mg (R 384 696.49) if substituting for Felodipine-Hexal® 10 mg.

Table 4.28: Potential cost saving of nifedipine containing items in 2006

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
NIFEDIPINE	Adalat 5 mg Cap	188	109.94	118.67	20 668.53	Innovator		
	Adalat 10 mg Cap	455	106.05	149.34	48 253.63			
	Adalat Retard 10 mg	507	171.77	79.93	87 085.66	No generic substitution on extended or sustained release nifedipine formulations (MCC 2003:3)		
	Adalat Retard 20 mg	555	303.07	115.46	168 202.22			
	Adalat XL 30 mg Tab	35 687	206.32	41.58	7 362 957.79			
	Adalat XL 60 mg Tab	14 458	267.35	29.28	3 865 350.60			
	Cardifen TM 5 mg Cap	1 450	51.25	26.90	74 316.41	9 635.51	11 033.02	53.38%
	Cardifen TM 10 mg Cap	1 765	83.60	45.31	147 548.69	38 036.63	10 217.00	21.17%
	Cipalat Retard 20 mg	30 835	42.72	14.12	1 317 376.31			
	Nifedalat 10 mg Cap	931	37.03	20.12	34 474.21	16 848.30	31 405.33	65.08%
	Nifedalat 20 SR Tab	6 405	34.04	13.21	218 019.74			
	Sandoz nifedipine 10 mg	370	87.96	44.95	32 546.62	40 023.55	8 230.08	17.06%
	Vascard 30 SR	14 343	154.95	36.67	2 222 404.86			

No extended or sustained release nifedipine tablets are allowed to be substituted (MCC, 2003:3). Adalat® XL 30 mg is an extended release tablet and was the best selling nifedipine containing item in 2006 with a total of 35 687 items dispensed. Adalat® XL 30 mg could be seen in the 15th position on the list of the top CV items dispensed in 2006. Some cost saving could be achieved with generic substitution of the more expensive innovator drugs as shown by means of the following scenarios:

- A potential 65% saving off the total cost of Adalat® 10 mg could be achieved when Adalat® 10 mg should be substituted for Nifedalat® 10 mg.
- Substitution of Adalat® 5 mg with Cardifen® TM 5 mg could potentially result in a saving of R 11 033.02, a 53.4% saving off the total cost of Adalat® 5 mg.

Table 4.29: Potential cost saving of verapamil containing items in 2006

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
VERAPAMIL	Isoptin 40 mg Tab	829	60.12	87.42	49 835.74	Innovator		
	Isoptin 80 mg Tab	5	164.06	56.43	820.31			
	Isoptin SR 240 mg Tab	3 378	138.91	38.47	469 236.94			
	Isoptin 5 mg/2 ml Inj	11	143.22	380.06	1 575.41			
	Calcicard SR 240 mg	20 013	136.00	33.20	2 721 761.42	459 406.89	9 830.05	2.09%
	Ravamil SR 240 mg	11 231	134.91	37.20	1 515 120.42	455 709.80	13 527.14	2.88%
	Sandoz verapamil HCl 40 mg	1 213	31.15	13.40	37 789.82	25 826.68	24 009.06	48.18%
	Sandoz verapamil HCl 80 mg	1 015	61.20	18.45	62 115.22	305.99	514.32	62.70%
	Sandoz verapamil HCl 120 mg	490	76.78	33.36	37 623.11			
	Vasomil 40 mg Tab	3 712	23.93	9.85	88 826.90	19 837.69	29 998.05	60.19%
	Vasomil 80 mg Tab	2 666	55.95	20.87	149 159.06	279.74	540.57	65.90%
	Vasomil 5 mg/2 ml Inj	2	38.31	20.23	76.61	421.36	1 154.06	73.25%
	Verahexal 240 mg SR	27 131	102.02	23.14	2 767 818.78	344 612.87	124 624.07	26.56%

Verahexal® 240 SR was the verapamil containing product in 2006 with the most items dispensed (n = 27 131). More verapamil containing generics were dispensed than innovators. It was seen that the number of Verahexal® 240 mg SR items dispensed was eight times more than the innovator called Isoptin® SR 240 mg (n = 3 378). Different scenarios were created to show potential cost saving with generic substitution e.g.:

- A potential saving of 26.56% could be generated by substituting Isoptin® SR 240 mg for Verahexal® 240 mg SR.
- A 73.25% saving could potentially be saved if the Isoptin® injection were to be substituted for the Vasomil® injection.
- A potential saving of R 29 998.05 could be possible if all the Isoptin® 40 mg items were substituted for Vasomil® 40 mg.
- If Isoptin® 80 mg could be substituted for Vasomil® of the same strength a potential 65.9% of its total cost could be saved.

Table 4.30: CCB items of 2006 without generic equivalents on the market

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)
ISRAPIDINE	Dynacirc SRO 5 mg Cap	4 327	242.21	52.09	1 048 063.45
	Dynacirc 2.5 mg Tab	755	166.64	55.47	125 811.36
LERCANIDIPINE	Zanidip 10 mg Tab	5 617	151.21	34.26	849 341.98

Every year items without generics could be listed. Three such items existed in 2006.

- Syscor-CC® 20 mg, a nisoldipine containing product disappeared off the list of items without generics in 2006.
- The most expensive one of them was Dynacirc® SRO 5 mg at R 242.21 (SD = R 52.09) per item.
- The highest total cost of a product without a generic equivalent in 2007 could be seen with an isradipine containing product called Dynacirc® SRO with R 1 048 063.45.
- Zanidip® 10 mg, a lercanidipine containing product, was also seen without any generics on the South African market.

4.7.3 Potential cost saving of CCB items in 2007

In this section the potential cost saving with generic substitution of CCB items from 1 January to 31 December 2007 will be evaluated.

Table 4.31: Potential cost saving of amlodipine containing items in 2007

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
AMLODIPINE	Norvasc 5 mg Tab	25 396	135.94	30.49	3 452 238.03	Innovator		
	Norvasc 10 mg Tab	12 556	178.33	28.67	2 239 164.80			
	Almadin 5 mg Tab	680	67.28	13.07	45 753.66	1 708 764.63	1 743 473.40	50.50%
	Almadin 10 mg Tab	391	98.19	12.87	38 390.58	1 232 818.73	1 006 346.07	44.94%
	Amlate 5 mg Tab	63	81.55	15.08	5 137.55	2 071 003.49	1 381 234.54	40.01%
	Amlate 10 mg Tab	58	116.28	19.59	6 744.52	1 460 072.30	779 092.50	34.79%
	Amloc 5 mg Tab	59 987	105.10	19.73	6 304 645.67	2 669 124.67	783 113.36	22.68%
	Amloc 10 mg Tab	31 500	143.15	19.17	4 509 209.64	1 797 385.28	441 779.52	19.73%
	Amlodac 5 mg Tab	130	77.95	17.07	10 133.74	1 979 665.08	1 472 572.95	42.66%
	Amlodac 10 mg Tab	75	111.91	19.80	8 393.21	1 405 135.26	834 029.54	37.25%
	Amlosyn 5 mg Tab	1 321	107.16	24.05	141 561.45	2 721 494.76	730 743.27	21.17%
	Amlosyn 10 mg Tab	558	144.80	14.30	80 800.26	1 818 150.65	421 014.15	18.80%
	Austell amlodipine 5 mg Tab	138	89.36	19.87	12 331.95	2 269 436.25	1 182 801.78	34.26%
	Austell amlodipine 10 mg Tab	113	121.17	22.07	13 692.47	1 521 439.41	717 725.39	32.05%
	Calbloc 5mg Tab	115	88.16	29.25	10 138.61	2 238 957.74	1 213 280.29	35.14%
	Calbloc 10 mg Tab	46	128.03	23.49	5 889.56	1 607 593.81	631 570.99	28.21%
	Ciplavasc 5 mg Tab	3 999	68.12	11.57	272 410.72	1 729 968.15	1 722 269.88	49.89%
	Ciplavasc 10 mg Tab	2 502	103.16	11.69	258 096.99	1 295 230.14	943 934.66	42.16%
	Corvadil 5 mg Tab	135	68.55	30.63	9 254.87	1 741 012.43	1 711 225.60	49.57%
	Corvadil 10 mg Tab	92	88.41	35.64	8133.48	1 110 043.21	1 129 121.59	50.43%
	Cpl Alliance amlodipine 5 mg	13	76.10	34.83	989.27	1 932 576.99	1 519 661.04	44.02%
	Cpl Alliance amlodipine 10 mg	11	116.97	33.97	1 286.70	1 468 709.56	770 455.24	34.41%
	Indo amlodipine 5 mg Tab	1	138.01		138.01	3,504,901.96	-52,663.93	-1.53%
	Klodip-5 mg Tab	661	80.55	20.34	53 244.51	2 045 684.68	1 406 553.35	40.74%
	Lomanor 5 mg Tab	889	97.55	26.21	86 724.72	2 477 458.93	974 779.10	28.24%
	Lomanor 10 mg Tab	403	129.99	34.29	52 387.09	1 632 189.34	606 975.46	27.11%
	Sandoz amlodipine 5 mg Tab	559	105.76	21.84	59 118.12	2 685 802.82	766 435.21	22.20%
	Sandoz amlodipine 10 mg Tab	518	145.43	12.36	75 334.21	1 826 054.71	413 110.09	18.45%

In 2007 it was noticed that Amloc® 5 mg (a generic amlodipine containing tablet) was the CCB with the most items dispensed (Table 4.15). From Table 4.31 it was seen that a

relatively large number of amlodipine generics entered the market in 2007. It was also noted that more Amloc® 5 mg and 10 mg (the generic equivalent) were dispensed as the original Norvasc® of the same strength. Different potential cost saving scenarios were created e.g.:

- It was also noticed that there was one Indo®-amlodipine 5 mg item dispensed but at a cost higher than the average cost of Norvasc® 5 mg (R 135.94 SD = R 30.49).
- Amloc 5mg, the Norvasc® 5 mg generic with the largest number of items dispensed in 2007 was only 22.7% cheaper than the innovator product.
- The biggest potential saving with a 5 mg product could be achieved when substituting Norvasc® 5 mg for Almadin® 5 mg.
- An amount of R 1 129 121.59 could potentially be saved with the substitution of all Norvasc® 10 mg items for Corvadil® 10 mg (50.43%).
- In 2007, only one Indo® amlodipine 5 mg medicine item was dispensed. This item had a higher cost than the average cost per medicine item of the innovator (Norvasc® 5 mg).

Table 4.32: Potential cost saving of diltiazem containing items in 2007

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
DILTIAZEM	Tilazem 60 mg Tab	535	210.63	129.10	112 688.62	Innovator		
	Tilazem 90 mg Tab	447	255.01	91.16	113 990.87			
	Tilazem 180 CR	521	233.97	43.45	121 896.85			
	Tilazem 240 CR	156	244.74	58.62	38 179.59			
	Dilatam 60 mg Tab	1 682	88.08	32.09	148 152.68	47 123.47	65 565.15	58.18%
	Sandoz diltiazem 60mg	2 345	74.67	28.54	175 104.16	39 949.14	72 739.48	64.55%
	Zildem 60 mg Tab	2 891	108.00	40.98	312 224.46	57 779.34	54 909.28	48.73%
	Zildem 90 mg Tab	4 039	246.88	66.25	997 140.19	110 354.46	3 636.41	3.19%
	Zildem 180 mg SR	10 203	191.30	27.82	1 951 870.05	99 669.15	22 227.70	18.23%
	Zildem 240 mg SR	3 902	189.23	22.93	738 375.07	29 519.86	8 659.73	22.68%

Zildem® 180 mg SR was the diltiazem containing item with the most items dispensed in 2007 and could be seen in the 13th position of the top CCB items dispensed in 2007. Some scenarios were created to calculate the potential cost saving opportunities with generic substitution:

- If Zildem® 180 mg SR were to be used to substitute Tilazem® 180 CR a potential amount of R 22 227.70 could be saved.
- A saving of 64.55% could be attained if Sandoz® diltiazem 60 mg could be used for substituting Tilazem® 60 mg.
- Approximately 10% of patients using a 90 mg diltiazem product were using the innovator Tilazem® 90 mg and if these patients had used Zildem® 90 mg instead of the innovator a 3.2% (R 3 636.41) reduction in the treatment cost could have been achieved.

Table 4.33: Potential cost saving of felodipine containing items in 2007

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
FELODIPINE	Plendil 2.5 mg Tab	3 989	182.90	39.28	729 597.00	No generic available		
	Plendil 5 mg Tab	3 548	210.58	46.36	747 147.74	Innovator		
	Plendil 10 mg Tab	1 185	254.90	50.14	302 050.67			
	Felodipine-Hexal 5 mg Tab	13 239	108.76	22.09	1 439 820.31	385 866.19	361 281.55	48.35%
	Felodipine-Hexal 10 mg Tab	4 754	148.59	20.31	706 373.33	176 073.28	125 977.39	41.71%

Felodipine-Hexal® 5 mg was the felodipine containing item of which there were 13 239 items dispensed in 2007, the highest quantity of any felodipine containing product dispensed in 2007. Some scenarios were created to show potential cost saving with felodipine generic substitution:

- If Felodipine-Hexal® 5 mg had been used to substitute Plendil® 5 mg, a potential amount of R 361 281.55 could be saved, which would be 48.35% of the total cost of Plendil® 5 mg in 2007.
- A possible saving of R 125 977.39 could be made by substituting Plendil® 10 mg for Felodipine-Hexal® 10 mg.

Table 4.34: Potential cost saving of nifedipine containing items in 2007

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
NIFEDIPINE	Adalat 5 mg Cap	45	55.14	76.41	2 481.52	Innovator		
	Adalat 10 mg Cap	215	46.84	93.38	10 069.68			
	Adalat Retard 10 mg	565	145.91	102.87	82 440.58	No generic substitution on extended or sustained release nifedipine formulations (MCC 2003:3)		
	Adalat Retard 20 mg	411	281.41	127.36	115 658.27			
	Adalat XL 30 mg Tab	35 359	216.74	49.82	7 663 566.38			
	Adalat XL 60 mg Tab	14 778	280.83	36.35	4 150 072.39			
	Bio-nifedipine 5 mg	5	30.20	32.93	151.00	1 359.00	1 122.52	45.24%
	Bio-nifedipine 10 mg	14	21.99	19.89	307.82	4 727.24	5 342.44	53.05%
	Cardifen TM 5 mg Cap	1 202	53.56	30.19	64 374.99	2 410.05	71.47	2.88%
	Cardifen TM 10 mg Cap	1 554	77.54	45.80	120 491.50	16 670.32	-6 600.64	-65.55%
	Cipalat Retard 20 mg	23 636	41.50	14.30	980 968.20			
	Nifedalat 10 mg Cap	758	39.17	23.73	29 693.52	8 422.30	1 647.38	16.36%
	Nifedalat 20 SR Tab	4 269	37.23	14.09	158 949.39			
	Sandoz nifedipine 10 mg	41	79.75	48.23	3 269.67	17 145.83	-7 076.15	-70.27%
	Vascard 30 SR	11 981	161.97	41.08	1 940 565.83			

An interesting fact noticed was that even though the average cost of the innovator Adalat® 10 mg (R 46.84 SD = R 93.38) was lower than some of the generics (Cardifen® 10 mg and Sandoz® nifedipine 10 mg) Cardifen® 10 mg (R 77.54 SD = R 45.80) still dispensed more items than Adalat® 10 mg. Extended or sustained release nifedipine containing products are not allowed to be substituted according to the Medicines Control Council of South Africa (MCC, 2003:3). Some cost saving scenarios with generic substitution were shown of nifedipine containing medicine items:

- A possible 53.1% could be saved if Bio-nifedipine® 10 mg could be used as a generic substitute for Adalat® 10 mg, although only 14 items were dispensed in 2007.
- More Cardifen® 5 mg (n = 1 202) items were dispensed even though Bio-nifedipine® (n = 5) was the least expensive 5 mg generic on the market.

Table 4.35: Potential cost saving of verapamil containing items in 2007

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
VERAPAMIL	Isoptin 40 mg Tab	620	61.19	35.87	37 937.90	Innovator		
	Isoptin SR 240 mg Tab	3 078	147.91	41.83	455 254.74			
	Isoptin 5 mg/2ml Inj	4	28.07	32.57	112.27			
	Calcicard SR 240 mg	15 426	142.74	35.21	2 201 939.45	439 360.15	15 894.59	3.49%
	Ravamil SR 240 mg	11 662	141.59	36.72	1 651 212.18	435 811.28	19 443.46	4.27%
	Sandoz verapamil HCl 40 mg	705	30.72	13.60	21 656.08	19 045.06	18 892.84	49.80%
	Sandoz verapamil HCl 80 mg	448	61.61	19.20	27 601.10			
	Sandoz verapamil HCl 120 mg	407	75.60	28.32	30 768.09			
	Vasomil 40 mg Tab	2 901	25.77	10.72	74 750.98	15 975.74	21 962.16	57.89%
	Vasomil 80 mg Tab	2 096	58.12	23.13	121 816.74			
	Vasomil 5 mg/2ml Inj	1	0.00		0.00			
	Verahexal 240 mg SR	25 414	110.06	25.33	2 797 106.82	338 769.76	116 484.98	25.59%

Isoptin® 80 mg was apparently discontinued in the year 2007, as it was not seen on the medicine claims database, and joined Isoptin® 120 mg on the discontinued list. No potential cost saving were calculated for the generic equivalents of these discontinued products for the year 2007.

More generic equivalents than original verapamil containing items were dispensed in 2007. Verahexal® 240 mg SR is a generic equivalent of Isoptin® SR 240 mg and could be found among the top verapamil containing products dispensed in 2007 and was found in 4th among the top CCBs dispensed in 2007 (Table 4.17). Different potential cost saving scenarios were created for verapamil containing medicine items:

- There were two generic products for possible generic substitution of Isoptin® 40 mg. The biggest potential saving was with substituting the innovator for Vasomil® 40 mg.
- Verahexal® 240 mg SR dispensed the most items in 2007 for any verapamil containing product and has the potential of saving 25.6% when used for substituting Isoptin® SR 240 mg.

Table 4.36: CCB items of 2007 without generic equivalents on the market

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)
ISRAPIDINE	Dynacirc SRO 5 mg Cap	3 389	254.49	61.85	862 454.98
	Dynacirc 2.5 mg Tab	512	176.65	70.79	90 445.96
LERCANIDIPINE	Zanidip 10 mg Tab	7 941	160.37	36.08	1 273 502.45
	Zanidip 20 mg Tab	266	201.03	26.56	53 474.74

Isradipine and lercanidipine are the pharmacological active ingredients in 2007 without generic equivalents on the market.

- Zanidip® 10 mg (n = 7 941) were mostly prescribed at an average cost per item of R160.37 (SD = R 36.08) and a total cost of R 1 273 502.45.
- The most expensive item in this table (Table 4.36) is Dynacirc® SRO 5 mg at an average cost per item of R 254.49 (SD = R 61.85).

4.7.4 Potential cost saving of CCB items in 2008

In this section the potential cost saving with generic substitution of CCB items from 1 January to 31 December 2008 will be evaluated.

Table 4.37: Potential cost saving of amlodipine containing items in 2008

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
AMLODIPINE	Norvasc 5 mg Tab	16 012	132.80	36.22	2 126 413.90	Innovator		
	Norvasc 10 mg Tab	8 273	175.13	38.87	1 448 826.76			
	Almadin 5 mg Tab	1 939	69.39	12.20	134 556.18	1 111 146.75	1 015 267.15	47.75%
	Almadin 10 mg Tab	1 385	103.03	8.64	142 700.84	852 392.82	596 433.94	41.17%
	Amlate 5 mg Tab	430	65.29	12.36	28 075.70	1 045 460.72	1 080 953.18	50.83%
	Amlate 10 mg Tab	380	105.35	7.94	40 033.52	871 571.87	577 254.89	39.84%
	Amloc 5 mg Tab	57 156	97.27	20.19	5 559 824.67	1 557 560.23	568 853.67	26.75%
	Amloc 10 mg Tab	32 574	133.12	19.08	4 336 209.18	1 101 291.17	347 535.59	23.99%
	Amlodac 5 mg Tab	250	68.22	15.08	17 054.92	1 092 333.52	1 034 080.38	48.63%
	Amlodac 10 mg Tab	228	104.89	16.86	23 915.60	867 779.64	581 047.12	40.10%
	Amlosyn 5 mg Tab	620	108.96	20.90	67 556.53	1 744 701.87	381 712.03	17.95%
	Amlosyn 10 mg Tab	232	144.42	22.28	33 504.87	1 194 766.33	254 060.43	17.54%
	Austell amlodipine 5mg Tab	876	66.71	13.60	58 437.98	1 068 160.89	1 058 253.01	49.77%
	Austell amlodipine 10mg Tab	615	100.49	12.50	61 801.73	831 358.88	617 467.88	42.62%
	Calbloc 5 mg Tab	203	70.98	16.35	14 407.93	1 136 452.09	989 961.81	46.56%
	Calbloc 10 mg Tab	155	101.88	18.27	15 791.09	842 836.69	605 990.07	41.83%
	Ciplavasc 5 mg Tab	13 663	70.84	12.67	967 822.31	1 134 214.36	992 199.54	46.66%
	Ciplavasc 10 mg Tab	8 220	107.00	10.82	879 577.16	885 248.40	563 578.36	38.90%
	Corvadil 5 mg Tab	137	80.94	21.77	11 089.11	1 296 049.85	830 364.05	39.05%
	Corvadil 10 mg Tab	114	120.99	15.48	13 792.42	1 000 918.34	447 908.42	30.92%
	CPL Alliance amlodipine 5mg	211	58.43	21.00	12 328.23	935 543.22	1 190 870.68	56.00%
	CPL Alliance amlodipine 10mg	170	93.09	27.88	15 825.32	770 134.54	678 692.22	46.84%
	Indo amlodipine 5 mg Tab	644	66.77	15.33	42 998.40	1 069 084.44	1 057 329.46	49.72%
	Klodip-5 mg	1 886	70.55	15.01	133 061.83	1 129 685.06	996 728.84	46.87%
	Lomanor 5 mg Tab	5 105	96.22	18.76	491 183.82	1 540 614.17	585 799.73	27.55%
	Lomanor 10 mg Tab	2 457	130.93	21.60	321 697.73	1 083 193.05	365 633.71	25.24%
	PharmaDynamics amlodipine besilate 10 mg	300	86.78	23.36	26 033.12	717 906.67	730 920.09	50.45%
	Sandoz amlodipine 5 mg Tab	880	71.80	20.81	63 180.05	1 149 589.73	976 824.17	45.94%
	Sandoz amlodipine 10 mg Tab	907	106.60	25.21	96 683.47	881 876.90	566 949.86	39.13%

Even more amlodipine products were marketed in 2008 than in 2007. Some scenarios were created to show the cost saving potential of generic substitution:

- It appeared that generic substitution for the different Amloc® equivalents would not result in significantly big cost saving.
- A product even less expensive than Amlate® 5 mg was seen on the 2008 database. It was called CPL Alliance® amlodipine 5 mg. It had a cost of R 58.43 (SD = R 21.00) per item and it is more than half the cost (56%) of Norvasc® 5 mg.
- PharmaDynamics® amlodipine besilate 10 mg was 50.45% less expensive than Norvasc® 10mg and would result in the biggest saving if Norvasc® 10 mg were to be substituted for it.
- The smallest potential saving could be achieved with substitution of the innovator for an Amlosyn® generic in the case of the 5 mg and 10 mg product.

Table 4.38: Potential cost saving of diltiazem containing items in 2008

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
DILTIAZEM	Tilazem 60 mg Tab	718	193.04	89.66	138 603.14	Innovator		
	Tilazem 90 mg Tab	301	254.19	99.95	76 510.74			
	Tilazem 180 CR	484	245.69	103.80	118 913.62			
	Tilazem 240 CR	153	246.83	32.09	37 765.53			
	Dilatam 60 mg Tab	2 411	91.97	35.07	221 749.09	66 037.27	72 565.87	52.36%
	Sandoz diltiazem 60 mg	166	68.82	30.16	11 423.90	49 411.81	89 191.33	64.35%
	Zildem 60 mg Tab	3 366	116.21	45.26	391 146.68	83 435.33	55 167.81	39.80%
	Zildem 90 mg Tab	2 844	249.31	64.65	709 048.90	75 043.50	1 467.24	1.92%
	Zildem 180 mg SR	8 830	198.63	31.87	1 753 918.91	96 137.80	22 775.82	19.15%
	Zildem 240 mg SR	3 331	194.26	17.90	647 086.37	29 722.07	8 043.46	21.30%

More generic equivalents of items containing diltiazem were dispensed than the original products (Tilazem®) in 2008.

Possible cost saving scenarios of diltiazem containing medicine items were created to show potential savings in 2008 e.g.:

- From this table (Table 4.38) it is clear that the largest cost saving potential would be substituting Tilazem® 60 mg for Sandoz® diltiazem 60 mg.
- The cost of Zildem® 90 mg increased from R 246.88 (SD = R 66.25) and has the potential of a relatively small cost saving (1.92%) when used as a substitute for Tilazem® 90 mg.

Table 4.39: Potential cost saving of felodipine containing items in 2008

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
FELODIPINE	Plendil 2.5 mg Tab	3 007	188.06	31.04	565 509.05	No generic available		
	Plendil 5mg Tab	2 674	218.19	55.02	583 429.77	Innovator		
	Plendil 10 mg Tab	759	265.15	53.03	201 248.92			
	Felodipine-Hexal 5 mg Tab	12 602	111.69	22.96	1 407 481.26	298 651.40	284 778.37	48.81%
	Felodipine-Hexal 10 mg Tab	4 819	152.53	20.55	735 035.80	115 769.28	85 479.64	42.47%

No new felodipine containing products entered the market and relatively not much in this table (Table 4.39) changed from the previous years.

- Felodipine-Hexal® 5 mg was yet again the most popular felodipine containing product in 2008 (n = 12 602) and was 48.8% less costly than its innovator (Plendil® 5 mg).

Table 4.40: Potential cost saving of nifedipine containing items in 2008

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
NIFEDIPINE	Adalat 5 mg Cap	31	48.51	47.50	1 503.88	Innovator		
	Adalat 10 mg Cap	172	36.71	60.19	6 314.94			
	Adalat Retard 10 mg	448	122.59	101.16	54 919.47	No generic substitution on extended or sustained release nifedipine formulations (MCC 2003:3)		
	Adalat Retard 20 mg	316	253.94	146.51	80 244.78			
	Adalat XL 30 mg Tab	31 231	223.24	53.72	6 971 950.16			
	Adalat XL 60 mg Tab	13 398	290.65	37.62	3 894 138.20			
	Adco-Vascard 30 SR Caps	10 866	166.22	43.13	1 806 170.49			
	Bio-nifedipine 5 mg	78	26.86	15.51	2 094.95	832.61	671.27	44.64%
	Bio-nifedipine 10 mg	29	6.07	7.71	176.14	1 044.69	5 270.25	83.46%
	Cardifen TM 5 mg Cap	923	49.50	34.82	45 688.39	1 534.50	-30.62	-2.04%
	Cardifen TM 10 mg Cap	1 184	71.55	44.48	84 711.22	12 306.02	-5 991.08	-94.87%
	Cipalat Retard 20 mg	32 695	46.50	15.40	1 520 444.10			
	Nifedalat 10 mg Cap	708	38.43	25.48	27 210.45	6 610.45	-295.51	-4.68%
	Nifedalat 20 SR Tab	3 357	38.22	15.09	128 289.72			
	Sandoz Nifedipine 10 mg	15	62.04	37.26	930.58	10 670.65	-4 355.71	-68.97%

Cipalat® Retard 20 mg was the best selling nifedipine containing item in 2008. It was also the 2nd most dispensed CCB in 2008. In this table (Table 4.40) of nifedipine containing products of 2008 a few interesting facts were observed e.g.:

- Four of the seven generic products evaluated were more expensive than the innovator.
- The costs of Adalat® 5 mg and 10 mg decreased dramatically from R 113.65 (SD = R 95.85) and R154.93 (SD = R 175.39) respectively in 2005 to the current costs reported in the table (Table 4.40). This is a decrease of 57.3% in the cost of Adalat® 5 mg and 76.3% in the cost of Adalat® 10 mg. The costs of the generic products also decreased but not as dramatically.
- Bio-nifedipine® 10 mg was noted to be 83.46% less expensive than the average cost of the innovator and still only 29 items were dispensed.
- Bio-nifedipine® 5 mg was also found to be less expensive than the innovator.
- Cardifen® 10 mg was found to be almost double the cost of Adalat® 10mg.

Table 4.41: Potential cost saving of verapamil containing items in 2008

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)	Cost of items if substituted with generic (R)	Potential cost saving when substituted with generic (R)	Potential % saved
VERAPAMIL	Isoptin 40 mg Tab	521	63.34	37.55	32 998.62	Innovator		
	Isoptin SR 240 mg Tab	2845	158.02	45.60	449 578.76			
	Isoptin 5 mg/2ml Inj	4	40.63	16.10	162.50			
	Calcicard SR 240 mg	11 119	149.06	36.16	1 657 346.32	424 062.44	25 516.32	5.68%
	Ravamil SR 240 mg	9 396	146.17	38.02	1 373 420.48	415 855.82	33 722.94	7.50%
	Sandoz verapamil HCl 40 mg	652	34.64	13.30	22 588.44	18 049.97	14 948.65	45.30%
	Sandoz verapamil HCl 80 mg	384	60.86	22.02	23 370.73			
	Sandoz verapamil HCl 120 mg	318	75.38	27.29	23 969.57			
	Vasomil 40 mg Tab	2 459	26.73	11.53	65 727.41	13 925.98	19 072.64	57.80%
	Vasomil 80 mg Tab	2 027	60.40	23.67	122 439.69			
	Vasomil 5 mg/2ml Inj	1	22.02		22.02	88.08	74.42	45.80%
	Verahexal 240 mg SR	27 289	113.35	26.37	3 093 145.48	322 474.22	127 104.54	28.27%

Some potential cost saving scenarios with verapamil containing medicine items were depicted below:

- Verahexal® 240 mg SR was the verapamil containing product with the most items dispensed in 2008 and with a potential 28.3% saving if Isoptin® SR 240 mg were to be substituted for it.
- Vasomil® 40 mg was 57.8% less expensive than Isoptin® 40 mg.
- Vasomil® 40 mg was in the 27th position on the list of CCB items ranked by the number of items dispensed in 2008 (Appendix Table A.5).
- A saving of R 14 948.65 would have been possible if all Isoptin 40mg items had been substituted for Sandoz® verapamil HCl 40 mg.

Table 4.42: CCB items of 2008 without generic equivalents on the market

Active ingredient	Registered trade name	Total items	Average cost per item (R)	SD	Total cost (R)
ISRAPIDINE	Dynacirc 2.5 mg Tab	356	187.51	69.55	66 752.48
	Dynacirc SRO 5 mg Cap	2 662	269.08	68.69	716 295.26
LERCANIDIPINE	Zanidip 10 mg Tab	8 370	162.69	32.40	1 361 680.91
	Zanidip 20 mg Tab	1 096	207.74	31.08	227 684.10

Dynacirc® containing isradipine and Zanidip® containing lercanidipine were the products without a generic substitute on the market in 2008.

- The most items were dispensed of Zanidip® 10 mg (n = 8 370), even more than the previous year (n = 7 941) at an average of R162.69 (SD = R 32.40) per item and a total cost of R 1 361 680.91.
- The most expensive item in Table 4.42 was the same as in the year 2007 namely Dynacirc® SRO 5 mg at an average cost of R 269.08 (SD = R 68.69) per medicine item.
- A total of 2 662 of these medicine items was dispensed in 2008.

In Section 4.7 of this thesis it was observed that medicine items still had relatively large deviations in costs that should not necessarily be because of the SEP structure discussed in Section 2.5.2.1.2 of this study. The pricing structure of medicine items is not in the scope of this study and further studies on this matter will be needed.

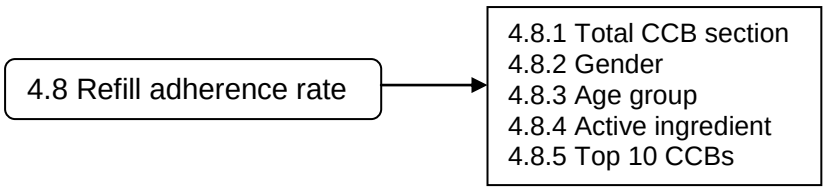
To summarise Section 4.7 of this study Table 4.43 was drawn up from Table 4.19 to Table 4.41 to show the possible maximum and minimum amount to be saved through generic substitution, taking into consideration that the rand-value was calculated across different formulations and strengths of the specified active ingredients. Table 4.43 consisted only of CCB active ingredients with generic equivalents available on the South African market.

Table 4.43: Possible maximum and minimum amounts to be saved through generic substitution according to active ingredients

CCB active ingredient	2005		2006		2007		2008	
	Minimum possible saving (R)	Maximum possible saving (R)	Minimum possible saving (R)	Maximum possible saving (R)	Minimum possible saving (R)	Maximum possible saving (R)	Minimum possible saving (R)	Maximum possible saving (R)
Amlodipine	717 482.86	1 608 203.85	485 686.99	1 335 073.50	413 110.09	1 743 473.40	254 060.43	1 190 870.68
Diltiazem	11 337.07	91 734.13	7 011.92	81 367.96	3 636.41	72 739.48	1 467.24	89 191.33
Felodipine	261 949.96	720 477.61	165 499.61	495 005.24	125 977.39	361 281.55	85 479.64	284 778.37
Nifedipine	17 907.19	60 333.82	8 230.08	31 405.33	-7 076.15	5 342.44	-5 991.08	5 270.25
Verapamil	1 260.68	124 579.78	514.32	124 624.07	15 894.59	116 484.98	74.42	127 104.54

According to Table 4.43 the highest potential saving with generic substitution would be among amlodipine containing items in each of the study years. It was also noticed that some generic substitutions could be relatively more expensive than the innovators, e.g. in 2007 it was seen that the average cost of Sandoz® nifedipine 10 mg (R 79.75 SD = R 48.23) was 70.27% (R 32.91) more expensive than the average cost of the innovator called Adalat® 10 mg. If cost is a major object of medicine usage generic substitution should be implemented carefully.

4.8 Refill-adherence rate of CCB medicine items



In this section the refill-adherence rate (also known as compliance) of patients on the PBM database using CCB medicine items will be examined. The refill-adherence rate of the CCB medicine items was determined from 2005 to 2008 for those individual CCB items that were dispensed to patients more than once during the study period, as explained in Section 3.3.5.5. The refill-adherence rate will be expressed as a percentage.

The refill-adherence rates were divided into three categories according to their refill-adherence rate percentages as stated below.

1	**Unacceptable low adherence rate**	< 80% refill-adherence rate
2	**Acceptable adherence rate**	>80% ≤ 120% refill-adherence rate
3	**Unacceptable high adherence rate**	>120% refill-adherence rate

The total days supplied indicated the total days an individual patient was supplied with an individual CCB medicine item. Below follows the total days supplied criteria used during the study:

Total days supplied categories	Total days supplied of medication
1	≤ 60 days
2	> 60≤ 90 days
3	> 90≤ 120 days
4	> 120≤ 180 days
5	> 180≤ 360 days
6	> 360≤ 720 days
7	> 720≤ 1080 days
8	>1080 days

This total days supplied classification has already been discussed in Section 3.3.5.5 of this study.

4.8.1 Refill-adherence rate of the patients using CCB medicine items

In this section the refill-adherence rate of all the CCB medicine items that were dispensed more than once during the study period will be examined and divided into the 3 groups according to their refill-adherence rate as discussed in Section 3.3.5.5.

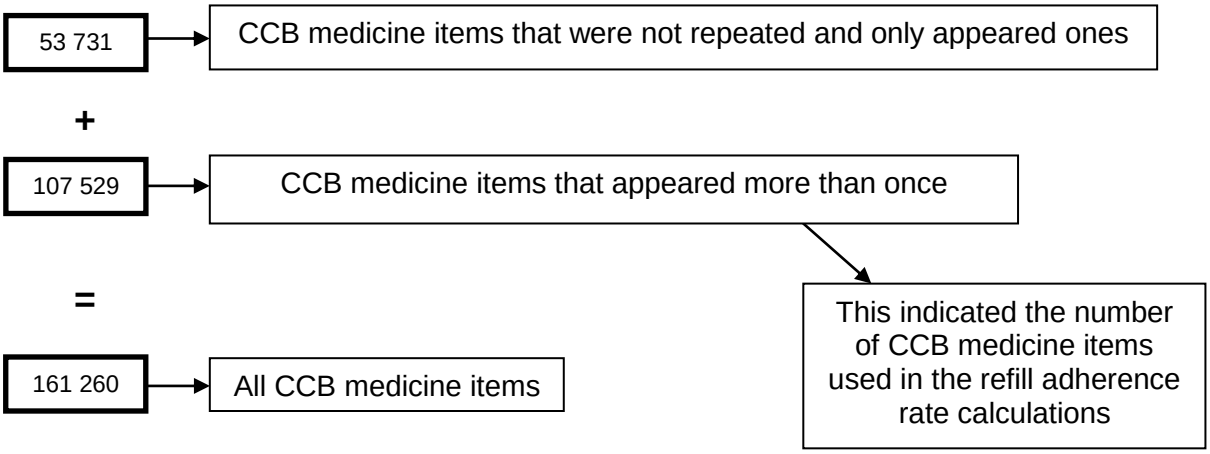


Figure 4.15: The number of medicine items used to calculate the refill-adherence rates

From Figure 4.15 it could be gathered that 53 731 of the total CCB medicine items (161 260) were not used in the refill-adherence rate equation because they had not been dispensed more than once during the study period.

Calculation showed that the CCB medicine items that had been dispensed more than once during the study period had a refill-adherence rate of 90.04% (SD = 142.31) during the study period from 2005 to 2008.

Table 4.44: Refill-adherence rates of the CCB medicine items used during the study period

Total number of CCB items used in the refill-adherence rate equations	1	2	3
10 7529	35.65%	60.34%	4.01%

According to Table 4.44 was noted that only 60.34% of CCB items were used with acceptable refill-adherence rates during the study (Section 3.3.5.5). Approximately 4% of CCB medicine items had an adherence rate of over 120%. More than a third of the CCB medicine items used had unacceptable low adherence rates from 2005 to 2008.

Table 4.45: Percentage adherence according to the total days supplied of CCB medicine items during the study period

Total days supplied category	Percentage of CCB medicine items dispensed
1	44.92%
2	5.66%
3	4.47%
4	7.39%
5	13.75%
6	13.69%
7	6.12%
8	3.99%
Total number of CCB medicine items	161 260

Table 4.45 indicated that 44.92% of specific CCB medicine items used by patients during the study period were used for shorter than 60 days. A percentage of 13.75% was calculated for CCB items used for > 180 ≤ 360 days and 13.69% had been used from 2005 to 2008 for > 360≤ 720 days.

4.8.2 Refill-adherence rate of CCB medicine items according to gender

In this section the refill-adherence rate of CCB medicine items will be examined by gender (Section 3.3.6.3) and divided into the three groups according to their refill-adherence rates, as discussed in Section 3.3.5.5.

A number of medicine items were not used in the refill-adherence rate equations as they were not dispensed more than once for a specific patient during the study period. These numbers of unused items were also tabulated.

The average refill-adherence rate for female patients was 88.89% (SD = 135.82) and 91.46% (SD = 149.93) for male patients. This could be seen as acceptable according to Bester & Hammann (2007:20).

Table 4.46: Refill-adherence rates of CCB medicine items according to gender during the study period

Gender	Total number of CCB items used in the refill-adherence rate equations	1	2	3	Number of items not included in the equations	Average refill-adherence rate	SD
Female	59 281	36.29%	59.68%	4.02%	31312	88.89%	135.82
Male	48 216	34.85%	61.15%	4%	22406	91.46%	149.93
Unknown	32	43.75%	53.13%	3.13%	13	75.45%	32.99

- It was noted that a higher percentage of male patients using CCB medicine items (61.15%) had an acceptable refill-adherence rate than female patients using CCB medicine items (59.68%) even though more female patients used a CCB medicine item during the study period than male patients (Table 4.8).
- From Table 4.46 it was also noted that 4% of male patients had an unacceptable high adherence rate.
- More than a third of patients from both genders had unacceptable low adherence rates with the usage of CCB medicine items with their lowest refill-adherence rate present with female patients (36.29%).

Table 4.47: Percentage adherence according to the total days supplied of CCB medicine items per gender during the study period

Days supply category	Gender		
	Female	Male	Unknown
1	46.27%	43.27%	44.44%
2	5.54%	5.81%	4.44%
3	4.43%	4.53%	4.44%
4	7.11%	7.75%	4.44%
5	13.12%	14.55%	17.78%
6	13.31%	14.19%	11.11%
7	6.07%	6.19%	13.33%
8	4.16%	3.78%	-
Total number of CCB medicine items	90 593	70 622	45

According to Table 4.46 the following could be noted:

- A slightly higher percentage of female CCB users used a CCB medicine item for shorter than 60 days compared to male patients.
- A percentage of 14.55% of CCB items used by male patients were used for > 180 ≤ 360 days compared to the 13.12% of CCB medicine items used for the same number of days by female users.
- A larger percentage of CCB items were used for > 360 ≤ 720 days by male patients (14.19%) than by female patients (13.31%).
- More female patients (4.16%) compared to male patients (3.78%) used their CCB medicine items for more than 1080 days.

4.8.3 Refill-adherence rate of CCB medicine items according to age groups

In this section the refill-adherence rate of CCB medicine items will be examined by age groups (Section 3.3.6.2) and divided into the 3 groups according to their compliance as discussed in Section 3.3.5.5.

A number of medicine items were not used in the refill-adherence rate equations as they were not dispensed more than once for a specific patient during the study period. These numbers of unused items were also tabulated.

Table 4.48: Refill-adherence rates of CCB medicine items according to age groups during the study period

Age group	Total number of CCB items used in the refill-adherence rate equations	1	2	3	Number of items not included in the equations	Average refill-adherence rate	SD
1	64	35.94%	56.25%	7.81%	264	93.6%	94.19
2	235	54.47%	39.15%	6.38%	792	101.22%	279.29
3	1 436	47.91%	46.66%	5.43%	2380	84.34%	153.03
4	8 233	49.93%	45.21%	4.86%	8590	88.2%	196.52
5	21 787	43.49%	52.32%	4.19%	14547	86.27%	154.10
6	26 590	34.63%	61.19%	4.18%	11697	90.82%	142.95
7	4 9187	29.89%	66.47%	3.64%	15461	91.71%	123.16

According to the average refill-adherence rate tabulated in Table 4.48 the following could be noted:

- Patients aged ≤ 15 years had an average refill-adherence rate of 93.6% (SD = 94.19) with the use of their CCB medicine items.
- The refill-adherence rate of patients aged > 55 ≤ 65 years with their CCB medicine items was 90.82% (SD = 142.95) and a refill-adherence rate of 91.71% (SD = R 123.16) was seen with the use of CCBs by patients older than 65 years.
- The "worst" refill-adherence rate was seen in patients aged > 25 ≤ 35 years (84.34% SD = 153.03).

Table 4.48 also displayed the following:

- CCB medicine items used by patients older than 65 years of age had the best refill-adherence rate. It should be noted that patients over 65 years used more items per patient than any other age group (Table 4.8) during the study period. Because of the high number of items per patient seen with patients older than 65 years, Bester and Hammann (2007:18) and Section 2.4 of this study indicated that older patients with multiple diseases should have worse adherence rates. The identification of multiple diseases in the patients aged over 65 was beyond the scope of this study.
- The CCB medicine items used by patients aged > 15 ≤ 25 years had the worst refill-adherence rates, only 39.15% had an acceptable refill-adherence rate with the use of their CCB medicine items and had 60.85% unacceptable refill-adherence rates (54.47% unacceptable low refill-adherence rate and 6.38% unacceptable high refill-adherence rate) with their CCB medication regimens.
- A higher percentage of CCB medicine items used by patients aged > 25 ≤ 35 years had an unacceptable adherence rate (53.34% combined unacceptable high and low refill-adherence rates) than an acceptable refill-adherence rates (46.66%).
- The highest unacceptable high refill-adherence rate was seen with patients aged ≤ 15 years (7.81%).

Table 4.49: Percentage adherence according to the total days supplied of CCB medicine items according to age groups during the study period

Days supply category	Age groups						
	1	2	3	4	5	6	7
1	85.98%	86.27%	75.03%	64.12%	52.85%	41.97%	34.58%
2	3.05%	2.63%	4.85%	5.35%	5.86%	5.96%	5.55%
3	1.22%	2.14%	3.07%	3.96%	4.50%	4.92%	4.46%
4	3.66%	2.53%	5.06%	6.08%	7.59%	8.03%	7.46%
5	2.74%	3.21%	6.97%	10.36%	13.06%	14.77%	15.04%
6	2.13%	2.24%	3.75%	7.32%	10.86%	14.53%	17.28%
7	0.61%	0.88%	0.97%	2.02%	3.64%	6.05%	9.05%
8	0.61%	0.10%	0.31%	0.80%	1.64%	3.76%	6.57%
Total number of CCB medicine items	328	1 027	3 816	16 823	36 334	38 287	64 645

The total CCB medicine items increased as the age of the patients increased as seen in Table 4.8. Table 4.49 reflected information such as the following:

- More than 85% (86.27%) of CCB medicine items used by patients >15 ≤ 25 years were used for shorter than 60 days.
- The smallest percentage of patients who used a CCB medicine item for shorter than 60 days were patients older than 65 years.
- The patients older than 65 years (6.57%) showed the highest percentage of patients who used their CCB medicine items for more than 1080 days.
- Only 0.31% and 0.8% of patients aged > 25 ≤ 35 years and > 35 ≤ 45 years respectively used their CCB medicine items for more than 1080 days.

4.8.4 Refill-adherence rate of CCB medicine items by active ingredients

In this section the refill-adherence rate of CCB medicine items according to active ingredients (Section 3.3.6.5.3) will be examined and divided into the 3 groups according to their compliance as discussed in Section 3.3.5.5.

As stated before, a number of medicine items were not used in the refill-adherence rate equations as they were not dispensed more than once for a specific patient during the study period. These numbers of unused items were also tabulated.

Table 4.50: Refill-adherence rates of CCB medicine items by active ingredients during the study period

Active ingredients	Total number of CCB items used in the refill-adherence rate equations	1	2	3	Number of items not included in the equations	Average refill-adherence rate	SD
Amlodipine	42 060	32.45%	62.96%	4.59%	19 065	93.39%	143.4
Diltiazem	6 811	32.8%	63.78%	3.33%	2 677	92.51%	137.60
Felodipine	6 869	30.72%	66.19%	3.09%	2 521	91.65%	140.35
Israpidine	796	27.26%	69.85%	2.89%	206	90.36%	115.64
Lercanidipine	1 869	26.97%	67.95%	5.08%	647	92.32%	84.46
Nifedipine	32 288	41.5%	54.4%	4.09%	21 887	86.11%	151.13
Nisoldipine	1	100%	-	-	-	99.45%	-
Verapamil	16 835	36.96%	60.04%	2.99%	6 728	87.28%	130.31

- The highest average refill-adherence rate was noted with CCB medicine items containing amlodipine (93.39% SD = 143.4).
- Nifedipine had a refill-adherence rate of 86.11% and verapamil had a refill-adherence rate of 87.28% (SD = 130.31) of the items CCB medicine items that were dispensed more than once during the study period.
- Nifedipine containing CCB medicine items had the worst acceptable refill-adherence rate (54.4%) of all active ingredients and 41.5% of nifedipine were used with unacceptable low adherence rates.
- The best acceptable refill-adherence rate can be attached to with the isradipine containing products (69.85%).
- A relatively good acceptable refill rate was seen with products containing lercanidipine (67.95%) as well as felodipine (66.2%). It was also noted that 5.08% of lercanidipine usage occurred with unacceptable high refill-adherence rates.
- The most frequently used CCB active ingredient during the study period, amlodipine, had an acceptable refill-adherence rate of 62.96% and an unacceptable high and low refill-adherence rate of 32.45% and 4.59% respectively.
- It was noted that only 60.04% of verapamil containing CCB medicine items had an acceptable adherence rate as by definition in Section 3.3.5.5.

Table 4.51: Percentage adherence according to the total days supplied of CCB medicine items by active ingredients during the study period

Total days supplied category	Active ingredients							
	Amlodipine	Diltiazem	Felodipine	Israpidine	Lercanidipine	Nifedipine	Nisoldipine	Verapamil
1	42.82%	38.71%	37.11%	29.94%	36.33%	52.97%	-	39.05%
2	6.26%	5.35%	5.45%	3.49%	6.32%	5.12%	-	5.56%
3	5.09%	4.30%	4.30%	2.79%	4.89%	3.93%	-	4.30%
4	8.28%	7.02%	7.54%	3.59%	7.31%	6.69%	-	6.93%
5	14.59%	13.34%	13.56%	11.38%	15.62%	12.72%	100%	14.07%
6	14.20%	14.13%	16.06%	17.37%	17.81%	11.87%	-	14.88%
7	6.04%	8.59%	8.73%	13.07%	8.86%	4.22%	-	8.09%
8	2.72%	8.55%	7.24%	18.36%	2.86%	2.49%	-	7.11%
Total number of CCB medicine items	61 125	9 488	9 390	1 002	2 516	54 175	1	23 563

According to the days supplies of CCB pharmacological active ingredients shown in Table 4.51 it was noted that:

- More than half of the nifedipine containing medicine items used (52.97%), were used for shorter than 60 days.
- Israpidine containing medicine items had the lowest percentage of users discontinuing treatment in shorter than 60 days (29.94%) and the highest percentage of users using it for more than 1080 days (18.36%).
- Approximately 43% (42.82%) of patients using amlodipine containing medicine items, used it for shorter than 60 days and 14.59% of amlodipine items were used for > 180 ≤ 360 days and 2.72% of them used it for more than 1080 days.
- Diltiazem containing items showed a relatively high percentage (8.55%) of items being used for more than 1080 days.

4.8.5 Refill-adherence rate of CCB medicine items of the top CCB medicine items dispensed during the study period

In this section the refill-adherence rate of the most frequently dispensed CCB medicine items during the study period will be examined and divided into the 3 groups according to their compliance as discussed in Section 3.3.5.5. The criteria inclusion of items on the most dispensed list during the study period was discussed in Section 4.6 and these CCB medicine

items could also be seen in Table 4.15 where the top CCB medicine items were evaluated per year from 2005 to 2008.

The number of medicine items not used in the refill-adherence rate equations were also tabulated in Table 4.52 as they were not dispensed more than once for a specific patient during the study period.

Table 4.52: Refill-adherence rates of the top CCB medicine items dispensed during the study period

Registered trade name	Total number of CCB items used in the refill-adherence rate equations	1	2	3	Number of items not included in the equations	Average refill-adherence rate	SD
Amloc 5 mg	14 147	31.89%	64.14%	3.97%	5 679	91.15%	120.6
Cipalat Retard 20 mg	5 650	38.02%	57.54%	4.44%	3 122	86.24%	123.74
Amloc 10 mg	7 985	34.15%	61.94%	3.91%	2 951	92.67%	150.7
Adalat XL 30 mg	9 742	47.11%	48.93%	3.96%	7 003	87.17%	192.64
Verahexal 240 SR	6 451	32.83%	64.25%	2.91%	1 779	87.03%	94.13
Norvasc 5 mg	8 015	36.59%	60.19%	3.22%	4 039	89.65%	149.52
Ciplavasc 5 mg	2 265	22.3%	66.45%	11.26%	828	107.54%	164.7
Adalat XL 60 mg	3 661	40.18%	55.83%	3.99%	1 971	89.85%	163.21
Felodipine-Hexal 5 mg	2 969	28.22%	68.71%	3.07%	858	94.31%	152.11
Calcicard SR 240 mg	4 357	40.58%	56.67%	2.75%	1 853	90.37%	174.51
Adco-Vascard 30 mg SR	1 354	24.89%	68.98%	6.13%	401	95.08%	103.97
Norvasc 10 mg	3870	36.95%	59.15%	3.9%	1826	96.04%	191.67

- Amloc® 5 mg showed an average refill-adherence rate of 91.15% (SD = 120.6) during the study period.
- Cipalat® Retard was the 2nd most dispensed in 2008 (Table 4.15) and had a refill-adherence rate of 86.24% (SD = 123.74).

From the above table (Table 4.52) the following could be observed:

- The highest percentage of acceptable refill-adherence rates was seen with Adco-Vascard® 30 mg SR (68.98%).
- Felodipine-Hexal® 5 mg had an acceptable refill-adherence rate percentage of 68.71% and an unacceptable high and low refill-adherence rate 28.22% and 3.07% respectively.
- The lowest unacceptable high refill-adherence rate was seen with Calcicard® SR 240 mg (2.75%).

- Ciplavasc® had the highest percentage of all evaluated CCB medicine items with regard to the unacceptable high refill adherence rate.
- Amloc® 5 mg was the CCB medicine item with the most items dispensed in 2006, 2007 and 2008 according to data from the PBM data as shown in Table 4.15. From Table 4.52 dispensing for 5 679 Amloc® 5 mg items had occurred only once per patient and therefore these items were excluded from the refill-adherence rate calculations. It was found that 64.14% of Amloc® 5 mg medicine items had an acceptable refill-adherence rate, 31.89% an unacceptable low adherence rate and 3.97% unacceptable high refill-adherence rate.
- A sub 50% acceptable refill-adherence rate (48.93%) was seen with Adalat® XL 30 mg, 47.11% had an unacceptable low refill-adherence rate and an unacceptable high refill-adherence rate of 3.96%.
- It was calculated that 58.18% of the total number of Adalat® XL 30 mg medicine items were dispensed more than once during the study period and could be used in the refill-adherence rate equation.
- A relatively low percentage was noted with the acceptable refill-adherence rates of Adalat® XL 60 (55.83%).

Table 4.53: Percentage adherence according to the total days supplied of the top CCB medicine items dispensed during the study period

Days supplied category	Registered trade name											
	Amloc 5 mg	Cipalat Retard 20 mg	Amloc 10 mg	Adalat XL 30 mg	Verahexal 240 SR	Norvasc 5 mg	Ciplavasc 5 mg	Adalat XL 60 mg	Felodipine-Hexal 5 mg	Calcicard SR 240 mg	Adco-Vascard 30 SR	Norvasc 10 mg
1	39.19%	49.82%	37.64%	54.93%	30.77%	44.79%	39.54%	45.69%	32.19%	40.37%	34.87%	43.93%
2	5.90%	5.13%	6.28%	5.60%	5.65%	5.30%	7.02%	5.47%	4.57%	5.30%	6.61%	5.71%
3	5.05%	3.83%	5.14%	3.52%	4.84%	4.24%	6.37%	4.35%	4.02%	4.25%	7.52%	4.30%
4	7.57%	8.39%	9.16%	5.51%	7.93%	6.36%	16.29%	6.37%	8.02%	6.28%	7.98%	6.37%
5	15.42%	13.70%	16.21%	10.12%	15.61%	11.97%	18.72%	11.75%	14.42%	14.91%	35.16%	12.20%
6	16%	16.94%	16.44%	10.52%	17.38%	15.13%	11.96%	13.21%	17.53%	14.01%	7.81%	15.33%
7	7.85%	2.19%	6.72%	5.43%	8.13%	7.66%	0.10%	6.92%	9.82%	9.61%	0.06%	7.71%
8	3.01%	-	2.40%	4.38%	9.70%	4.55%	-	6.23%	9.41%	5.27%	-	4.46%
Total number of CCB medicine items	19 826	8 772	10 936	16 745	8 230	12 054	3 093	5 632	3 827	6 210	1 755	5 696

- According to Table 4.53 it appeared that 30.77% of Verahexal® 240 mg SR items were used for shorter than 60 days and 9.7% were used for 1080 days.
- The data analysed also showed that 32.19% of Felodipine-Hexal® 5 mg items and more than half of Adalat® XL 30 mg (54.93%) were used for shorter than 60 days.
- The usage of Ciplavasc® 5 mg items indicated that 18.72% of the items used, were used for > 180≤ 360 days.
- A larger percentage of Adco-Vascard® was used for > 180 ≤ 360 days (35.16%) compared to the percentage of patients using it for shorter than 60 days.
- A smaller percentage of Amloc® 10 mg items were used for shoter than 60 days compared to Amloc® 5 mg.
- With regards to Norvasc® 5 mg, 44.79% were used for shorter than 60 days, 15.13% were used for > 360 ≤ 720 days and 4.55% were used for more than 1080 days.

4.8.6 Financial implications of the usage of the most frequently dispensed CCB medicine items during the study period

In this section of the study the financial implications of the usage of the top CCB medicine items dispensed during the study period will be analysed. The cost of these CCB medicine items will be analysed according to the refill-adherence rates as specified in Section 3.3.5.5 as well as the CCB medicine items not included in the refill-adherence rate analysis because they were not repeated more than once during the study period. This section is a cost analysis of the percentages and numbers shown in Table 4.52.

The criteria inclusion of items on the most often dispensed list during the study period were discussed in Section 4.6 and these CCB medicine items could also be seen in Table 4.15 where the top CCB medicine items were evaluated per year from 2005 to 2008.

Table 4.54: Financial implications of the use of the top CCB medicine items dispensed during the study period according to adherence rates

Registered trade name	Cost of items not repeated more than once (R)	Cost of items with unacceptable low refill-adherence rate (R)	Cost of items with a acceptable refill-adherence rate (R)	Cost of items with unacceptable high refill-adherence rate (R)
Amloc 5 mg	544 363.64	4 042 664.89	13 498 503.50	383 601.04
Cipalat Retard 20 mg	115 139.72	614 860.66	1 704 288.09	59 773.91
Amloc 10 mg	384 580.65	3 255 104.61	9 424 083.80	276 666.17
Adalat XL 30 mg	1 316 347.86	8 273 480.33	18 219 581.53	538 589.60
Verahexal 240 SR	180 088.18	2 635 812.39	8 179 757.96	180 414.90
Norvasc 5 mg	521 250.59	3 916 526.04	11 007 837.60	274 722.62
Ciplavasc 5 mg	55 153.52	197 599.05	869 136.37	118 344.09
Adalat XL 60 mg	504 318.92	3 721 431.94	10 768 997.85	230 003.44
Felodipine-Hexal 5 mg	85 245.88	1 001 197.74	4 179 195.47	69 546.42
Calcicard SR 240 mg	246 383.04	2 849 356.38	5 962 317.34	113 528.15
Adco-Vascard 30 mg SR	61 768.59	283 070.14	1 349 086.18	112 245.58
Norvasc 10 mg	318 096.21	2 429 522.94	6 725 546.11	197 053.64
Total cost of the medicine items evaluated	4 332 736.80	33 220 627.11	91 888 331.80	2 554 489.56

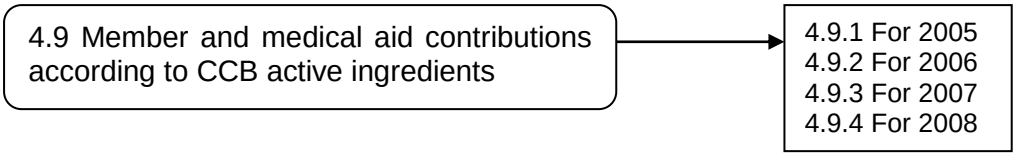
- The cost of the Amloc® 5 mg items used with unacceptable refill adherence (high and low combined) was R 4 426 265.93. This was 3.28 times more than the cost of Amloc® 5 mg used with an acceptable refill-adherence rate. The cost of the Amloc® 5 mg items, dispensed only once during the study period, was R 544 363.64.
- The 61.94% of Amloc® 10 mg used with an acceptable refill-adherence rate (Table 4.52) had a cost of R 9 424 083.80.

- The most costly CCB medicine item as per average cost per medicine item , as seen in Appendix Table A.2 to Appendix Table A.,) during the study period was Adalat® XL 60 mg. It was seen that the cost of these Adalat® items dispensed only once to a patient during the study period were R 504 318.92. From Table 4.52 could be seen that only 55.83% of the Adalat® XL 60 mg items were used with an acceptable refill-adherence rate. The cost of these CCB items used with an unacceptable refill-adherence rate was noted to be R 3 951 435.38.
- Norvasc® 5 mg was the top CCB medicine item dispensed in 2005 (Table 4.15). According to Table 4.54 the cost of the Norvasc® 5 mg items can be classified in the following manner:
    - Used with an unacceptable low adherence rate it was R 3 916 526.04
    - Used with an acceptable refill-adherence rate it was R 11 007 837.60
    - Used with an unacceptable high refill-adherence rate it was R 274 722.62
- Adco-Vascard® 30 SR showed an acceptable refill-adherence rate of almost 70% over the study years, which was the highest percentage of the items on Table 4.52, and the cost of the items used with an unacceptable refill-adherence rate was R 395 315.72 (Table 4.54).

From this section it was clear that the financial implications of non-adherent use of CCB medicine items are relatively large and efforts should be made to promote better adherence by patients. Better adherence results in more therapeutic benefits and has financial benefits for members and the different medical aids involved.

4.9 Member and medical aid contributions according to CCB active ingredients

In this section contribution by the member and by the medical aid for CCB active ingredients will be examined per year. These contributions will be expressed as a percentage.



4.9.1 Contributions per CCB active ingredients in 2005

Figure 4.16 indicate the member and medical aid contributions of CCB active ingredients in 2005.

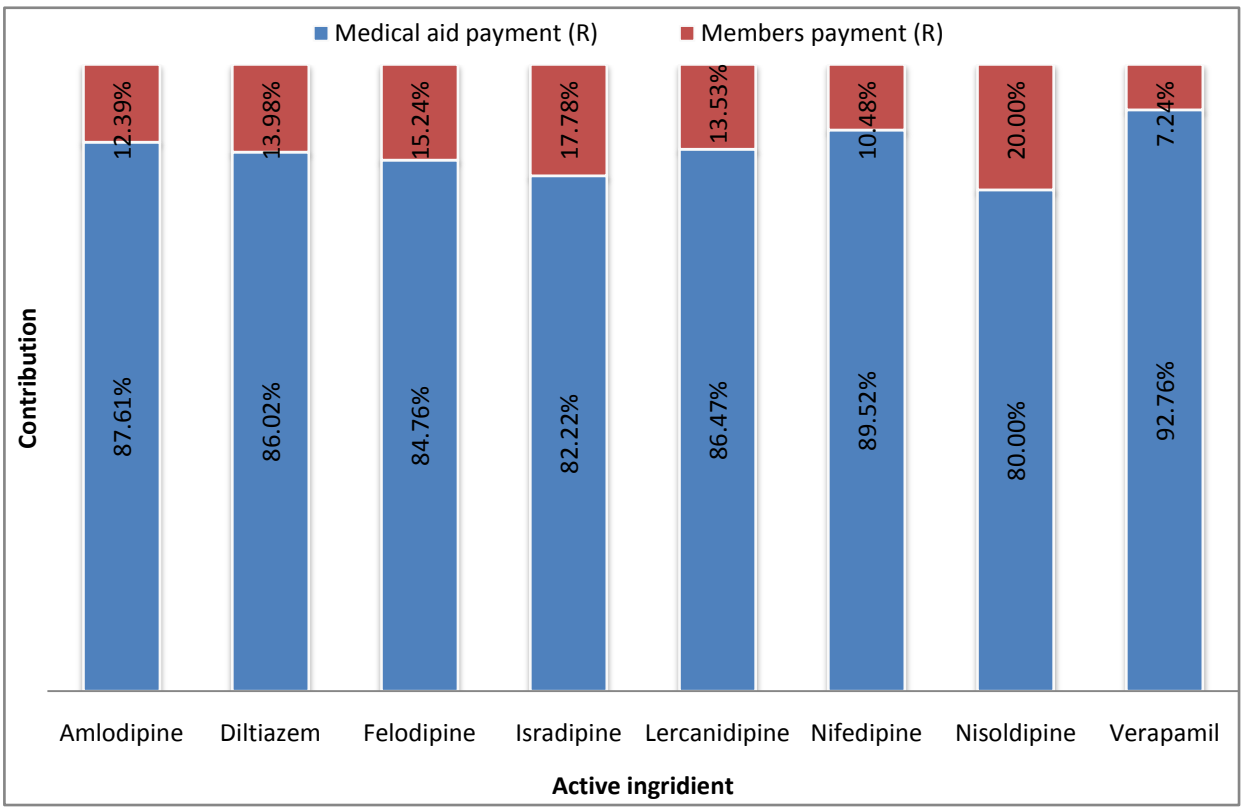


Figure 4.16: Member and medical aid contributions of CCB active ingredients in 2005 (calculated from Appendix Table A.6)

According to Figure 4.16 the following can be observed:

- The medical aid covered 92.76% for verapamil containing CCB medicine items in 2005. From Figure 4.11 it was seen that 21% of all CCB medicine items dispensed in 2005 were verapamil containing items.
- An amount of R 12 156 207.61 (Appendix Table A.6) which represented 89.52% of the total cost for nifedipine, the most used CCB in 2005 (Figure 4.11), was paid by the medical aid in 2005.
- Amlodipine was the active ingredient in Norvasc® 5 mg, the top selling CCB medicine item in 2005, and the medical aid contributed 87.6% to the total cost of amlodipine containing medicine items.
- The highest percentage of patient contribution was seen with nisoldipine containing CCB medicine items (20%). Only seven nisoldipine containing CCB medicine items were dispensed in 2005 under the trade name Syscor-CC® 20 mg.

4.9.2 Contributions per CCB active ingredients in 2006

Figure 4.17 indicate the member and medical aid contributions of CCB active ingredients in 2006.

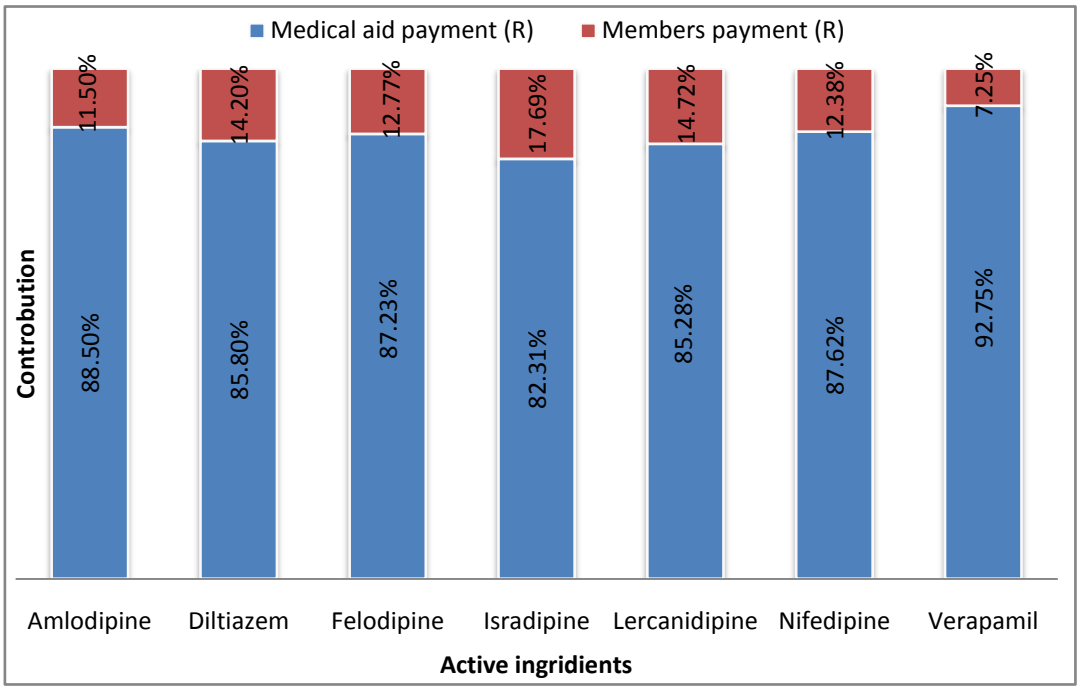


Figure 4.17: Member and medical aid contributions of CCB active ingredients in 2006 (calculated from Appendix Table A.6)

- The CCB active ingredient with the highest medical aid contribution was verapamil (92.75%) and the patient contribution was recorded as 7.25%.
- The medical aid contributions increased from 84.76% in 2005 to 87.23% in 2006 for felodipine containing CCB medicine items.
- Amlodipine, the most used item in 2006 (33%) according to Figure 4.12, had a 0.89% increase in the medical aid contribution from 2005 (87.61%) to 2006 (88.5%).
- The CCB active ingredient with the highest member contribution was isradipine with the medical aid covering only 82.31% of the cost in 2006 and R 207 622.01 (Appendix Table A.6) needed to be "paid" from the patient's pocket.

4.9.3 Contributions per CCB active ingredients in 2007

Figure 4.18 indicate the member and medical aid contributions of CCB active ingredients in 2007.

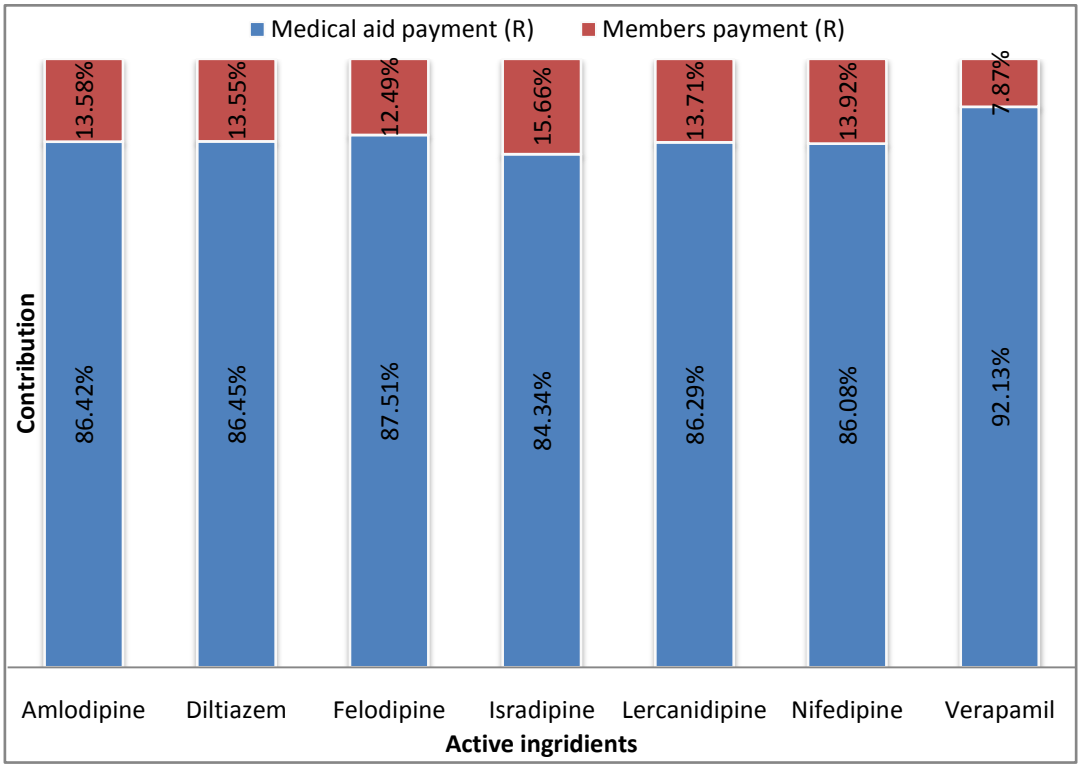


Figure 4.18: Member and medical aid contributions of CCB active ingredients in 2007 (calculated from Appendix Table A.6)

- As the usage of amlodipine increased from 2006 to 2007 to 39% of the total CCB medicine items dispensed in 2007 (Figure 4.13), the medical aid contribution decreased to 86.42%.

- Isradipine was the active ingredient contained in Dynacirc® and was still the CCB active ingredient with the highest patient contribution percentage in 2007 (15.66%).
- It was seen that 92.13% of verapamil containing CCB medicine items were covered by medical aid which accounted for R6 836 176.50 (Appendix Table A.6).
- The medical aid contribution for diltiazem increased from 85.8% in 2006 to 86.45% in 2007.

4.9.4 Contributions per CCB active ingredients in 2008

Figure 4.19 indicate the member and medical aid contributions of CCB active ingredients in 2008.

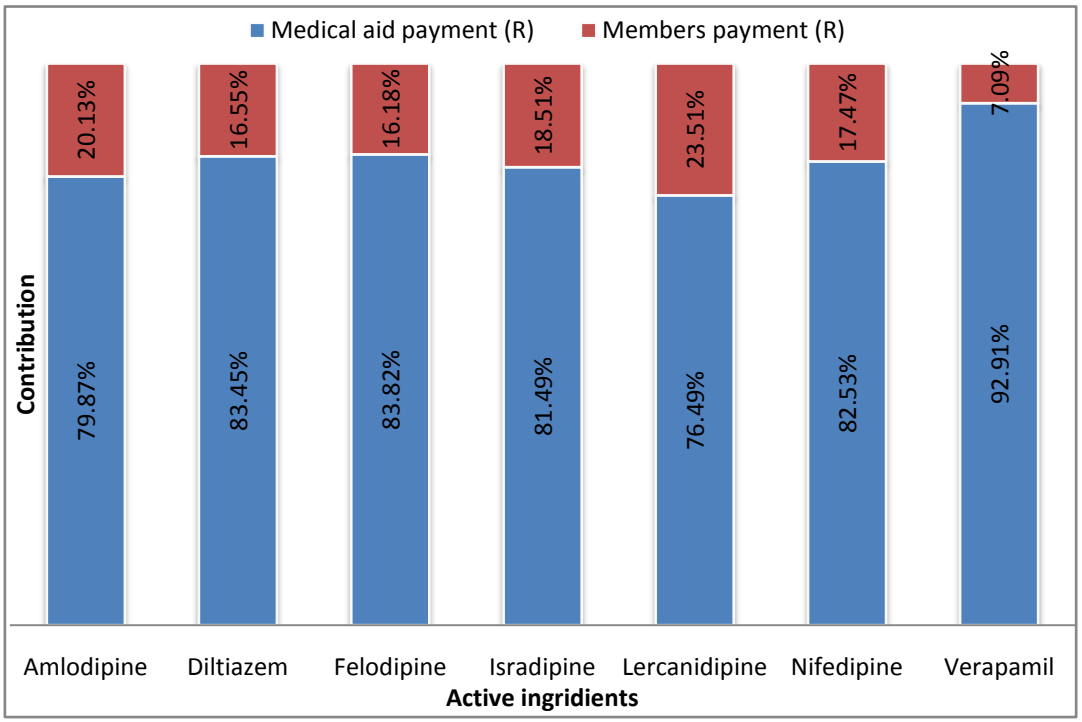


Figure 4.19: Member and medical aid contributions of CCB active ingredients in 2008 (calculated from Appendix Table A.6)

- Lercanidipine was the active ingredient in 2008 with the highest patient contribution covering 23.51% of the total lercanidipine cost.
- The most used CCB active ingredient in 2008, amlodipine, that represented 42% of all CCB active ingredients used in 2008 (Figure 4.14), had a decline of 6.55% in the contribution by medical aids (79.87%) during the study year of 2008.
- The medical aid contribution for verapamil containing CCB items increased to 92.91% in 2008.

- According to Figure 4.19 the medical aid contribution percentage for CCB medicine items containing isradipine decreased from 84.34% in 2007 to 81.49% in 2008.

To conclude Section 4.9, the active ingredients with the highest patient contribution percentages were CCB medicine items without generic equivalents on the South African market during the study period. Verapamil was the CCB active ingredient with the highest medical aid contribution percentages over all four of the study years.

Table 4.55 was compiled to illustrate the percentage of a calculated simple average payment made by the medical aid and members for CCB medicine items during the study period.

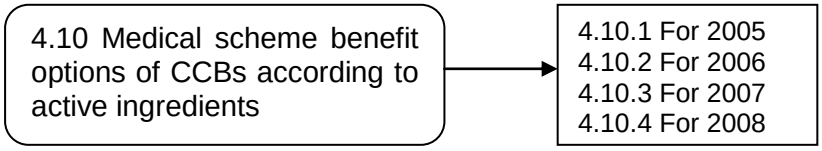
Table 4.55: The percentage of a calculated simple average payment made by the medical aid and members for CCB medicine items during the study period

Year	Average percentage of member contributions (SD)	Average percentage of medical aid contributions (SD)
2005	13.83% (4.01)	86.17% (4.01)
2006	12.93% (3.22)	87.07% (3.22)
2007	12.97% (2.44)	87.03% (2.44)
2008	17.06% (5.06)	82.94% (5.06)

This aspect was not further investigated but it seems that a trend of larger co-payments by members for their CCB medicine items may be a concern. Patients pay more for “the same benefits” because the percentages of payments made by the medical aids decreased during the study period and this illustrated the decreasing patient cover by medical aids.

4.10 Medical scheme benefit options of CCBs according to active ingredients

In this section the benefit options of the CCB medicine items according to the PBM will be evaluated. It should be noted that hypertension and angina are both conditions on the PMB chronic disease list and should be registered by the medical aid accordingly. For the classification of medical scheme benefit options Section 3.3.6.6 should be referred to.



It should be noted that the medical scheme benefit options were not altered in any way by the researcher and were used as they were received from the PBM. The reasons for the inclusions of CCBs into the different medical scheme benefit options were beyond scope of this study. The PBM refers to the benefit options as “drug status”.

4.10.1 CCBs claims according to medical scheme benefit options for 2005

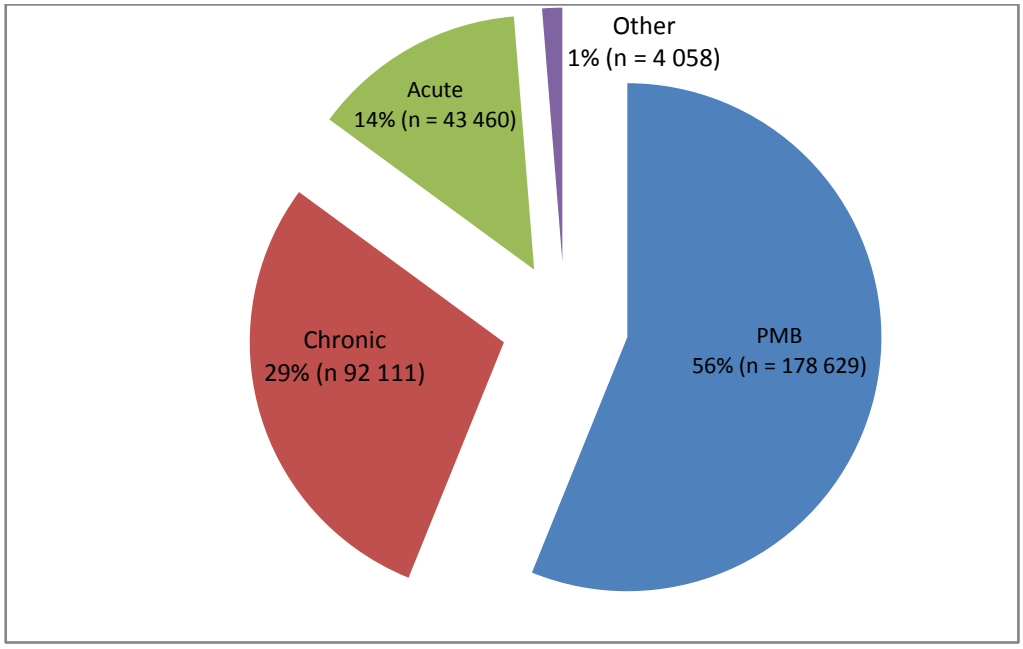


Figure 4.20: Medical scheme benefit options of CCBs dispensed in 2005

Figure 4.20 revealed the following information:

- More than half the CCBs dispensed to patients were indicated for a condition found on the CDL and covered as PMB by medical aid.

- In 29.4% of cases CCB medicine items were claimed from the chronic options of patients.
- It was seen that in 2005 14% of CCBs dispensed were paid for out of the money saved by patients on their medical aid account on the acute option.

4.10.2 CCBs claims according to medical scheme benefit options for 2006

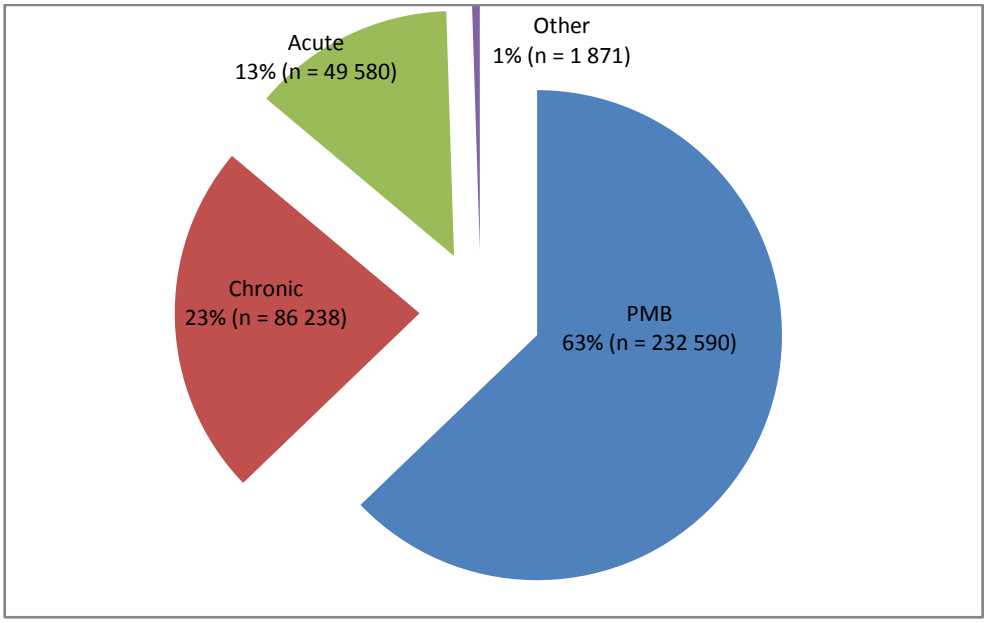


Figure 4.21: Medical scheme benefit options of CCBs dispensed in 2006

- In 2006 it was seen that the CCB items dispensed were done so indicated for a condition on the PMB list increased to 63% from 56% as seen in 2005.
- The other percentages of medical scheme benefit options decreased accordingly.
- Items submitted as acute decreased slightly by 1% from the percentage seen in 2005.

4.10.3 CCBs claims according to medical scheme benefit options for 2007

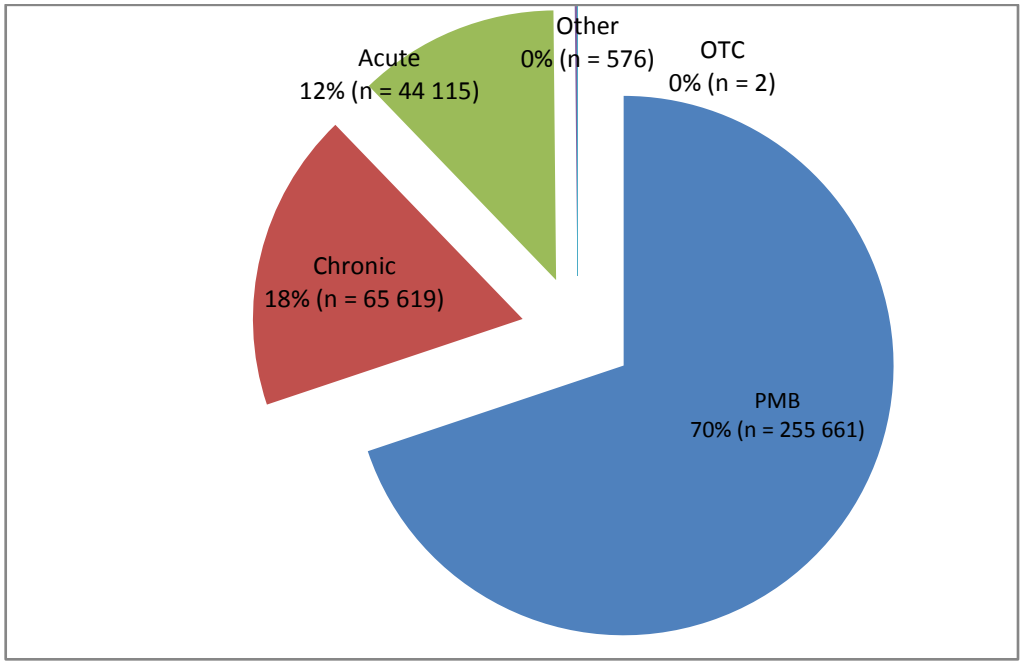


Figure 4.22: Medical scheme benefit options of CCBs dispensed in 2007

The following could be noted (2007):

- The CCBs indicated for a condition on the list of PMBs increased to 70%.
- Two items were dispensed as OTC items. This could only have been a mistake as these OTC items should be scheduled as S2 and below.

4.10.4 CCBs claims according to medical scheme benefit options for 2008

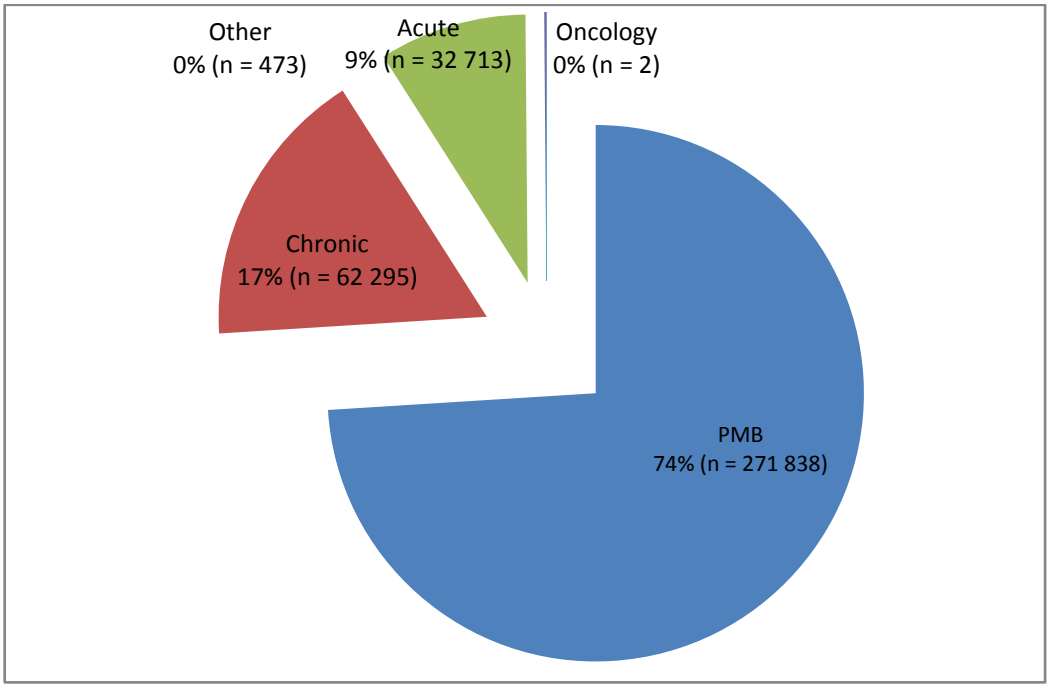


Figure 4.23: Medical scheme benefit options of CCBs dispensed in 2008

- In 2008 74% of CCBs dispensed were done so indicated for a PMB condition as discussed in Section 2.5.2.1.1.
- Medicine items submitted through the acute option decreased to 9%.
- In 2008 some CCB items were submitted as oncology. Early literature suggested that CCB medicine items could develop cancer, not the treatment thereof, but a recent article by Debes *et al.* (2004:257) stated that cancer in CCB medicine users is the result of genetic origin. These patients have a history of cancers in their families.

Table 4.56 was compiled from Figure 4.20 to Figure 4.23 to indicate the percentages of the medical aids' benefit options during the study period. Only three major classifications namely acute, chronic and PMB were compiled in Table 4.56.

Table 4.57: Percentages of the medical aids benefit options during the study period

Year	Medical scheme benefit options	Number of medicine items dispensed*	Percent*
2005	PMB	178 629	56.13%
2006		232 590	62.81%
2007		255 661	69.86%
2008		271 838	74.01%
2005	Chronic	92 111	28.94%
2006		86 238	23.29%
2007		65 619	17.93%
2008		62 295	16.96%
2005	Acute	43 460	13.66%
2006		49 580	13.39%
2007		44 115	12.05%
2008		32 713	8.91%

* Items dispensed and representing percentages were taken from Figure 4.20 to Figure 4.23

From Table 4.56 was noted that percentage of CCB items claimed on PMB increased during the study period. Chronic and acute benefit options decreased over the study period from 2005 to 2008. As previously mentioned the medical scheme benefit options should be investigated in-depth as such an investigation was not part of this study.

4.11 Prescribers of CCBs

In this section the different prescribers of CCBs (Section 3.3.6.4) will be evaluated for each study year.

It should be noted that the classification of the prescribers was taken from the medicine claims database and no alterations were made to the classification system.

Table 4.57: Prescribers of CCB medicine items in the study period

Year	Prescriber	Total number of items prescribed	Total cost of items prescribed (R)	Cost per medicine item (R)	SD	Percentage of items per prescriber (%)	Percentage of total cost (%)	CPI	*d*-Value *
2005	Cardiologists	19 222	2 925 305.54	152.19	66.83	6.04%	6.55%	1.08	0.26
	General medical practitioners	241 736	33 020 995.29	136.60	67.75	75.96%	73.93%	0.97	
	Other	18 794	2 782 548.77	148.06	67.64	5.91%	6.23%	1.05	
	Group specialists	38 125	5 880 311.69	154.24	68.77	11.98%	13.17%	1.10	
	Thoracic surgery	381	56 169.13	147.43	67.40	0.12%	0.13%	1.05	
2006	Cardiologists	22 448	3 267 427.51	145.56	63.46	6.06%	6.54%	1.08	0.25
	General medical practitioners	279 817	36 693 387.64	131.13	64.83	75.53%	73.46%	0.97	
	Other	21 975	3 170 374.56	144.27	64.57	5.93%	6.35%	1.07	
	Group specialists	45 729	6 744 964.74	147.50	64.87	12.34%	13.50%	1.09	
	Thoracic surgery	491	71 238.27	145.09	68.81	0.13%	0.14%	1.08	
2007	Cardiologists	22 469	3 343 783.59	148.82	67.57	6.14%	6.50%	1.06	0.22
	General medical practitioners	274 658	37 725 619.18	137.35	66.43	75.03%	73.37%	0.98	
	Other	22 359	3 287 608.01	147.04	69.74	6.11%	6.39%	1.05	
	Group specialists	46 041	6 981 817.32	151.64	66.48	12.58%	13.58%	1.08	
	Thoracic surgery	522	80 223.10	153.68	74.47	0.14%	0.16%	1.09	
2008	Cardiologists	20 487	3 007 466.12	146.80	69.47	5.58%	6.18%	1.11	0.46
	General medical practitioners	282 380	36 239 484.88	128.34	68.08	76.85%	74.50%	0.97	
	Other	20 440	2 948 731.77	144.26	74.71	5.56%	6.06%	1.09	
	Group specialists	43 680	6 376 856.44	145.99	69.77	11.89%	13.11%	1.10	
	Thoracic surgery	450	72 687.08	161.53	71.58	0.12%	0.15%	1.22	

* It should be noted that the *d*-value in Table 4.55 was calculated between the prescriber with the highest and prescriber with the lowest average cost of each year.

In the 2005 section of Table 4.57 the following could be observed:

- There were 75.96% of CCB medicine items prescribed by GPs at an average cost of R 136.60 (SD = R 67.75).
- The total cost of all the items prescribed by GPs represented 73.93% of the total cost of CCB medicine items in 2005.
- An approximate portion of 12% of CCB items in 2005 were prescribed to patients by group specialists and had the highest average cost per item prescribed (R 154.24 SD = R 68.77) in 2005 and could be seen as relatively expensive CCB items according to the CPI value calculated at 1.10.
- It was noted that 6% of CCB items in 2005 were prescribed by cardiologists at an average cost of R 152.19 (SD = R 66.83) per medicine item.
- A *d*-value was calculated for the average cost of items by group specialists and GPs and the *d*-value showed (0.26). The difference in average cost per item was of no practical importance (Section 3.3.7.3).

In 2006 the following could be observed:

- Most of the CCB medicine items were prescribed by GPs (75.53%) at a total cost of73.46% of the total expenditure of CCB items in 2006.
- The CPI value of CCB items prescribed by GPs indicated that it was the most inexpensive (Section 3.3.5.4) CCB items dispensed in 2006.
- It was found that 22 448 CCB medicine items (6.06%) dispensed in 2006 were prescribed by cardiologists at an average cost of R 145.56 (SD = R 63.46) per item.
- A *d*-value in 2006 indicated in Table 4.57 was calculated between the average cost of items by group specialists and GPs and the *d*-value showed (0.25). The difference in average cost per item was of no practical importance (Section 3.3.7.3).

According to Table 4.57 information for 2007 included the following:

- A number of 274 658 (75.03%) items dispensed in 2007 were prescribed by a GP.
- The average cost of a CCB item prescribed by GPs was R 137.35 (SD = R 66.43) and this was the lowest average cost per item in all the examined groups of prescribers.
- Group specialists prescribed more than a quarter of all CCB medicine items dispensed in 2007.
- A CPI value of 1.08 showed that items prescribed by group specialists were relatively more expensive than CCB items prescribed by GPs (CPI = 0.98).

- The most expensive average cost per CCB medicine item was prescribed by thoracic surgeons (R 153.68 SD = R 74.47) in 2007.
- A *d*-value in 2007 was calculated between the average cost of items by thoracic surgery and GPs and the *d*-value showed (0.22) the difference in average cost per item was of no practical importance (Section 3.3.7.3).

According to the 2008 information in Table 4.57 the following could be noted:

- The percentage of CCB medicine items prescribed by cardiologists decreased to 5.58% in 2008.
- The percentage of CCB items prescribed by GPs increased by 1.82% from 2007 (75.03%) to 2008 (76.85%) as the overall use of CCB items increased during the study period (Table 4.5).
- The most expensive average cost per CCB item was seen with the items dispensed by thoracic surgeons (R 161.53 SD = R 71.58) but items prescribed by thoracic surgeons represented only 0.12% of all CCB items dispensed in 2008.
- CCB items prescribed by thoracic surgeons had a CPI value of 1.22 and could be considered as relatively expensive (Section 3.3.5.4).
- The lowest average cost per CCB medicine item in 2008 was seen prescribed by GPs (R 128.34 SD = R 68.08).
- A *d*-value for 2008 was calculated between the average cost of items by thoracic surgery and GPs as the average cost per item of these two prescribers showed to be the highest and lowest, as described in the above remarks. The *d*-value was calculated to be 0.46. This was the highest *d*-value calculated in this section (Section 4.11) but still indicated the difference in average cost per item between these two prescribers was of no practical importance (Section 3.3.7.3).

4.12 Chapter summary

In this chapter the results of the empirical investigation were outlined. The main focus was on CCB medicine items and this was analysed in different age groups, gender and prescribers. Cost saving through generic substitution was investigated. Refill-adherence rates were analysed and the top 10 CCBs were determined for each of the study years.

In the following chapter (chapter 5) the conclusions made in this study as well as a number recommendations will be documented.

CHAPTER 5

Conclusions and Recommendations

5.1 Introduction

In this chapter the conclusions of this study will be discussed. Recommendations will also be made for future studies.

5.2 Conclusions

The conclusions made in this study will be discussed in line with objectives as formulated earlier in chapters one and three of this study.

5.2.1 Literature review

The specific research objectives of the literature review as stated in chapter one and chapter three will be mentioned and discussed together with relevant conclusions.

5.2.1.1 The first objective was to determine the general indications and future uses of CCB medicine products.

Section 2.2 of this study supplied general information on CCB preparations. It was pointed out that CCBs are generally indicated for hypertensive and anginal patients (Snyman, 2009:103). In section 2.3.9 of this study it was noted that CCB medicine items could in future also be used for antimigraine treatment (Donald & Warkentin, 2009:1; Ogbru, 2009) because CCBs have a vasodilatory effect. Another possibility attached to CCB medicine items is that they may possibly be used to counter the iron overload that causes tissue damage after myocardial infarct (Oudit, 2005:73). The countering action of CCBs with regard bronchoconstriction could see CCBs being indicated for asthmatic patients (Barnes ,1983:3; Boushey, 2009:340; Gomes *et al.*, 2007:1117), especially patients suffering from hypertension or angina pectoris (Barnes, 1983:4). An article found by Wisner and her team of researchers (2002:1) stated that verapamil is effective in female manic patients, but further research would be necessary.

Some added effects of CCB medicine items were also noted. It was stated (Ikeda *et al.,* 2009:52; Clunn *et al.,* 2009:4) that amlodipine has a very useful effect in patients with atherosclerosis as it reduces the intimae-media thickness of the carotid artery. Opie *et al.*

*(*2000:9) found that verapamil, if taken for a minimum of two years, lowers blood cholesterol slightly.

5.2.1.2 The second objective was to determine conditions for which the use of CCB medication is considered as the preferred therapy.

In section 2.3.4.1 was mentioned that dihydropyridine CCBs, especially amlodipine, are favoured for use in pregnancy because of their antihypertensive effect (Southern African Hypertension Society, 2006; Weber-Schoendorfen *et al*., 2008:1)

In section 2.3.4.2 of this study was stated that non-dihydropyridine CCBs are the therapy preferred for the treatment of the black hypertensive patients (Southern African Hypertension Society, 2006). Non-dihydropyridine CCBs are also selected for patients suffering from tachycardia (Southern African Hypertension Society, 2006).

5.2.1.3 The third objective was to determine the possible uses of drug utilisation review, pharmaco-economic, pharmaco-epidemiology, prescribed daily dosages and cost analysis with regard to CCB usage.

An important part of this study was to identify possible instruments for measuring medicine usage. This section listed some possible instruments to use.

Possible uses of DUR include the following as described in section 2.9:

- Making estimates of the numbers of patients exposed to drugs within a given time period. These estimates may either refer to all drug users, regardless of when they started to use the drug (prevalence), or focus on patients who started to use the drug within the selected period (incidence).
- Describing the extent of use at a certain time and/or in a certain area (e.g. country, region, community, hospital). Such descriptions are most meaningful when they are part of a continuous evaluation system (when the patterns are followed over time and trends in drug use can be described).
- Estimating (e.g. on the basis of epidemiological data on a disease) to what extent drugs are properly used, overused, or underused.
- Describing the pattern or profile of drug use (alternative drugs used for particular conditions and to what extent).
- Comparing observed patterns of drug use with current recommendations or guidelines for the treatment of a certain disease.

- Applying quality indicators to drug utilisation patterns, e.g. so-called DU90% that reflects the number of drugs that account for 90% of drug prescriptions and adherence.
- Relating the number of adverse effects to the number of patients exposed in order to assess the potential magnitude of the problem. It could be detected that the reaction is more common in a certain age group, under certain conditions or at a special dose level, improving the information on proper use to assure a safer use. By doing so withdrawal of the drug from the market may be avoided.

DUR combined with pharmaco-epidemiology can be used to determine prevalence of CCB medicine items and side-effects. This approach was implemented in chapter 4 of this study.

Pharmaco-economic aspects were discussed in section 2.8. CMA (cost-minimisation analysis) was used in section 4.7 of this study and it could be used to promote generic substitution of especially CCB medicine items. The cost aspects of CCBs were analysed throughout chapter 4 including per gender (Section 4.2.2) as well as in the specified age groups (Section 4.2.3).

PDD (prescribed daily dosage) of all the CCB active ingredients were analysed and tabulated in section 2.3.8 (Table 2.1) as well as the dosages of the different age groups. PDD as such was not further analysed in this study but is definitely recommended.

5.2.2 Empirical investigation

The specific research objectives of the empirical study as stated in Chapter 1 and Chapter 3 are included to accompany discussions on conclusions in the section below.

5.2.2.1 The forth objective was to analyse the general prescribing patterns of CCB's and the identification of possible changes from 2005 to 2008.

It was observed seen that the percentage of CCB medicine items dispensed increased from 2005 to 2008. A greater percentage of patients used a CCB medicine item at the end of the study period compared to the first year. An average annual increase of 0.48% in the patients using CCBs was noted with a 1.93% increase in CCB using patients over the study period. An increase of 0.61% of the percentage of CCB items dispensed over the study period was noted (table 4.6).

In comparison with the total database, that showed an increase of 16.41% in the average cost per medicine item, a slight decrease of 4.84% was recorded in the average cost per

cardiovascular medicine item during the four- year study period. A decrease of 5.66% in the average cost per CCB medicine item was also recorded during the time period (Section 4.3).

5.2.2.2 The fifth objective was to determine the possible difference in the prescribing patterns between various age groups and genders of patients using CCBs

From section 4.3.2 it was noted that in general men received more CCBs than female patients during the study period. An exception could be noted in 2007 when a relatively higher percentage of female patients received a CCB medicine item in comparison with the male patients in that year. The percentage of male patients who used a CCB medicine items according to the medicine claims database ranged from 4.14% to 6.02% and the percentage of female users ranged from 3.51% to 4.95% during the study period. The amount spent by females on CCB medicine items ranged from 2.25% to 2.54% of the total cost spent on medicine items and for male patient it ranged from 2.72% to 3% during the study period. The CPI value in female patients using CV items were less than in male patients using CV items of the same year throughout and it could be concluded that the CV treatment of female patients was relatively less expensive compared to those of male patients (table 4.8).

Information contained in table 4.9 indicated that the use of CCBs increased as the patients' age advanced. A higher percentage of patients over 65 years of age used a CCB medicine item during the study period than any other patient age group. The percentage for patients older than 65 years ranged from 13.82% to 17.98% during the study period. The percentage of CCB medicine items used by these patients increased by 1.52% during the study period. The percentage of CCB medicine items used by patients in age group 2 (>15 ≤ 25 years) ranged from 0.04% to 0.05% of the total medicine items used by these patients during the study period and the number of items used by patient in age group 5 (> 45 ≤ 55 years) calculated as percentages between 1.46% and 2.05%.

Patients aged 65 years and older had the highest expenditure on CCB medicine items ranging from R 23 236 624.54 to R 25 881 167.07, rendering percentages between 4.38% and 4.56% of the total expenditure during the study period for patients older than 65 years. Patients in age group 4 (>35 ≤45 years) used between 1.04% and 1.19% of their total medicine expenditure on CCB medicine items during the study period (table 4.9).

5.2.2.3 The sixth objective was to determine the differences in the prescribing patterns of CCBs between general practitioners and specialists.

As noted in chapter 4.11 of the study GPs prescribed more than 70% of the CCB medicine items used during the study period. Cardiologists were responsible for approximately 6% of

the CCB medicine items prescribed in a year. The average prices of the CCBs prescribed by GPs were relatively lower than the average cost of CCBs by any of the specialist prescribers analysed in this study. The highest average cost per CCB medical items prescribed was seen by group specialists (in 2005 and 2006) and thoracic surgeons (in 2007 and 2008). The *d*-values calculated indicated that the difference in the average cost was of no practical significance ($d < 0.8$).

5.2.2.4 The seventh objective was to establish refill-adherence rates with regard to CCBs by using data from a medicine claims database.

According to the medicine claims database 60.34% (n = 10 752) of the patients who used a CCB during the study period had an acceptable refill-adherence rate according to the requirements stated in section 3.3.5.5. It was also noted that male patients (91.46%) were more adherent to their CCB medical items compared to female patients (88.89%). A higher percentage of patients aged over 65 years (91.71%) had an acceptable refill-adherence rate compared to any other patient age group. It was further noted that the highest percentage of acceptable refill-adherence rate occurred with israpidine containing medicine items. Patients using nifedipine containing CCB medicine items had the worst refill-adherence rate (54.4%) of all CCB active ingredients compared and 41.5% of nifedipine containing items were used with unacceptable low refill-adherence rates. The highest percentage of acceptable refill-adherence rate was indicated with Adco-Vascard® 30 SR usage (68.98%). A lower than 50% acceptable refill-adherence rate (48.93%) could be attached to Adalat® XL 30 mg that showed the lowest percentage of all items included in the refill-adherence calculations.

5.2.2.5 The eighth objective was to establish potential savings that could be generated by means of generic substitution of CCBs in the private health care sector of South Africa.

The biggest potential cost saving by means of generic substitution could be achieved with CCB medicine items containing amlodipine. This was noted throughout the study period. If all Norvasc® 10 mg (innovator) items used in 2005 were to be substituted for Nortwin® of the same strength a possible 38.8% could be saved off the total cost of Norvasc® 10 mg in that year. A potential 50.50% saving of the total cost of Norvasc® 5 mg in 2007 could be achieved should Norvasc® 5 mg be substituted for Almadin® 5 mg. Generic substitution of amlodipine containing medicine items could have resulted in potential savings ranging between R 254 060.43 and R 1 910 870.68 in 2008.

However, care should be taken, because not all generic equivalents are less expensive than the innovators and generic substitution will not always result in cost saving (Section 4.7). During the study period it was noted that some nifedipine generic equivalents presented with a higher average cost per medicine item than the innovator medicine item and were, therefore, relatively more expensive. In 2007 it was seen that if all Adalat ®10 mg items were to be substituted with Sandoz® nifedipine 10 mg, a loss of R 7 076.15 would be achieved. In 2008 some loses could also be seen when the nifedipine containing innovator was to be substituted with some generic equivalents thereof.

Cardifen® 5 mg, a generic equivalent to Adalat® 5 mg (innovator), could have resulted in an amount of R 11 033.02 (53.38%) saved, had the innovator been substituted for the generic (2006).

Plendil® is the innovator medicine item containing felodipine. A generic of that product is marketed as Felodipine-Hexal® which was available in a 5 mg and 10 mg tablet form during the study period. Generic substitution of felodipine containing medicine items had the potential of saving between R 261 949.96 and R 720 477.61 in 2005. It was also noted that an amount of R 127 104.54 could be saved should generic substitution be applied to verapamil containing medicine items (Table 4.43).

5.3 Recommendations

- As discussed in section 4.7 of this thesis, some medicine items still revealed relatively large deviations in costs. However, the pricing structure of medicine items was not within the scope of this study. Further studies on this matter would be beneficial.

- It was noted that a considerable number of CCB medicine items were not recorded as PMB items by the medical schemes during the study period. The reasons for the inclusion of CCBs as a chronic on the PMB (prescribed minimum benefits) options should be investigated as CCBs could be considered as qualifying for PMB status.

- Results and findings of this study showed that refill-adherence rates pertaining to CCB medicine items allowed much scope for improvement. An in-depth study investigating the relationship between the financial aspects, reasons for poor adherence and adherence rates would be strongly recommended.

- The possible CCB-related drug-drug interactions with various other medication items should be investigated and clinically evaluated as this section has not yet received adequate attention.

- Combination therapy for cardiovascular conditions should be analysed more extensively as the majority these conditions require combination therapy.

5.4 Chapter summary

In this chapter conclusions pertaining to the objectives of the literature review as well the empirical investigation were presented. Recommendations for further studies with regard to cardiovascular medicine usage were also stated. With this the specific research objectives of this study (Section 3.2.1) were attained.

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APPENDIX

Table A.1: *d*-Values of the total database, the cardiovascular items and CCB items per gender

	Year	Gender	Total number of patients	Total number of Rx	Total number of items dispensed	Total cost of items dispensed (R)	Average cost per item (R)	SD	*d* Value	d Value per gender with total database	d Value per gender with cardio-vascular
Total medicine database	2005	Female	842 386	5 036 494	11 750 190	1 084 626 865.29	92.31	158.69	0.01		
		Male	665 505	3 348 219	7 734 461	733 769 633.85	94.87	176.88			
	2006	Female	868 891	5 336 202	12 699 707	1 162 254 536.29	91.52	188.12	0.02		
		Male	688 091	3 565 328	8 403 158	796 360 401.04	94.77	208.10			
	2007	Female	654 348	4 754 911	11 509 346	1 138 188 990.86	98.89	300.67	0.01		
		Male	523 841	3 154 355	7 562 466	779 508 488.81	103.08	356.74			
	2008	Female	538 254	4 062 385	9 893 928	1 057 274 453.63	106.86	416.84	0.01		
		Male	436 243	2 713 478	6 545 325	728 596 560.22	111.32	465.21			
Cardiovascular medicine usage	2005	Female	134 538	978 261	1 400 663	183 041 895.37	130.68	77.47	0.11	0.24	
		Male	107 557	797 077	1 232 903	172 102 228.60	139.59	80.66		0.25	
	2006	Female	138 006	1 058 054	1 539 707	194 789 701.98	126.51	75.63	0.11	0.19	
		Male	111 945	871 842	1 374 067	185 699 175.19	135.15	79.44		0.19	
	2007	Female	117 210	990 732	1 465 522	189 594 111.56	129.37	74.78	0.10	0.10	
		Male	93 444	807 998	1 300 463	178 489 288.29	137.25	78.67		0.10	
	2008	Female	108 959	932 970	1 400 223	175 887 779.94	125.61	72.10	0.07	0.04	
		Male	89 888	776 748	1 269 536	166 677 528.47	131.29	76.02		0.04	
CCB medicine usage	2005	Female	27 746	176 797	178 266	24 659 535.70	138.33	67.41	0.07	0.29	0.10
		Male	21 379	138 467	139 822	19 983 730.18	142.92	68.96		0.27	0.04
	2006	Female	30 739	204 966	206 619	27 560 062.17	133.39	64.41	0.05	0.22	0.09
		Male	24 016	162 289	163 693	22 366 310.49	136.64	65.82		0.20	0.02
	2007	Female	28 692	204 123	205 679	28 547 578.27	138.80	66.45	0.06	0.13	0.13
		Male	21 865	158 693	160 284	22 859 239.24	142.62	67.54		0.11	0.07
	2008	Female	28 064	201 124	202 485	26 803 965.72	132.38	68.66	0.00	0.06	0.09
		Male	22 537	163 387	164 952	21 841 260.57	132.41	69.74		0.05	0.01

Table A.2: CCB medicine items ranked from most dispensed to least dispensed for the year 2005

Position	Registered trade name	Active ingredient	Number of medicine Items dispensed	Average cost per tablet (R)	SD	Average cost per medicine item (R)	SD	Total cost per medicine item (R)	Percentage of total prevalence (%)	Percentage of total cost (%)	CPI
1	Norvasc 5 mg tab	Amlodipine	39 825	4.62	0.49	138.62	26.97	5 520 457.90	12.51%	12.36%	0.99
2	Adalat XL 30 mg tab	Nifedipine	30 814	6.91	0.43	206.06	38.42	6 349 524.99	9.68%	14.22%	1.47
3	Cipalat retard 20 mg	Nifedipine	27 409	0.82	0.15	42.93	13.91	1 176 686.07	8.61%	2.63%	0.31
4	Verahexal 240 SR	Verapamil	24 815	3.54	0.23	101.47	23.35	2 518 002.35	7.80%	5.64%	0.72
5	Amloc 5 mg tab	Amlodipine	20 418	3.48	0.34	103.73	19.15	2 117 962.12	6.42%	4.74%	0.74
6	Calcicard SR 240 mg	Verapamil	19 264	4.76	0.34	134.48	33.46	2 590 537.72	6.05%	5.80%	0.96
7	Norvasc 10 mg tab	Amlodipine	17 127	6.17	0.67	182.36	26.65	3 123 337.31	5.38%	6.99%	1.30
8	Adalat xl 60 mg tab	Nifedipine	12 313	9.22	0.50	269.24	32.05	3 315 190.96	3.87%	7.42%	1.92
9	Vascard 30 SR	Nifedipine	11 126	4.80	0.28	152.01	31.57	1 691 219.93	3.50%	3.79%	1.08
10	Felodipine-Hexal 5 mg	Felodipine	10 967	3.43	0.20	103.26	16.51	1 132 403.19	3.45%	2.54%	0.74
11	Zildem 180 mg SR	Diltiazem	10 934	5.96	0.31	181.40	25.07	1 983 379.68	3.44%	4.44%	1.29
12	Ravamil SR 240 mg	Verapamil	10 864	4.81	0.26	135.00	35.45	1 466 680.92	3.41%	3.28%	0.96
13	Amloc 10 mg tab	Amlodipine	9 879	4.72	0.41	140.47	17.67	1 387 717.41	3.10%	3.11%	1.00
14	Plendil 5 mg tab	Felodipine	7 100	6.80	0.70	204.73	33.28	1 453 591.74	2.23%	3.25%	1.46
15	Nifedalat 20 SR tab	Nifedipine	5 501	0.75	0.16	33.15	12.56	182 363.79	1.73%	0.41%	0.24
16	Zildem 90 mg tab	Diltiazem	5 233	4.44	0.30	232.38	59.65	1 216 030.01	1.64%	2.72%	1.66
17	Plendil 2.5 mg tab	Felodipine	5 160	5.68	0.31	172.62	28.98	890 712.04	1.62%	1.99%	1.23
18	Dynacirc SRO 5 mg cap	Israpidine	5 100	7.73	0.40	243.13	49.95	1 239 959.94	1.60%	2.78%	1.73
19	Zildem 240 mg SR	Diltiazem	4 660	5.97	0.29	179.70	14.45	837 413.58	1.46%	1.87%	1.28
20	Vasomil 40 mg tab	Verapamil	3 765	0.40	0.06	25.00	10.20	94 130.28	1.18%	0.21%	0.18
21	Zildem 60 mg tab	Diltiazem	3 473	2.08	0.25	109.18	40.49	379 166.12	1.09%	0.85%	0.78
22	Isoptin SR 240 mg tab	Verapamil	3 182	5.04	0.31	140.62	40.00	447 460.44	1.00%	1.00%	1.00
23	Sandoz diltiazem 60 mg	Diltiazem	2 899	1.23	0.15	71.81	25.52	208 181.80	0.91%	0.47%	0.51
24	Vasomil 80 mg tab	Verapamil	2 888	0.84	0.09	54.82	19.86	158 324.90	0.91%	0.35%	0.39

Table A.2: CCB medicine items ranked from most dispensed to least dispensed for the year 2005 (continued)

Position	Registered trade name	Active ingredient	Number of medicine Items dispensed	Average cost per tablet (R)	SD	Average cost per medicine item (R)	SD	Total cost per medicine item (R)	Percentage of total prevalence (%)	Percentage of total cost (%)	CPI
25	Felodipine-Hexal 10 mg tab	Felodipine	2 744	4.68	0.16	140.31	17.96	384 997.51	0.86%	0.86%	1.00
26	Plendil 10 mg tab	Felodipine	2 410	8.30	0.74	249.00	31.11	600 085.53	0.76%	1.34%	1.77
27	Cardifen TM 10 mg cap	Nifedipine	1 940	1.45	0.15	84.73	42.19	164 380.30	0.61%	0.37%	0.60
28	Dilatam 60 mg tab	Diltiazem	1 725	1.50	0.22	84.38	28.98	145 554.33	0.54%	0.33%	0.60
29	Zanidip 10 mg tab	Lercanidipine	1 527	5.12	0.24	148.85	26.81	227 292.82	0.48%	0.51%	1.06
30	Cardifen tm 5 mg cap	Nifedipine	1 437	1.08	0.19	54.16	28.60	77 825.03	0.45%	0.17%	0.39
31	Sandoz Verapamil HCl 40 mg	Verapamil	1 280	0.51	0.24	31.02	14.43	39 709.56	0.40%	0.09%	0.22
32	Sandoz Verapamil HCl 80 mg	Verapamil	1 014	0.98	0.16	57.86	18.11	58 671.40	0.32%	0.13%	0.41
33	Nifedalat 10 mg cap	Nifedipine	975	0.74	0.22	41.73	21.64	40 686.98	0.31%	0.09%	0.30
34	Dynacirc 2.5 mg tab	Israpidine	974	4.18	0.30	164.18	53.15	159 910.64	0.31%	0.36%	1.17
35	Adalat retard 20 mg	Nifedipine	917	6.98	0.63	325.98	105.60	298 919.22	0.29%	0.67%	2.32
36	Isoptin 40mg tab	Verapamil	785	0.78	0.12	53.53	31.08	42 024.95	0.25%	0.09%	0.38
37	Tilazem 180 CR	Diltiazem	760	7.41	0.41	228.83	44.33	173 907.86	0.24%	0.39%	1.63
38	Tilazem 60 mg	Diltiazem	689	3.78	0.62	204.95	100.84	141 212.32	0.22%	0.32%	1.46
39	TILAZEM 90 mg	DILTIAZEM	639	5.61	0.51	257.19	87.89	164 341.55	0.20%	0.37%	1.83
40	Adalat retard 10 mg	Nifedipine	623	4.07	0.50	184.76	78.34	115 103.48	0.20%	0.26%	1.32
41	Sandoz nifedipine 10 mg	Nifedipine	581	1.49	0.22	86.96	40.47	50 525.47	0.18%	0.11%	0.62
42	Sandoz Verapamil HCl 120 mg	VERAPAMIL	575	1.75	0.17	77.14	29.96	44 355.68	0.18%	0.10%	0.55
43	Adalat 10 mg cap	Nifedipine	533	4.55	1.43	154.93	175.39	82 576.04	0.17%	0.18%	1.10
44	Nortwin 5 mg	Amlodipine	503	3.00	1.63	90.07	51.11	45 306.77	0.16%	0.10%	0.64
45	Adalat 5 mg cap	Nifedipine	301	3.70	0.79	113.65	95.85	34 208.74	0.09%	0.08%	0.81
46	Nortwin 10 mg	Amlodipine	218	3.73	1.99	111.61	59.81	24 331.02	0.07%	0.05%	0.80
47	Tilazem 240 CR	Diltiazem	194	7.87	0.55	238.14	24.85	46 199.35	0.06%	0.10%	1.70
48	Amlosyn 5 mg tab	Amlodipine	119	3.32	0.13	98.24	13.67	11 690.10	0.04%	0.03%	0.70
49	Amlosyn 10 mg tab	Amlodipine	49	4.63	0.15	135.42	16.82	6 635.34	0.02%	0.01%	0.96

Table A.2: CCB medicine items ranked from most dispensed to least dispensed for the year 2005 (continued)

Position	Registered trade name	Active ingredient	Number of medicine Items dispensed	Average cost per tablet (R)	SD	Average cost per medicine item (R)	SD	Total cost per medicine item (R)	Percentage of total prevalence (%)	Percentage of total cost (%)	CPI
50	Isoptin 80 mg tab	Verapamil	14	3.31	0.20	147.91	78.72	2 070.74	0.00%	0.00%	1.05
51	Isoptin 5 mg/2 ml inj.	Verapamil	8	18.38	15.21	33.96	23.17	271.70	0.00%	0.00%	0.24
52	Syscor-cc 20 mg	Nisoldipine	7	9.92	-	297.73	-	2 084.11	0.00%	0.00%	2.12
53	A-Lennon nifedipine 5 mg	Nifedipine	1	0.08	-	16.69	-	16.69	0.00%	0.00%	0.12

Table A.3: CCB medicine items ranked from most dispensed to least dispensed for the year 2006

Position	Registered trade name	Active ingredient	Number of medicine Items dispensed	Average cost per tablet (R)	SD	Average cost per medicine item (R)	SD	Total cost per medicine item (R)	Percentage of total prevalence (%)	Percentage of total cost (%)	CPI
1	Amloc 5 mg tab	Amlodipine	45 129	3.34	0.21	99.42	16.64	4 486 700.61	12.18%	8.98%	0.74
2	Adalat xl 30 mg tab	Nifedipine	35 687	6.91	0.56	206.32	41.58	7 362 957.79	9.63%	14.74%	1.53
3	Norvasc 5 mg tab	Amlodipine	35 076	4.37	0.35	131.75	24.23	4 621 227.02	9.47%	9.25%	0.98
4	Cipalat retard 20 mg	Nifedipine	30 835	0.81	0.16	42.72	14.12	1 317 376.31	8.32%	2.64%	0.32
5	Verahexal 240 SR	Verapamil	27 131	3.54	0.24	102.02	23.14	2 767 818.78	7.32%	5.54%	0.76
6	Amloc 10 mg tab	Amlodipine	22 797	4.58	0.28	136.30	14.70	3 107 299.00	6.15%	6.22%	1.01
7	Calcicard SR 240 mg	Verapamil	20 013	4.80	0.31	136.00	33.20	2 721 761.42	5.40%	5.45%	1.01
8	Norvasc 10 mg tab	Amlodipine	16 476	5.85	0.52	173.52	21.52	2 858 890.03	4.45%	5.72%	1.29
9	Adalat xl 60 mg tab	Nifedipine	14 458	9.18	0.66	267.35	29.28	3 865 350.60	3.90%	7.74%	1.98
10	Vascard 30 SR	Nifedipine	14 343	4.78	0.26	154.95	36.67	2 222 404.86	3.87%	4.45%	1.15
11	Felodipine-Hexal 5 mg tab	Felodipine	13 200	3.39	0.19	102.69	18.23	1 355 480.75	3.56%	2.71%	0.76
12	Ravamil SR 240 mg tab	Verapamil	11 231	4.79	0.32	134.91	37.20	1 515 120.42	3.03%	3.03%	1.00
13	Zildem 180 mg SR	Diltiazem	10 464	5.96	0.36	181.03	23.78	1 894 249.21	2.82%	3.79%	1.34
14	Nifedalat 20sr tab	Nifedipine	6 405	0.75	0.13	34.04	13.21	218 019.74	1.73%	0.44%	0.25
15	Zanidip 10 mg tab	Lercanidipine	5 617	5.09	0.41	151.21	34.26	849 341.98	1.52%	1.70%	1.12
16	Plendil 5 mg tab	Felodipine	4 948	6.75	0.93	202.73	36.49	1 003 105.15	1.34%	2.01%	1.50
17	Zildem 90 mg tab	Diltiazem	4 884	4.43	0.34	231.84	59.35	1 132 315.31	1.32%	2.27%	1.72
18	Plendil 2.5 mg tab	Felodipine	4 682	5.67	0.39	174.14	32.52	815 308.68	1.26%	1.63%	1.29
19	Felodipine-Hexal 10 mg tab	Felodipine	4 526	4.67	0.24	140.69	19.08	636 768.35	1.22%	1.27%	1.04
20	Dynacirc SRO 5 mg cap	Israpidine	4 327	7.71	0.50	242.21	52.09	1 048 063.45	1.17%	2.10%	1.80
21	Zildem 240 mg SR	Diltiazem	4 291	5.95	0.44	179.20	20.04	768 939.93	1.16%	1.54%	1.33
22	Vasomil 40 mg tab	Verapamil	3 712	0.39	0.10	23.93	9.85	88 826.90	1.00%	0.18%	0.18
23	Isoptin SR 240 mg tab	Verapamil	3 378	5.04	0.34	138.91	38.47	469 236.94	0.91%	0.94%	1.03

Table A.3: CCB medicine items ranked from most dispensed to least dispensed for the year 2006 (continued)

Position	Registered trade name	Active ingredient	Number of medicine Items dispensed	Average cost per tablet (R)	SD	Average cost per medicine item (R)	SD	Total cost per medicine item (R)	Percentage of total prevalence (%)	Percentage of total cost (%)	CPI
24	Sandoz diltiazem 60 mg	Diltiazem	3 300	1.26	0.18	71.38	25.88	235 551.73	0.89%	0.47%	0.53
25	Zildem 60 mg tab	Diltiazem	3 274	2.05	0.24	104.63	39.75	342 547.17	0.88%	0.69%	0.78
26	Vasomil 80 mg tab	Verapamil	2 666	0.83	0.10	55.95	20.87	149 159.06	0.72%	0.30%	0.41
27	Dilatam 60 mg tab	Diltiazem	1 770	1.46	0.17	83.57	30.44	147 919.51	0.48%	0.30%	0.62
28	Cardifen tm 10 mg cap	Nifedipine	1 765	1.44	0.28	83.60	45.31	147 548.69	0.48%	0.30%	0.62
29	Plendil 10 mg tab	Felodipine	1 558	8.24	0.88	246.92	34.56	384 696.49	0.42%	0.77%	1.83
30	Cardifen tm 5 mg cap	Nifedipine	1 450	1.07	0.18	51.25	26.90	74 316.41	0.39%	0.15%	0.38
31	Amlosyn 5 mg tab	Amlodipine	1 213	3.31	0.27	99.78	18.43	121 031.73	0.33%	0.24%	0.74
32	Sandoz verapamil HCl 40 mg	Verapamil	1 213	0.55	0.27	31.15	13.40	37 789.82	0.33%	0.08%	0.23
33	Sandoz verapamil HCl 80 mg	Verapamil	1 015	1.00	0.18	61.20	18.45	62 115.22	0.27%	0.12%	0.45
34	Nifedalat 10 mg cap	Nifedipine	931	0.70	0.20	37.03	20.12	34 474.21	0.25%	0.07%	0.27
35	Isoptin 40 mg tab	Verapamil	829	0.81	1.37	60.12	87.42	49 835.74	0.22%	0.10%	0.45
36	Dynacirc 2.5 mg tab	Israpidine	755	4.16	0.33	166.64	55.47	125 811.36	0.20%	0.25%	1.24
37	Tilazem 60 mg tab	Diltiazem	629	3.72	0.71	200.74	96.13	126 265.55	0.17%	0.25%	1.49
38	Tilazem 180 CR	Diltiazem	622	7.27	0.84	225.64	47.51	140 346.60	0.17%	0.28%	1.67
39	Amlosyn 10 mg tab	Amlodipine	620	4.62	0.19	137.00	11.78	84 940.92	0.17%	0.17%	1.02
40	Adalat retard 20 mg	Nifedipine	555	7.17	0.61	303.07	115.46	168 202.22	0.15%	0.34%	2.25
41	Adalat retard 10 mg	Nifedipine	507	4.07	0.69	171.77	79.93	87 085.66	0.14%	0.17%	1.27
42	Tilazem 90 mg	Diltiazem	492	5.55	0.49	254.77	87.47	125 347.03	0.13%	0.25%	1.89
43	Sandoz verapamil HCl 120 mg	Verapamil	490	1.84	0.19	76.78	33.36	37 623.11	0.13%	0.08%	0.57
44	Adalat 10mg cap	Nifedipine	455	4.77	1.17	106.05	149.34	48 253.63	0.12%	0.10%	0.79
45	Sandoz nifedipine 10mg	Nifedipine	370	1.46	0.19	87.96	44.95	32 546.62	0.10%	0.07%	0.65
46	Adalat 5mg cap	Nifedipine	188	3.42	0.99	109.94	118.67	20 668.53	0.05%	0.04%	0.82
47	Tilazem 240 CR	Diltiazem	147	7.60	1.58	226.90	47.73	33 354.07	0.04%	0.07%	1.68
48	Isoptin 5mg/2ml Inj	Verapamil	11	25.74	4.74	143.22	380.06	1 575.41	0.00%	0.00%	1.06

Table A.3: CCB medicine items ranked from most dispensed to least dispensed for the year 2006 (continued)

Position	Registered trade name	Active ingredient	Number of medicine Items dispensed	Average cost per tablet (R)	SD	Average cost per medicine item (R)	SD	Total cost per medicine item (R)	Percentage of total prevalence (%)	Percentage of total cost (%)	CPI
49	Isoptin 80mg tab	Verapamil	5	3.42	0.17	164.06	56.43	820.31	0.00%	0.00%	1.22
50	Nortwin 10mg	Amlodipine	5	0.00	-	0.01	-	0.05	0.00%	0.00%	0.00
51	Nortwin 5mg	Amlodipine	5	0.00	-	0.01	-	0.05	0.00%	0.00%	0.00
52	Amlate 10mg tab	Amlodipine	3	3.96	0.50	118.95	14.99	356.84	0.00%	0.00%	0.88
53	Amlate 5mg tab	Amlodipine	3	3.12	0.05	93.69	1.53	281.06	0.00%	0.00%	0.69
54	Sandoz-amlodipine 10 mg	Amlodipine	2	4.80	-	144.04	-	288.08	0.00%	0.00%	1.07
55	Vasomil 5mg/2ml Inj	Verapamil	2	25.15	1.63	38.31	20.23	76.61	0.00%	0.00%	0.28

Table A.4: CCB medicine items ranked from most dispensed to least dispensed for the year 2007

Position	Registered trade name	Active ingredient	Number of medicine Items dispensed	Average cost per tablet (R)	SD	Average cost per medicine item (R)	SD	Total cost per medicine item (R)	Percentage of total prevalence (%)	Percentage of total cost (%)	CPI
1	Amloc 5 mg tab	Amlodipine	59 987	3.53	0.37	105.10	19.73	6 304 645.67	16.39%	12.26%	0.75
2	Adalat XL 30 mg tab	Nifedipine	35 359	7.23	0.80	216.74	49.82	7 663 566.38	9.66%	14.90%	1.54
3	Amloc 10 mg tab	Amlodipine	31 500	4.79	0.45	143.15	19.17	4 509 209.64	8.61%	8.77%	1.02
4	Verahexal 240 SR	Verapamil	25 414	3.80	0.31	110.06	25.33	2 797 106.82	6.94%	5.44%	0.78
5	Norvasc 5 mg tab	Amlodipine	25 396	4.49	0.60	135.94	30.49	3 452 238.03	6.94%	6.71%	0.97
6	Cipalat retard 20 mg	Nifedipine	23 636	0.80	0.13	41.50	14.30	980 968.20	6.46%	1.91%	0.30
7	Calcicard SR 240 mg	Verapamil	15 426	5.04	0.44	142.74	35.21	2 201 939.45	4.21%	4.28%	1.02
8	Adalat XL 60 mg tab	Nifedipine	14 778	9.62	0.93	280.83	36.35	4 150 072.39	4.04%	8.07%	2.00
9	Felodipine-Hexal 5 mg tab	Felodipine	13 239	3.61	0.37	108.76	22.09	1 439 820.31	3.62%	2.80%	0.77
10	Norvasc 10 mg tab	Amlodipine	12 556	6.01	0.81	178.33	28.67	2 239 164.80	3.43%	4.35%	1.27
11	Vascard 30 SR	Nifedipine	11 981	4.98	0.39	161.97	41.08	1 940 565.83	3.27%	3.77%	1.15
12	Ravamil SR 240 mg tab	Verapamil	11 662	5.02	0.49	141.59	36.72	1 651 212.18	3.19%	3.21%	1.01
13	Zildem 180mg SR	Diltiazem	10 203	6.28	0.50	191.30	27.82	1 951 870.05	2.79%	3.80%	1.36
14	Zanidip 10 mg tab	Lercanidipine	7 941	5.34	0.56	160.37	36.08	1 273 502.45	2.17%	2.48%	1.14
15	Felodipine-Hexal 10 mg tab	Felodipine	4 754	4.93	0.31	148.59	20.31	706 373.33	1.30%	1.37%	1.06
16	Nifedalat 20 SR tab	Nifedipine	4 269	0.80	0.14	37.23	14.09	158 949.39	1.17%	0.31%	0.27
17	Zildem 90 mg tab	Diltiazem	4 039	4.69	0.39	246.88	66.25	997 140.19	1.10%	1.94%	1.76
18	Ciplavasc 5 mg tab	Amlodipine	3 999	2.26	0.25	68.12	11.57	272 410.72	1.09%	0.53%	0.48
19	Plendil 2.5 mg tab	Felodipine	3 989	5.95	0.57	182.90	39.28	729 597.00	1.09%	1.42%	1.30
20	Zildem 240 mg SR	Diltiazem	3 902	6.28	0.59	189.23	22.93	738 375.07	1.07%	1.44%	1.35
21	Plendil 5 mg tab	Felodipine	3 548	6.98	1.23	210.58	46.36	747 147.74	0.97%	1.45%	1.50
22	Dynacirc SRO 5 mg cap	Israpidine	3 389	7.95	0.75	254.49	61.85	862 454.98	0.93%	1.68%	1.81
23	Isoptin SR 240 mg tab	Verapamil	3 078	5.31	0.49	147.91	41.83	455 254.74	0.84%	0.89%	1.05
24	Vasomil 40 mg tab	Verapamil	2 901	0.43	0.10	25.77	10.72	74 750.98	0.79%	0.15%	0.18

Table A.4: CCB medicine items ranked from most dispensed to least dispensed for the year 2007 (continued)

Position	Registered trade name	Active ingredient	Number of medicine Items dispensed	Average cost per tablet (R)	SD	Average cost per medicine item (R)	SD	Total cost per medicine item (R)	Percentage of total prevalence (%)	Percentage of total cost (%)	CPI
25	Zildem 60 mg tab	Diltiazem	2 891	2.20	0.34	108.00	40.98	312 224.46	0.79%	0.61%	0.77
26	Ciplavasc 10 mg tab	Amlodipine	2 502	3.45	0.27	103.16	11.69	258 096.99	0.68%	0.50%	0.73
27	Sandoz diltiazem 60 mg	Diltiazem	2 345	1.31	0.18	74.67	28.54	175 104.16	0.64%	0.34%	0.53
28	Vasomil 80 mg tab	Verapamil	2 096	0.90	0.14	58.12	23.13	121 816.74	0.57%	0.24%	0.41
29	Dilatam 60 mg tab	Diltiazem	1 682	1.53	0.16	88.08	32.09	148 152.68	0.46%	0.29%	0.63
30	Cardifen TM 10 mg cap	Nifedipine	1 554	1.44	0.26	77.54	45.80	120 491.50	0.42%	0.23%	0.55
31	Amlosyn 5mg tab	Amlodipine	1 321	3.49	0.50	107.16	24.05	141 561.45	0.36%	0.28%	0.76
32	Cardifen TM 5mg cap	Nifedipine	1 202	1.13	0.30	53.56	30.19	64 374.99	0.33%	0.13%	0.38
33	Plendil 10 mg tab	Felodipine	1 185	8.48	1.36	254.90	50.14	302 050.67	0.32%	0.59%	1.81
34	Lomanor 5 mg tab	Amlodipine	889	3.26	0.77	97.55	26.21	86 724.72	0.24%	0.17%	0.69
35	Nifedalat 10mg cap	Nifedipine	758	0.72	0.17	39.17	23.73	29 693.52	0.21%	0.06%	0.28
36	Sandoz verapamil HCl 40 mg	Verapamil	705	0.47	0.17	30.72	13.60	21 656.08	0.19%	0.04%	0.22
37	Almadin 5 mg tab	Amlodipine	680	2.26	0.33	67.28	13.07	45 753.66	0.19%	0.09%	0.48
38	Klodip-5 mg	Amlodipine	661	2.66	0.50	80.55	20.34	53 244.51	0.18%	0.10%	0.57
39	Isoptin 40 mg tab	Verapamil	620	0.82	0.21	61.19	35.87	37 937.90	0.17%	0.07%	0.44
40	Adalat retard 10mg	Nifedipine	565	4.19	0.90	145.91	102.87	82 440.58	0.15%	0.16%	1.04
41	Sandoz amlodipine 5 mg tab	Amlodipine	559	3.56	0.52	105.76	21.84	59 118.12	0.15%	0.11%	0.75
42	Amlosyn 10 mg tab	Amlodipine	558	4.84	0.38	144.80	14.30	80 800.26	0.15%	0.16%	1.03
43	Tilazem 60 mg tab	Diltiazem	535	3.67	0.95	210.63	129.10	112 688.62	0.15%	0.22%	1.50
44	Tilazem 180 CR	Diltiazem	521	7.64	0.64	233.97	43.45	121 896.85	0.14%	0.24%	1.67
45	Sandoz amlodipine 10 mg	Amlodipine	518	4.85	0.41	145.43	12.36	75 334.21	0.14%	0.15%	1.04
46	Dynacirc 2.5mg tab	Israpidine	512	4.31	0.57	176.65	70.79	90 445.96	0.14%	0.18%	1.26
47	Sandoz verapamil HCl 80 mg	Verapamil	448	0.98	0.11	61.61	19.20	27 601.10	0.12%	0.05%	0.44
48	Tilazem 90 mg tab	Diltiazem	447	5.89	0.52	255.01	91.16	113 990.87	0.12%	0.22%	1.82

Table A.4: CCB medicine items ranked from most dispensed to least dispensed for the year 2007 (continued)

Position	Registered trade name	Active ingredient	Number of medicine Items dispensed	Average cost per tablet (R)	SD	Average cost per medicine item (R)	SD	Total cost per medicine item (R)	Percentage of total prevalence (%)	Percentage of total cost (%)	CPI
49	Adalat retard 20mg	Nifedipine	411	7.36	1.28	281.41	127.36	115 658.27	0.11%	0.22%	2.00
50	Sandoz verapamil HCl 120 mg	Verapamil	407	1.95	0.17	75.60	28.32	30 768.09	0.11%	0.06%	0.54
51	Lomanor 10 mg tab	Amlodipine	403	4.43	1.07	129.99	34.29	52 387.09	0.11%	0.10%	0.93
52	Almadin 10 mg tab	Amlodipine	391	3.28	0.41	98.19	12.87	38 390.58	0.11%	0.07%	0.70
53	Zanidip 20 mg tab	Lercanidipine	266	6.96	0.37	201.03	26.56	53 474.74	0.07%	0.10%	1.43
54	Adalat 10 mg cap	Nifedipine	215	4.58	1.55	46.84	93.38	10 069.68	0.06%	0.02%	0.33
55	Tilazem 240 CR	Diltiazem	156	8.05	0.91	244.74	58.62	38 179.59	0.04%	0.07%	1.74
56	Austell amlodipine 5 mg tab	Amlodipine	138	2.99	0.64	89.36	19.87	12 331.95	0.04%	0.02%	0.64
57	Corvadil 5 mg tab	Amlodipine	135	2.33	0.89	68.55	30.63	9 254.87	0.04%	0.02%	0.49
58	Amlodac 5 mg tab	Amlodipine	130	2.57	0.51	77.95	17.07	10 133.74	0.04%	0.02%	0.55
59	Austell amlodipine 10 mg tab	Amlodipine	113	4.09	0.63	121.17	22.07	13 692.47	0.03%	0.03%	0.86
60	Calbloc 5 mg tab	Amlodipine	105	2.93	0.62	91.51	22.49	915.14	0.03%	0.00%	0.06
61	Corvadil 10 mg tab	Amlodipine	89	2.94	1.14	144.95	11.60	434.84	0.02%	0.00%	0.03
62	Amlodac 10 mg tab	Amlodipine	75	3.73	0.66	111.91	19.80	8 393.21	0.02%	0.02%	0.80
63	Amlate 5 mg tab	Amlodipine	63	2.72	0.50	81.55	15.08	5 137.55	0.02%	0.01%	0.58
64	Amlate 10 mg tab	Amlodipine	58	3.94	0.54	116.28	19.59	6 744.52	0.02%	0.01%	0.83
65	Adalat 5 mg cap	Nifedipine	45	3.43	1.59	55.14	76.41	2 481.52	0.01%	0.00%	0.39
66	Calbloc 10mg tab	Amlodipine	41	4.25	0.78	131.51	1.57	657.53	0.01%	0.00%	0.11
67	Sandoz nifedipine 10 mg	Nifedipine	41	1.44	0.19	79.75	48.23	3 269.67	0.01%	0.01%	0.57
68	Bio-nifedipine 10 mg	Nifedipine	14	0.32	0.17	21.99	19.89	307.82	0.00%	0.00%	0.16
69	CPL alliance amlodipine 5 mg	Amlodipine	13	2.54	1.16	76.10	34.83	989.27	0.00%	0.00%	0.54
70	CPL alliance amlodipine 10 mg	Amlodipine	11	3.90	1.13	116.97	33.97	1 286.70	0.00%	0.00%	0.83
71	Calbloc 5 mg tab	Amlodipine	10	3.24	0.18	87.84	18.70	9 223.47	0.00%	0.02%	6.57

Table A.4: CCB medicine items ranked from most dispensed to least dispensed for the year 2007 (continued)

Position	Registered trade name	Active ingredient	Number of medicine Items dispensed	Average cost per tablet (R)	SD	Average cost per medicine item (R)	SD	Total cost per medicine item (R)	Percentage of total prevalence (%)	Percentage of total cost (%)	CPI
72	Bio-nifedipine 5 mg	Nifedipine	5	0.61	0.48	30.20	32.93	151.00	0.00%	0.00%	0.21
73	Calbloc 10 mg tab	Amlodipine	5	4.38	0.05	127.61	23.44	5 232.03	0.00%	0.01%	7.45
74	Isoptin 5mg/2ml Inj	Verapamil	4	14.03	16.28	28.07	32.57	112.27	0.00%	0.00%	0.20
75	Corvadil 10 mg tab	Amlodipine	3	4.83	0.39	86.50	34.61	7 698.64	0.00%	0.01%	18.27
76	Indo amlodipine 5 mg tab	Amlodipine	1	2.30	0.00	138.01	0.00	138.01	0.00%	0.00%	0.98
77	Vasomil 5mg/2ml Inj	Verapamil	1	0.00	0.00	0.00	0.00	0.00	0.00%	0.00%	0.00

Table A.5: CCB medicine items ranked from most dispensed to least dispensed for the year 2008

Position	Registered trade name	Active ingredient	Number of medicine Items dispensed	Average cost per tablet (R)	SD	Average cost per medicine item (R)	SD	Total cost per medicine item (R)	Percentage of total prevalence (%)	Percentage of total cost (%)	CPI
1	Amloc 5 mg tab	Amlodipine	57 156	3.26	0.47	97.27	20.19	5 559 824.67	15.56%	11.43%	0.73
2	Cipalat retard 20 mg	Nifedipine	32 695	0.88	0.17	46.50	15.40	1 520 444.10	8.90%	3.13%	0.35
3	Amloc 10 mg tab	Amlodipine	32 574	4.46	0.51	133.12	19.08	4 336 209.18	8.87%	8.91%	1.01
4	Adalat XL 30 mg tab	Nifedipine	31 231	7.43	0.83	223.24	53.72	6 971 950.16	8.50%	14.33%	1.69
5	Verahexal 240 SR	Verapamil	27 289	3.92	0.33	113.35	26.37	3 093 145.48	7.43%	6.36%	0.86
6	Norvasc 5 mg tab	Amlodipine	16 012	4.42	0.95	132.80	36.22	2 126 413.90	4.36%	4.37%	1.00
7	Ciplavasc 5 mg tab	Amlodipine	13 663	2.36	0.27	70.84	12.67	967 822.31	3.72%	1.99%	0.54
8	Adalat XL 60 mg tab	Nifedipine	13 398	9.94	0.94	290.65	37.62	3 894 138.20	3.65%	8.01%	2.20
9	Felodipine-Hexal 5mg tab	Felodipine	12 602	3.73	0.37	111.69	22.96	1 407 481.26	3.43%	2.89%	0.84
10	Calcicard SR 240 mg	Verapamil	11 119	5.22	0.50	149.06	36.16	1 657 346.32	3.03%	3.41%	1.13
11	Adco-Vascard 30 SR caps	Nifedipine	10 866	5.10	0.43	166.22	43.13	1 806 170.49	2.96%	3.71%	1.26
12	Ravamil SR 240 mg tab	Verapamil	9 396	5.19	0.54	146.17	38.02	1 373 420.48	2.56%	2.82%	1.10
13	Zildem 180 mg SR	Diltiazem	8 830	6.48	0.48	198.63	31.87	1 753 918.91	2.40%	3.61%	1.50
14	Zanidip 10 mg tab	Lercanidipine	8 370	5.51	0.56	162.69	32.40	1 361 680.91	2.28%	2.80%	1.23
15	Norvasc 10 mg tab	Amlodipine	8 273	5.88	1.24	175.13	38.87	1 448 826.76	2.25%	2.98%	1.32
16	Ciplavasc 10 mg tab	Amlodipine	8 220	3.58	0.27	107.00	10.82	879 577.16	2.24%	1.81%	0.81
17	Lomanor 5 mg tab	Amlodipine	5 105	3.24	0.48	96.22	18.76	491 183.82	1.39%	1.01%	0.73
18	Felodipine-Hexal 10mg tab	Felodipine	4 819	5.06	0.32	152.53	20.55	735 035.80	1.31%	1.51%	1.15
19	Zildem 60 mg tab	Diltiazem	3 366	2.25	0.34	116.21	45.26	391 146.68	0.92%	0.80%	0.88
20	Nifedalat 20 SR tab	Nifedipine	3 357	0.82	0.14	38.22	15.09	128 289.72	0.91%	0.26%	0.29
21	Zildem 240 mg SR	Diltiazem	3 331	6.48	0.56	194.26	17.90	647 086.37	0.91%	1.33%	1.47
22	Plendil 2.5 mg tab	Felodipine	3 007	6.14	0.42	188.06	31.04	565 509.05	0.82%	1.16%	1.42
23	Isoptin SR 240 mg tab	Verapamil	2 845	5.48	0.47	158.02	45.60	449 578.76	0.77%	0.92%	1.19
24	Zildem 90 mg tab	Diltiazem	2 844	4.87	0.39	249.31	64.65	709 048.90	0.77%	1.46%	1.88

Table A.5: CCB medicine items ranked from most dispensed to least dispensed for the year 2008 (continued)

Position	Registered trade name	Active ingredient	Number of medicine Items dispensed	Average cost per tablet (R)	SD	Average cost per medicine item (R)	SD	Total cost per medicine item (R)	Percentage of total prevalence (%)	Percentage of total cost (%)	CPI
25	Plendil 5 mg tab	Felodipine	2 674	7.18	1.26	218.19	55.02	583 429.77	0.73%	1.20%	1.65
26	Dynacirc SRO 5 mg cap	Israpidine	2 662	8.30	0.75	269.08	68.69	716 295.26	0.72%	1.47%	2.03
27	Vasomil 40 mg tab	Verapamil	2 459	0.46	0.13	26.73	11.53	65 727.41	0.67%	0.14%	0.20
28	Lomanor 10 mg tab	Amlodipine	2 457	4.43	0.63	130.93	21.60	321 697.73	0.67%	0.66%	0.99
29	Dilatam 60 mg tab	Diltiazem	2 411	1.60	0.16	91.97	35.07	221 749.09	0.66%	0.46%	0.69
30	Vasomil 80 mg tab	Verapamil	2 027	0.93	0.15	60.40	23.67	122 439.69	0.55%	0.25%	0.46
31	Almadin 5 mg tab	Amlodipine	1 939	2.33	0.28	69.39	12.20	134 556.18	0.53%	0.28%	0.52
32	Klodip-5 mg	Amlodipine	1 886	2.31	0.24	70.55	15.01	133 061.83	0.51%	0.27%	0.53
33	Almadin 10 mg tab	Amlodipine	1 385	3.46	0.24	103.03	8.64	142 700.84	0.38%	0.29%	0.78
34	Cardifen tm 10 mg cap	Nifedipine	1 184	1.51	0.41	71.55	44.48	84 711.22	0.32%	0.17%	0.54
35	Zanidip 20 mg tab	Lercanidipine	1 096	7.13	0.59	207.74	31.08	227 684.10	0.30%	0.47%	1.57
36	Cardifen TM 5 mg cap	Nifedipine	923	1.05	0.43	49.50	34.82	45 688.39	0.25%	0.09%	0.37
37	Sandoz amlodipine 10 mg	Amlodipine	907	3.56	0.82	106.60	25.21	96 683.47	0.25%	0.20%	0.81
38	Sandoz amlodipine 5mg tab	Amlodipine	880	2.36	0.58	71.80	20.81	63 180.05	0.24%	0.13%	0.54
39	Austell amlodipine 5mg tab	Amlodipine	876	2.19	0.29	66.71	13.60	58 437.98	0.24%	0.12%	0.50
40	Plendil 10 mg tab	Felodipine	759	8.82	1.36	265.15	53.03	201 248.92	0.21%	0.41%	2.00
41	Tilazem 60 mg tab	Diltiazem	718	3.85	0.95	193.04	89.66	138 603.14	0.20%	0.28%	1.46
42	Nifedalat 10 mg cap	Nifedipine	708	0.77	0.24	38.43	25.48	27 210.45	0.19%	0.06%	0.29
43	Sandoz verapamil HCl 40	Verapamil	652	0.55	0.21	34.64	13.30	22 588.44	0.18%	0.05%	0.26
44	Indo amlodipine 5 mg tab	Amlodipine	644	2.20	0.24	66.77	15.33	42 998.40	0.18%	0.09%	0.50
45	Amlosyn 5 mg tab	Amlodipine	620	3.59	0.49	108.96	20.90	67 556.53	0.17%	0.14%	0.82
46	Austell amlodipine 10 mg tab	Amlodipine	615	3.38	0.33	100.49	12.50	61 801.73	0.17%	0.13%	0.76
47	Isoptin 40 mg tab	Verapamil	521	0.84	0.23	63.34	37.55	32 998.62	0.14%	0.07%	0.48
48	Tilazem 180 CR	Diltiazem	484	7.87	0.98	245.69	103.80	118 913.62	0.13%	0.24%	1.86
49	Adalat retard 10mg	Nifedipine	448	4.23	1.08	122.59	101.16	54 919.47	0.12%	0.11%	0.93

Table A.5: CCB medicine items ranked from most dispensed to least dispensed for the year 2008 (continued)

Position	Registered trade name	Active ingredient	Number of medicine Items dispensed	Average cost per tablet (R)	SD	Average cost per medicine item (R)	SD	Total cost per medicine item (R)	Percentage of total prevalence (%)	Percentage of total cost (%)	CPI
50	Amlate 5 mg tab	Amlodipine	430	2.21	0.31	65.29	12.36	28 075.70	0.12%	0.06%	0.49
51	Sandoz verapamil HCl 80	Verapamil	384	0.94	0.22	60.86	22.02	23 370.73	0.10%	0.05%	0.46
52	Amlate 10 mg tab	Amlodipine	380	3.52	0.24	105.35	7.94	40 033.52	0.10%	0.08%	0.80
53	Dynacirc 2.5 mg tab	Israpidine	356	4.46	0.53	187.51	69.55	66 752.48	0.10%	0.14%	1.42
54	Sandoz verapamil HCl 120	Verapamil	318	2.02	0.19	75.38	27.29	23 969.57	0.09%	0.05%	0.57
55	Adalat retard 20 mg	Nifedipine	316	6.97	2.60	253.94	146.51	80 244.78	0.09%	0.16%	1.92
56	Tilazem 90 mg tab	Diltiazem	301	6.00	0.61	254.19	99.95	76 510.74	0.08%	0.16%	1.92
57	Pharma dynamics amlodipine besilate	Amlodipine	300	2.90	0.73	86.78	23.36	26 033.12	0.08%	0.05%	0.66
58	Amlodac 5 mg tab	Amlodipine	250	2.25	0.23	68.22	15.08	17 054.92	0.07%	0.04%	0.52
59	Amlosyn 10 mg tab	Amlodipine	232	4.82	0.74	144.42	22.28	33 504.87	0.06%	0.07%	1.09
60	Amlodac 10 mg tab	Amlodipine	228	3.52	0.52	104.89	16.86	23 915.60	0.06%	0.05%	0.79
61	CPL alliance amlodipine 5 mg	Amlodipine	211	1.93	0.68	58.43	21.00	12 328.23	0.06%	0.03%	0.44
62	Calbloc 5 mg tab	Amlodipine	203	2.36	0.39	70.98	16.35	14 407.93	0.06%	0.03%	0.54
63	Adalat 10 mg cap	Nifedipine	172	4.67	1.33	36.71	60.19	6 314.94	0.05%	0.01%	0.28
64	CPL alliance amlodipine 10 mg	Amlodipine	170	3.08	0.85	93.09	27.88	15 825.32	0.05%	0.03%	0.70
65	Sandoz diltiazem 60 mg	Diltiazem	166	1.29	0.24	68.82	30.16	11 423.90	0.05%	0.02%	0.52
66	Calbloc 1 0mg tab	Amlodipine	155	3.42	0.58	101.88	18.27	15 791.09	0.04%	0.03%	0.77
67	Tilazem 240 CR	Diltiazem	153	8.31	0.85	246.83	32.09	37 765.53	0.04%	0.08%	1.86
68	Corvadil 5 mg tab	Amlodipine	137	2.82	0.51	80.94	21.77	11 089.11	0.04%	0.02%	0.61
69	Corvadil 10 mg tab	Amlodipine	114	4.09	0.39	120.99	15.48	13 792.42	0.03%	0.03%	0.91
70	Bio-nifedipine 5 mg	Nifedipine	78	0.58	0.33	26.86	15.51	2 094.95	0.02%	0.00%	0.20
71	Adalat 5 mg cap	Nifedipine	31	2.73	1.36	48.51	47.50	1 503.88	0.01%	0.00%	0.37
72	Bio-nifedipine 10 mg	Nifedipine	29	0.26	0.09	6.07	7.71	176.14	0.01%	0.00%	0.05
73	Sandoz nifedipine 10 mg	Nifedipine	15	1.48	0.49	62.04	37.26	930.58	0.00%	0.00%	0.47
74	Isoptin 5mg/2ml inj	Verapamil	4	26.99	0.96	40.63	16.10	162.50	0.00%	0.00%	0.31

Table A.5: CCB medicine items ranked from most dispensed to least dispensed for the year 2008 (continued)

Position	Registered trade name	Active ingredient	Number of medicine Items dispensed	Average cost per tablet (R)	SD	Average cost per medicine item (R)	SD	Total cost per medicine item (R)	Percentage of total prevalence (%)	Percentage of total cost (%)	CPI
75	Vasomil 5mg/2ml inj	Verapamil	1	7.34		22.02		22.02	0.00%	0.00%	0.17

Table A.6: Member and medical aid contributions by CCB active ingredient 2005

Year	Active ingredient	Total number of medicine items dispensed	Total cost of medicine items (R)	Members payment (R)	Medical aid payment (R)
2005	Amlodipine	88 138	12 237 437.97	1 516 195.52	10 721 242.45
	Diltiazem	31 206	5 295 386.60	740 230.83	4 555 155.77
	Felodipine	28 381	4 461 790.01	679 915.91	3 781 874.10
	Isradipine	6074	1 399 870.58	248 894.61	1 150 975.97
	Lercanidipine	1 527	227 292.82	30 758.39	196 534.43
	Nifedipine	94 471	13 579 227.69	1 423 020.08	12 156 207.61
	Nisoldipine	7	2 084.11	416.85	1 667.26
	Verapamil	68 454	7 462 240.64	540 039.85	6 922 200.79
2006	Amlodipine	121 329	15 281 015.39	1 757 834.32	13 523 181.07
	Diltiazem	29 873	4 946 836.11	702 594.03	4 244 242.08
	Felodipine	28 914	4 195 359.42	535 821.67	3 659 537.75
	Isradipine	5 082	1 173 874.81	207 622.01	966 252.80
	Lercanidipine	5 617	849 341.98	125 011.43	724 330.55
	Nifedipine	107 949	15 599 205.27	1 931 400.72	13 667 804.55
	Verapamil	71 696	7 901 759.74	572 717.87	7 329 041.87
2007	Amlodipine	142 910	17 761 344.39	2 411 639.39	15 349 705.00
	Diltiazem	26 721	4 709 622.54	638 114.81	4 071 507.73
	Felodipine	26 715	3 924 989.05	490 338.47	3 434 650.58
	Isradipine	3 901	952 900.94	149 256.68	803 644.26
	Lercanidipine	8 207	1 326 977.19	181 867.61	1 145 109.58
	Nifedipine	94 833	15 323 060.74	2 132 306.94	13 190 753.80
	Verapamil	62 762	7 420 156.35	583 979.85	6 836 176.50
2008	Amlodipine	156 022	17 184 384.37	3 459 136.41	13 725 247.96
	Diltiazem	22 604	4 106 166.88	679 571.98	3 426 594.90
	Felodipine	23 861	3 492 704.80	565 182.26	2 927 522.54
	Isradipine	3 018	783 047.74	144 920.18	638 127.56
	Lercanidipine	9 466	1 589 365.01	373 659.97	1 215 705.04
	Nifedipine	95 451	14 624 787.47	2 554 701.40	12 070 086.07
	Verapamil	57 015	6 864 770.02	486 946.46	6 377 823.56