

**ASPECTS OF THE USAGE OF ANTINEOPLASTIC AND
IMMUNOMODULATING AGENTS IN A SECTION OF THE
PRIVATE HEALTH CARE SECTOR**

Wilmarie Rheeders

B. Pharm

Dissertation submitted in Pharmacy Practice, School of Pharmacy at the
Faculty of Health Sciences of the North-West University, Potchefstroom, in
partial fulfilment of the requirements for the degree Magister Pharmaciae.

Supervisor: Prof M.S. Lubbe
Co-supervisor: Dr. J.L. Duminy
Co-supervisor: Prof. M.P. Stander

Potchefstroom

November 2008

For all things are from Him, by Him, and for Him.

Glory belongs to Him forever! Amen. (Rom. 11:36)

ACKNOWLEDGEMENTS

To my Lord and Father whom I love, all the Glory! He gave me the strength, insight and endurance to finish this study.

I also want to express my sincere appreciation to the following people that have contributed to this dissertation:

- To Professor M.S. Lubbe, in her capacity as supervisor of this dissertation, my appreciation for her expert supervision, advice and time she invested in this study.
- To Dr. J.L. Duminy, oncologist and co-supervisor, for all the useful advice, assistance and time he put aside in the interest of this dissertation.
- To Professor M.P. Stander, in his capacity as co-supervisor of this study.
- To Professor J.H.P. Serfontein, for his guidance, time, effort and advice.
- To the Department of Pharmacy Practice as well as the NRF for the technical and financial support.
- To Anne-Marie, thank you for your patience, time and continuous effort you put into the data.
- To the Pharmacy Benefit Management company for providing the data for this dissertation.
- To Mrs. Elma de Kock for the language editing of this study.
- To Prof. Casper Lessing for the editing of the bibliography of this study.
- To my parents, Gert and Mariaan Breed - no words can express my gratitude, love and respect. Thank you for your faith in me and your support, encouragement and especially your prayers throughout my studies.
- To my dear brother, Marnus, who was in a serious car accident in June 2008 - the strength, perseverance and optimism with which you live your life encouraged me to give my best. You are always in my prayers.
- To my big brother, Gerbrand and sister-in-law, Melissa – thank you for your love, support and encouragement.
- To my husband, Danie – your love, continuous encouragement and never-ending faith in me has helped me through – you mean the world to me. I love you.
- To my family-in-law, thank you for your support.

- To my housemates and dear friends, Adri and Rinee - for their friendship, support, encouragement, patience and for listening, every time.
- To my friend Eugene, thank you for your loyal friendship, support, encouragement and all the coffees.
- To all my friends for their continuous support and friendship.
- To my fellow M-students, especially Anri, Corlee, Jenine, Mariet, Rial and Ulrich for their support, encouragement and friendship.

ABSTRACT

Title: Aspects of the usage of antineoplastic and immunomodulating agents in a section of the private health care sector.

Keywords: *Cancer, antineoplastic and immunomodulating agents, cancer medicine items, cancer treatment, pharmacoeconomics, cost of cancer.*

Cancer is a broad term used to describe more than 100 diseases that can affect any part of the body. Cancer is the uncontrollable division of abnormal cells in the human body, which can invade nearby tissue and spread through the bloodstream to other parts of the body (National Cancer Institute, 2007b). Cancer can affect people all over the world, from every race, society and age (Albrecht, 2006:3). The treatment of cancer is becoming more and more expensive as newer and more effective drugs enter the market (Niezen *et al.*, 2006:2887) and diagnosing and screening of cancer patients is showing remarkable progress (Meropol & Schulman, 2007:180).

The general objective of this study was to investigate and review the prescribing patterns of antineoplastic and immunomodulating agents in a section of the private health care sector of South Africa. This research can be classified as retrospective and quantitative. Data were obtained from a medicine claims database, of a pharmacy benefit management company. The study population consisted of all prescriptions, containing one or more cancer medicine items (classified according to the ATC classification), for the study period January 2005 to December 2006.

Different aspects of cancer were investigated in order to determine the international and national prevalence of cancer and types of cancer and cancer treatment. An overview of managed care aspects were given and through this study it is evident that pharmacoeconomic studies and other managed care aspects could play a major role as information system in the decision making about cancer treatments.

The prescribing patterns of antineoplastic and immunomodulating agents were reviewed, analysed and interpreted. It was determined that the number of cancer patients, the number of prescriptions containing one of more cancer drug and the number of cancer medicine items respectively comprised less than 1% of the total

number of patients, prescriptions and medicine items recorded on the total database. To the contrary, the total cost of cancer medicine items comprised 4.00% and 5.31% of the total cost of all medicine items (total database) in 2005 and 2006 respectively. This indicates the relatively high cost of cancer medicine items.

Almost 50% of all cancer patients are 59 years of age or older and the total cost of cancer medicine items claimed by patients 59 years and older comprised almost 60% of the total cost of all cancer medicine items claimed during the two study years respectively. Cancer medicine items claimed by patients ≤ 19 years of age comprised only 2% of all cancer medicine items claimed in both study years and less than 1% of the total cost of all cancer medicine items. Cancer medicine items claimed by patients between the age of 19 and 59 years of age comprised 45.32% and 44.80% of the total number of cancer medicine items in 2005 and 2006 respectively whilst the cost for these age groups comprised 40.81% and 40.73% of the total cost of cancer medicine items.

More than 70% of all cancer patients in 2005 and 2006 were females whilst male cancer patients comprised about 30% of all cancer patients. The number of cancer medicine items claimed by female cancer patients also comprised more than 70% of the total number of cancer medicine items claimed in 2005 and 2006, however, the total cost of cancer medicine items was divided almost even between male (45%) and female (55%) cancer patients for both study years. Therefore, according to this study, cancer medicine items claimed by male cancer patients are relatively more expensive than those claimed by female cancer patients.

In completion of this study, recommendations for further studies concerning cancer treatment and cost-effective usage of cancer medicine were formulated, including the influence of the nature of the cancer, the age and gender of the patients as well as the treatment costs of cancer.

OPSOMMING

Titel: Aspekte van die gebruik van antineoplastiese en immunomodulerende agente in 'n deel van die privaat-gesondheidsorgsektor.

Sleutelwoorde: *Kanker, antineoplastiese en immunomodulerende agente, kanker-medisyne-items, kankerbehandeling, farmako-ekonomie, koste van kanker.*

Kanker is die omvattende term wat gebruik word om meer as 100 siektes, wat enige deel van die liggaam kan aantast, te beskryf. Kanker is die onbeheerbare verdeling van abnormale selle in die menslike liggaam, wat nabygeleë weefsel kan binnedring en deur die bloedstroom kan versprei na ander dele van die liggaam (National Cancer Institute, 2007b). Kanker kan enige persoon affekteer, ongeag die ras, samelewingsgroep of ouderdom van die persoon (Albrecht, 2006:3). Die behandeling van kanker word al hoe duurder as gevolg van nuwe en meer effektiewe middels wat die mark betree (Niezen *et al.*, 2006:2887) en die diagnosering en die vroeë opsporing van kanker wat groot vordering toon (Meropol & Schulman, 2007:180).

Die algemene doelstelling van hierdie studie was om die medisinale voorskrifpatrone van antineoplastiese en immunomodulerende agente in 'n deel van die privaat-gesondheidsorgsektor te ondersoek. Hierdie navorsing kan as retrospektief en kwantitatief geklassifiseer word. Data is verkry vanaf 'n medisyne-eis databasis, van 'n farmaseutiese voordeel-bestuursmaatskappy. Die studiepopulasie het uit al die voorskrifte wat een of meer kankermedikasie-item bevat het, bestaan, vir die studieperiode wat strek vanaf Januarie 2005 tot Desember 2006.

Verskillende aspekte van kanker is ondersoek om die internasionale en nasionale voorkoms van kanker en kankerbehandeling te bepaal. 'n Oorsig van aspekte van bestuurde-gesondheidsorg is gedoen en deur hierdie studie het dit duidelik geblyk dat farmako-ekonomiese studies en ander bestuurde-gesondheidsorg aspekte 'n groot rol kan speel as inligtingssisteem in die behandelingsbesluite van kankerbehandeling.

Die voorskrifpatrone van antineoplastiese en immunomodulerende agente is bespreek, geanaliseer en geïnterpreteer. Daar is vasgestel dat die hoeveelheid kankerpatiënte, die hoeveelheid voorskrifte wat een of meer kankermedisyne-item bevat en die hoeveelheid kankermedisyne-items wat voorgeskryf is, onderskeidelik minder as 1% van die totale hoeveelheid pasiënte, voorskrifte en medisyne-items op die totale databasis omvat het. In teenstelling daarmee het die totale koste van kankermedisyne-items 4.00% (2005) en 5.31% (2006) van die totale koste van al die medisyne-items op die totale databasis beloop. Dit dui op die relatiewe hoë koste van kankermedisyne-items.

In 2005 en 2006 was ongeveer 50% van alle kanker pasiënte op die medisyne-eis databasis oor die ouderdom van 59 jaar en die totale koste van kankermedisyne-items wat deur pasiënte ouer as 59 jaar geëis is, het ongeveer 60% van die totale koste van alle kankermedisyne-items in beide studiejare beslaan. Kankermedisyne-items wat geëis is deur pasiënte ≤ 19 jaar, het slegs 2% van alle kankermedisyne-items, wat in onderskeidelik 2005 en 2006 geëis is, en minder as 1% van die totale koste van kankermedisyne-items in beide studiejare beslaan. Kankermedisyne-items wat deur pasiënte tussen die ouderdomme van 19 en 59 jaar geëis is, het 45.32% en 44.80% van die totale hoeveelheid kankermedisyne-items in 2005 en 2006 beslaan, terwyl die koste van kankermedisyne-items vir hierdie ouderdomsgroep 40.81% en 40.73% van die totale koste van kankermedisyne-items beloop het.

Meer as 70% van alle kankerpatiënte in 2005 en 2006 was vroulik, terwyl die oorblywende 30% manlike kankerpatiënte was. Die hoeveelheid kankermedisyne-items wat deur vroulike kanker pasiënte in beide studiejare geëis is, het ook meer as 70% van die totale hoeveelheid kankermedisyne-items beslaan, terwyl manlike kankerpatiënte die oorblywende kankermedisyne-items geëis het. Tog is die totale koste van kankermedisyne-items amper gelyk verdeel tussen manlike (45%) en vroulike (55%) kankerpatiënte, daarom kan daar afgelei word dat kankermedisyne-items wat deur manlike kankerpatiënte geëis is, dus relatief duurder was as die kankermedisyne-items wat deur vroulike kankerpatiënte geëis is.

As slotsom tot die studie word aanbevelings vir verdere studies rakende kanker-behandeling en die koste-effektiewe gebruik van kanker medisyne gemaak. Dit sluit aspekte soos die invloed van die aard van kanker, die ouderdom en geslag van die pasiënte asook die behandelingskoste van kanker in.

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CHAPTER 1

Introduction and problem statement

1.1 INTRODUCTION

This dissertation will focus on the usage patterns of antineoplastic and immunomodulating medicine items in the private health care sector in South Africa, according to the database of a pharmaceutical benefit management company. Data from 1 January 2005 to 31 December 2006 will be used in this investigation.

1.2 PROBLEM STATEMENT

Cancer can be defined as a disease of cells that causes a shift in the mechanisms that control and govern cell proliferation and differentiation (Chu & Sartorelli, 2004:898). The World Health Organization (WHO, 2006) defines cancer as a group of diseases that are characterized by the rapid formation of abnormal cells in the body, which can affect any part or organ and can spread through the body by means of metastasis. Metastasis is the movement or spread of cancer cells through the bloodstream or lymph system, from one organ or tissue to another (Matsui, 2006).

Cancer is a major burden worldwide and according to Varmus (2006:1162), minimally controlled by modern medicine. In the Cancer Facts & Figures report by the American Cancer Society (2008c:1), it is estimated that 1 437 180 new cancer cases will be diagnosed in 2008. It is also expected that 565 650 Americans will die of cancer in 2008, this adds up to more than 1500 persons a day.

In the Millennium review of the European Journal of Cancer, Sikora (1999:24) predicted that over the next 25 years there would be a dramatic increase in the number of people developing cancer worldwide. He also stated that 10 million new cancer patients are diagnosed globally each year and by the year 2020 there could be 20 million people diagnosed per year (Sikora, 1999:24). Of these patients, 70% will live in countries that, between them will have less than 5% of the resources for cancer control (Sikora, 1999:25). The death toll of cancer worldwide amounted to 7.6

million people in 2007, this is about 20 000 deaths a day. These cancer deaths are also expected to rise to 17.5 million cancer deaths in 2050 (Garcia *et al.*, 2007).

Treatment of cancer includes chemotherapy, radiotherapy, surgery and hormone therapy (National Cancer Institute, 2008a). New cancer approaches and modern anticancer drug development is currently of great interest for researchers and promise to play an immense role in cancer treatment in the next few years (Sikora, 2006:10). The four approaches in the development of novel therapies for cancer are mainly: small molecules, monoclonal antibodies, gene therapy and vaccines (Sikora, 2006:10).

According to the ATC codes of the WHO, there are five different levels in which drug groups are classified. All cancer drugs are included in the anatomical main group (1st level) "Antineoplastic and immunomodulating agents", which falls under the ATC code "L". The cancer drugs is then further divided into therapeutic subgroups (2nd level):

"L01" - Antineoplastic agents

"L02" - Endocrine therapy

"L03" - Immunostimulants

"L04" - Immunosuppressants

At level 3 and 4 the drugs are divided into chemical/pharmacological/therapeutic subgroups and level 5 is the chemical substance. The 2nd, 3rd and 4th levels are often used to identify pharmacological subgroups when that is considered more appropriate than therapeutic or chemical subgroups (WHO Collaborating Centre for Drug Statistics Methodology, 2008). The full ATC index for antineoplastic and immunomodulating agents is listed in Appendix A. The subgroup "Immunosuppressants" (L04) is not included in this study because the drugs included in "L04" are not exclusively used in cancer therapy.

One of the biggest obstacles to overcome in the immunological targeting of cancer is the cost of development, especially if therapies have to be tailored to individual patients (Sikora, 2006:10). A study done in the Netherlands shows that the introduction of new, expensive hospital drugs like trastuzumab (Herceptin®) and oxaliplatin (Eloxatin®) is the cause of a steep increase in expenditures for hospital drugs (Niezen *et al.*, 2006:2887). Trastuzumab (Herceptin®), a monoclonal antibody working against the HER2 protein that is over-expressed in 20-25% of patients with breast cancer, is a good example of the high cost of cancer drugs (Barret *et al.*,

2006:1118). In June 2006 the cost of one vial of Herceptin® was \$1 031.21 (Breast Cancer Network Australia, 2006), which amounts to about R7 784.98 (ZAR)¹. One of South Africa's largest medical schemes, Discovery Health Medical Scheme (2008), estimated that the cost of treating a 70kg woman with early breast cancer with Herceptin® will amount to R420 000 a year.

Over the past few years, there was outstanding development in cancer diagnosis, treatment and screening. All these factors are playing a role in the increasing cost of cancer care (Meropol & Sculman, 2007:180). According to Bosanquet and Sikora (2006a:1) the economics of cancer is not receiving the necessary attention to address these factors.

From the foregoing discussion, it is imperative that research should be performed on the cost and prescribing patterns of antineoplastic and immunomodulating agents.

1.3 RESEARCH QUESTIONS

The following research questions can be formulated from the foregoing discussion:

- What is cancer?
- What is the situation regarding cancer incidence and mortality, globally as well as in South Africa?
- What treatment options are available for cancer patients?
- What types of cancer is common in the private health care sector of South Africa and what is the pathology of the different cancers?
- What does managed care, pharmacoeconomics and drug utilisation review entail?
- What does the economics of cancer entail?
- How can cancer medicine items be classified?
- What is the difference in cost of cancer treatment in people from different age groups?
- What is the difference in treatment and cost of treatment between male and female cancer patients?

¹ 1 US dollar = R7.55

1.4 RESEARCH OBJECTIVES

The research objectives for this study are divided into general and specific objectives:

1.4.1 General objective

The general objective of this study was to investigate and review drug-prescribing patterns of antineoplastic and immunomodulating agents in a section of the private health care sector of South Africa by utilising a medicine claims database for a two-year period (2005 & 2006).

1.4.2 Specific research objectives

The research project consisted of two phases, the literature review and an empirical investigation.

1.4.2.1 Literature study

The specific objectives for this literature study were to:

- define cancer and put the disease into perspective, both globally and nationally;
- investigate the different cancer treatment approaches;
- describe different cancer types, in particular lung cancer, breast cancer, prostate cancer, colorectal cancer and lymphoma (Hodgkin's disease and non-Hodgkins lymphoma);
- define and describe the concepts: managed care, pharmacoeconomics and drug utilisation review;
- investigate the approach to cancer of some medical schemes in South Africa;
- determine the economics of cancer relative to treatment options;
- investigate the methods used to evaluate and value the quality of life of cancer patients.

1.4.2.2 Empirical investigation

By using a medicine claims database in a section of the private health care sector of South Africa, the specific objectives for this empirical study were to:

- determine the prevalence, cost and usage patterns of antineoplastic and immunomodulating agents in comparison to medicine in general;
- analyse the prescribing patterns for the top twenty cancer medicine items according to highest total cost, highest average cost and highest prevalence;
- determine the prevalence and cost associated with original, non-original and generic forms of cancer medicine items in the top twenty cancer medicine items according to highest total cost, highest average cost and highest prevalence;
- classification of cancer medicine items according to the different therapeutic, pharmacological and chemical subgroups;
- determine the prevalence and cost of cancer medicine items in the different therapeutic, pharmacological and chemical subgroups;
- determine the prevalence and cost of cancer agents associated with the different patient age groups;
- determine the prevalence and cost of cancer agents according to the gender of the patient;
- determine and analyse the prevalence and total cost of selected regimen therapy prescribed for five common types of cancer in the private health care sector of South Africa.

1.5 RESEARCH METHOD

The research method consists of two phases, namely a literature review and an empirical investigation.

1.5.1 Phase one: Literature review

The literature review includes an overview of the literature on cancer and the treatment thereof as well as the examination of managed care, pharmacoeconomics, drug utilisation review and its application to cancer.

1.5.2 Phase two: Empirical investigation

The method used in the empirical investigation consisted of the following phases:

- The selection of the research design
- the selection of the study population, using a database of a Pharmacy Benefit Management company (PBM) (see section 4.3);
- the selection of the measuring instruments (see section 4.7.3)
- data application and data analysis (see section 4.7)
- reliability and validity of the research instruments (see section 4.8)
- the report and discussion of the results of the empirical investigation (chapter 5);
- the recommendations based on the results of the empirical investigation (chapter 5).

A retrospective drug utilisation study will be done on data provided by a medicine claims database of a pharmacy benefit management company (PMB). The study period for this study was 1 January 2005 to 31 December 2006. The Statistical Analysis System (SAS for Windows, 9.1) will be used for comparisons and analysis. Permission to conduct the study was granted by the PBM's management as well as by the NWU Ethical Committee. The ethical permission was granted by the NWU for the study "Investigation of medicine usage patterns in a section of the private health care sector utilizing data from a Pharmaceutical Benefit Management (PBM) Company in South Africa" and the ethical committee awarded the study with the following permission number: NWU-0046-08-S5.

1.6 DIVISION OF CHAPTERS

The division of chapters will be as follows:

Chapter 1: Introduction

Chapter 2: Aspects of cancer management in the private health care sector of
South Africa

Chapter 3: Research methodology

Chapter 4: Results and discussion

Chapter 5: Conclusions, limitations and recommendations

1.7 SUMMARY

In this chapter an overview of the problem statement was presented. The research questions as well as the general and specific research objectives were described. The research method was stated as well as the division of chapters.

CHAPTER TWO

Aspects of cancer management in a section of the private health care sector of South Africa

2.1 INTRODUCTION

In chapter 1 the problem was stated, an approach was determined and the scope of the study was discussed. The focus of Chapter 2 will be the definition of cancer, the international and national cancer situation with specific reference to the different cancers prevalent in South Africa. Treatment of cancer and effects thereof will also be discussed. The terms managed care, pharmacoeconomics and drug utilisation review will be discussed briefly with special reference to economics of cancer as well as aspects of quality of life and value of life.

2.2 DEFINITION AND NATURE OF CANCER

2.2.1 Definition of cancer and oncology

Cancer is such a complex and complicated disease that it is difficult to define. The term “cancer” (KAN-ser) can be explained as the uncontrollable division of abnormal cells, which can invade nearby tissue and spread through the bloodstream and the lymphatic system (National Cancer Institute, 2007b).

The Cancer Fact Sheet of the World Health Organisation (2006) defines cancer as follows: *“Cancer is a generic term for a group of more than 100 diseases that can affect any part of the body. Other terms used are malignant tumours and neoplasms. One defining feature of cancer is the rapid creation of abnormal cells which grow beyond their usual boundaries, and which can invade adjoining parts of the body and spread to other organs, a process referred to as metastasis.”*

The word oncology is defined as the study and practice of the treatment of malignancy and has been derived from the word “oncos” which means: a malignant mass or tumour (Cohen, 1995:18). Oncology is thus the study of the branch of

medicine that deals with the study and treatment of malignant tumours (MSN Encarta, 2008).

2.2.2 The nature of the cancer disease

The previous Director of the National Institute of Health (NIH), Nobel Laurette and original discoverer of ongenes, Harold Varmus (2006:1162) said: *"The conquest of cancer continues to pose great challenges to medical science. The disease is notably complex, affecting nearly every tissue lineage in our bodies and arising from normal cells as a consequence of diverse mutations affecting many genes. It is also widespread and lethal; currently the second most common cause of death in the United States, and it is likely to become the most common in the near future."*

In a healthy body, normal body cells develop, divide, and die in a systematic and orderly way. At first, in the early years of a person's life, normal cells divide more rapidly. Later in life, cells in most parts of the body only divide to replace worn-out or dying cells and to repair injuries (American Cancer Society, 2007d). Cancer cells however continue to divide and grow, outliving normal cells and producing abnormal cells (Woman's Web, 2008). Cancer cells basically develop because of damage to DNA. This damaged DNA can be inherited or caused by exposure to elements in the environment e.g. smoking (American Cancer Society, 2007d).

2.3. CANCER IN PERSPECTIVE

In this section the international cancer situation as well as the situation of cancer in South Africa will be discussed.

2.3.1 International cancer situation

Cancer is a deadly, highly complex and devastating disease that affects people all over the world from every race, society and age (Albrecht, 2006:3), either directly or indirectly. In the GLOBOCAN 2002 database of the International Agency for Research on Cancer (IARC), Parkin and colleagues (2004) estimated that there were 10.9 million new cancer cases worldwide, with 24.6 million people living with cancer and 6.7 million people dying of cancer in the year 2002. As can be seen in figure 2.1, lung cancer, colorectal cancer and breast cancer were the most commonly diagnosed cancers in 2002. Cancer deaths were most common in lung cancer (1.18

million deaths), stomach cancer (700 000 deaths) and liver cancer (598 000 deaths) (Parkin *et al.*, 2004).

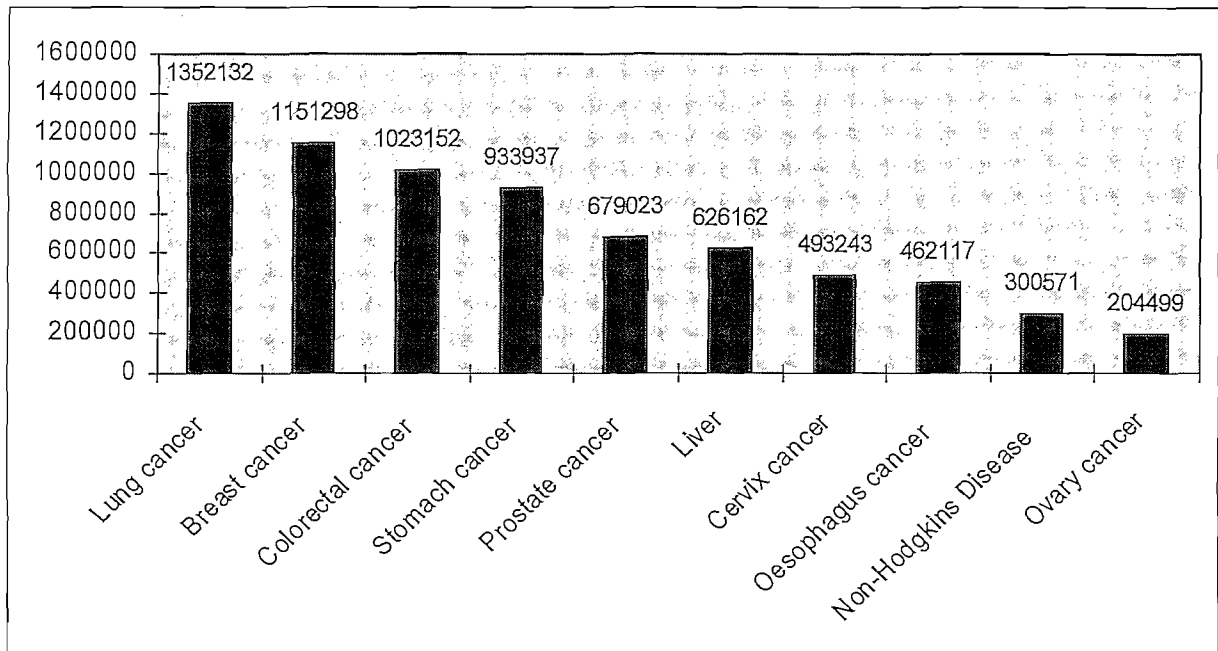


Figure 2.1 Top ten most commonly diagnosed cancers worldwide in 2002
(Adapted from the International Agency for Research on Cancer CancerBase
No. 5. version 2.0) (Parkin *et al.*, 2004)

2.3.2 Global cancer incidence, mortality and prevalence according to gender

A summary of the worldwide incidence, mortality and prevalence of 23 different cancers for each gender, as summarised by the International Agency for Research on Cancer: GLOBOCAN 2002, are given in table 2.1 and table 2.2.

As can be seen in table 2.1, the 5 cancers with the highest incidence during 2002, in males (in descending order) were lung, prostate, stomach, colorectal and liver cancer. Most deaths due to cancer in males were due to lung cancer with 848 132 deaths in 2002. Stomach cancer is the second deadliest cancer for men, followed by liver cancer, colorectal cancer and prostate cancer.

According to Parkin and colleagues (2004), cancer prevalence as presented in GLOBOCAN 2002, is based on diagnoses made within one, three and five years. This is because these time periods is most likely to be relevant to the different stages of cancer therapy, namely, initial treatment (one year), clinical follow-up (three years) and cure (five years).

Parkin and colleagues (2004) further state that cancer patients who are still alive five years after diagnosis of cancer are usually considered cured. This is because the death rates of such patients are comparable to any person in the general population. The 1-year and 5-year survival rate (prevalence) are also summarised in table 2.1.

According to table 2.2; the five most frequently diagnosed cancers (incidence), during 2002 in woman were breast, cervical, colorectal, lung and stomach cancer. Breast cancer also caused the most cancer deaths under woman (410 712 deaths in 2002, worldwide). Lung cancer, cervical cancer, stomach cancer and colorectal cancer also were under the top five most deadly female cancers worldwide (refer to table 2.2).

Breast cancer is an exception when it comes to survival rate – patients that are living with breast cancer is not considered cured after five years of diagnosis (Fiset, 2007). The current survival rate for all breast cancer stages is (Fiset, 2007):

- Five-year survival – 86%
- Ten-year survival – 76%

After 7 years of living with breast cancer the survival rate decreases. Also, woman with metastatic breast cancer has a 5-year survival rate of only 21% (Fiset, 2007).

Table 2.1 Global incidence, mortality and prevalence of cancer in males
(Parkin *et al.*, 2004)

CANCER SITE	Incidence ¹			Mortality ²			Prevalence ³	
	Cases	Crude Rate ⁴	ASR ⁵ (W)	Deaths	Crude Rate	ASR (W)	1-year	5-year
Oral cavity	175916	5.6	6.3	80736	2.6	2.9	133993	466683
Nasopharynx	55796	1.8	1.9	34913	1.1	1.2	40834	144277
Other pharynx	106219	3.4	3.8	67964	2.2	2.5	71982	215757
Oesophagus	315394	10.1	11.5	261162	8.4	9.6	121790	295076
Stomach	603419	19.3	22	446052	14.3	16.3	302067	951403
Colon and rectum	550465	17.6	20.1	278446	8.9	10.2	423416	1515221
Liver	442119	14.2	15.8	416882	13.3	14.9	113806	274539
Pancreas	124841	4	4.6	119544	3.8	4.4	30155	76241
Larynx	139230	4.5	5.1	78629	2.5	2.9	108722	396304
Lung	965241	30.9	35.5	848132	27.1	31.2	380807	938759
Melanoma of skin	79043	2.5	2.8	21952	0.7	0.8	73013	309690
Prostate	679023	21.7	25.3	221002	7.1	8.2	604506	2368659
Testis	48613	1.6	1.5	8878	0.3	0.3	41404	192239
Kidney etc.	129223	4.1	4.7	62696	2	2.3	94248	362404
Bladder	273858	8.8	10.1	108310	3.5	4	224742	860299
Brain, nervous system	108221	3.5	3.7	80034	2.6	2.8	50734	157685
Thyroid	37424	1.2	1.3	11297	0.4	0.4	31735	136671
Non-Hodgkin lymphoma	175123	5.6	6.1	98865	3.2	3.5	115493	427086
Hodgkin lymphoma	38218	1.2	1.2	14460	0.5	0.5	30306	129044
Multiple myeloma	46512	1.5	1.7	32696	1.1	1.2	32947	98176
Leukaemia	171037	5.5	5.8	125142	4	4.3	91332	290689
All sites but non-melanoma skin	5801839	185.7	210	3795991	121.5	138	3390545	11547465

¹ Incidence: Number of new cases arising in a given period (2002) in a specified population (global). It is expressed as an absolute number of cases per year.

² Mortality: Number of deaths occurring in a given period in a specified population.

³ Prevalence: Number of persons in a defined population who have been diagnosed with a type of cancer, and who are still alive at a given point in time.

⁴ Crude rate: Crude rate is calculated simply by dividing the number of new cancers observed during a given time period by the corresponding number of people in the population at risk. For cancer, it is expressed as an annual rate per 10 000 persons at risk.

⁵ ASR (age-standardised rate): An ASR is a summary measure of a rate that a population would have had if it had a standard age structure. Standardisation is necessary when comparing several populations

that differ with respect to age because age is an important risk factor in cancer. The World Standardised incidence rate was used and is also expressed per 100 000 persons.

**Table 2.2 Global incidence, mortality and prevalence of cancer in female
(Parkin *et al.*, 2004)**

CANCER SITE	Incidence			Mortality			Prevalence	
	Cases	Crude Rate	ASR (W)	Deaths	Crude Rate	ASR (W)	1-year	5-year
Oral cavity	98373	3.2	3.2	46723	1.5	1.5	75769	273356
Nasopharynx	24247	0.8	0.8	15419	0.5	0.5	17786	63235
Other pharynx	24077	0.8	0.8	16029	0.5	0.5	16630	52905
Oesophagus	146723	4.8	4.7	124730	4.1	3.9	54159	129394
Stomach	330518	10.7	10.4	254297	8.3	7.9	166436	522156
Colon and rectum	472687	15.4	14.6	250532	8.1	7.6	362911	1315195
Liver	184043	6	5.8	181439	5.9	5.7	46521	111446
Pancreas	107465	3.5	3.3	107479	3.5	3.3	26002	66596
Larynx	20011	0.7	0.6	11327	0.4	0.4	15463	57944
Lung	386891	12.6	12.1	330786	10.7	10.3	162377	423467
Melanoma of skin	81134	2.6	2.6	18829	0.6	0.6	75940	332953
Breast	1151298	37.4	37.4	410712	13.3	13.2	1060042	4406080
Cervical uteri	493243	16	16.2	273505	8.9	9	381033	1409265
Corpus uteri	198783	6.5	6.5	50327	1.6	1.6	183528	775542
Ovary etc.	204499	6.6	6.6	124860	4.1	4	153761	538499
Kidney etc.	79257	2.6	2.5	39199	1.3	1.2	57234	223235
Bladder	82699	2.7	2.5	36699	1.2	1.1	64673	249966
Brain, nervous system	81264	2.6	2.6	61616	2	2	37721	118861
Thyroid	103589	3.4	3.3	24078	0.8	0.8	89315	394698
Non-Hodgkin lymphoma	125448	4.1	4	72955	2.4	2.3	86221	324184
Hodgkin lymphoma	24111	0.8	0.8	8352	0.3	0.3	20178	87449
Multiple myeloma	39192	1.3	1.2	29839	1	0.9	27925	84521
Leukaemia	129485	4.2	4.1	97364	3.2	3.1	68394	221134
All sites but non-melanoma skin	5060657	164.3	162	2927896	95.1	92.1	3490957	13022650

¹ Incidence: Number of new cases arising in a given period (2002) in a specified population (global). It is expressed as an absolute number of cases per year.

² Mortality: Number of deaths occurring in a given period in a specified population.

³ Prevalence: Number of persons in a defined population who have been diagnosed with a type of cancer, and who are still alive at a given point in time.

4 Crude rate: Crude rate is calculated simply by dividing the number of new cancers observed during a given time period by the corresponding number of people in the population at risk. For cancer, it is expressed as an annual rate per 10 000 persons at risk.

5 ASR (age-standardised rate): An ASR is a summary measure of a rate that a population would have had if it had a standard age structure. Standardisation is necessary when comparing several populations that differ with respect to age because age is an important risk factor in cancer. The World Standardised incidence rate was used and is also expressed per 100 000 persons.

2.3.3 Cancer incidence in more developed and less developed regions

According to the statistics gathered by the International Agency for Research of Cancer (Parkin *et al.*, 2004) the top five cancers in more developed countries and regions differ from those in less developed countries and regions. Figure 2.2 and figure 2.3 shows the statistics.

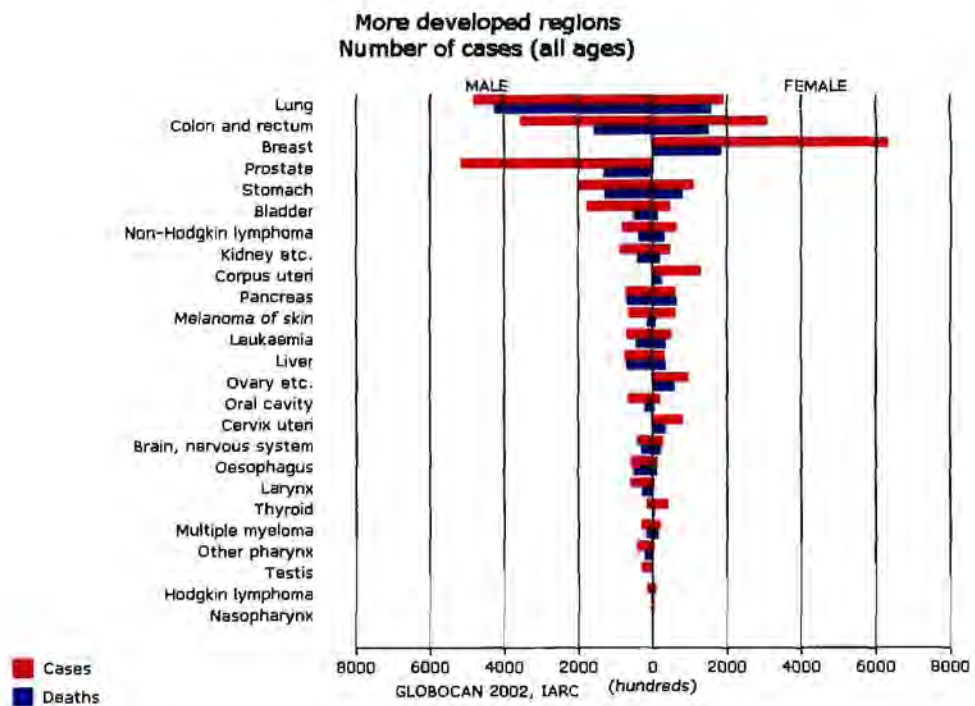


**Figure 2.2 Global statistics of cancer incidence in more developed regions
(Parkin *et al.*, 2004)**

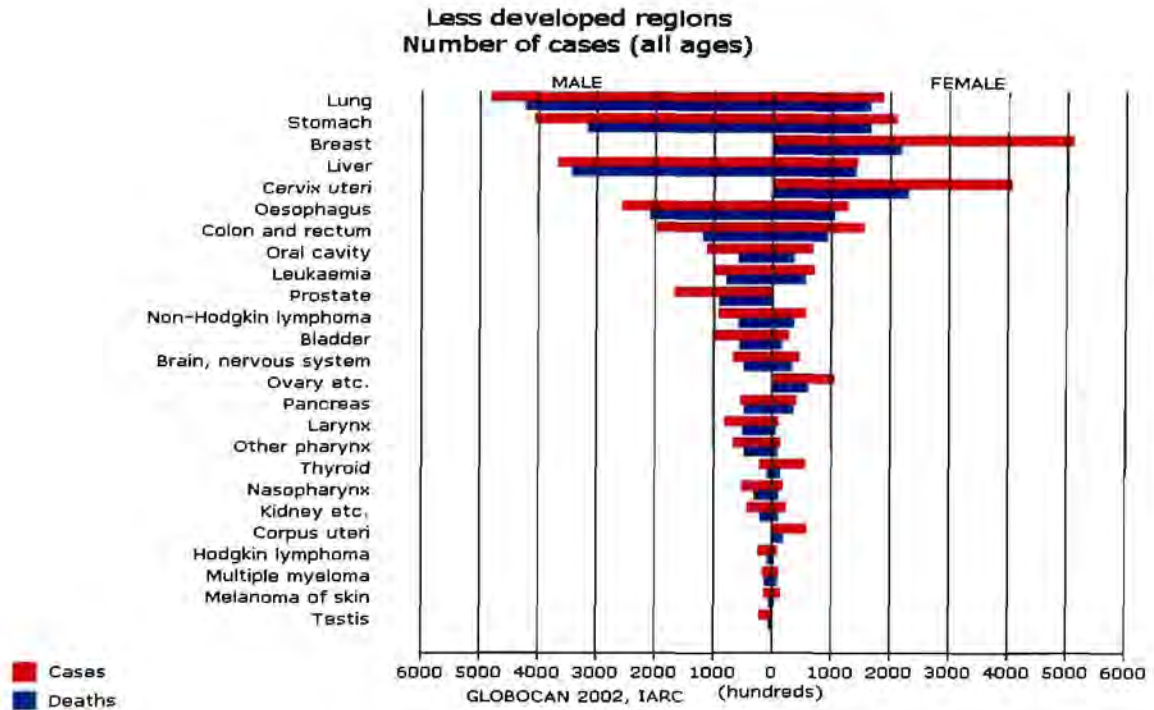


**Figure 2.3 Global statistics of cancer incidence in less developed regions
(Parkin *et al.*, 2004)**

According to figure 2.2, the cancer that is most frequently diagnosed in males in more developed regions is prostate cancer while in less developed regions prostate cancer is the 6th frequently diagnosed (see figure 2.3). More differences between the more developed regions and the less developed regions are that cervical cancer has the second highest incidence in less developed regions but in more developed regions it is the 7th most frequently diagnosed.

Less developed regions also had more liver cancer and oesophagus cancer while more developed regions had more bladder cancer and uterus cancer (Parkin *et al.*, 2004).

In a World Cancer Day press release the IARC (2008:1) stated that over the last few years, the majority of the global cancer burden has shifted to the medium- and low-resource countries in the world. This includes with and less than 0.1% of the population being covered by medically certified cause-of-death schemes.

Worldwide, cancer is a major burden and quickly becoming a force to reckon with (Ma & Yu, 2006:85). According to Harold Varmus (2006:1162) when cancer is

compared with other major diseases, it is commonly viewed as minimally controlled by modern medicine. He further states that death rates for cardiac, cerebrovascular and infectious diseases have declined by about two-thirds in the past 50 years while cancer's decline is relatively small in comparison. As presented in figure 2.4, the age-adjusted mortality rate of cancer hasn't changed much in 50 years' time.

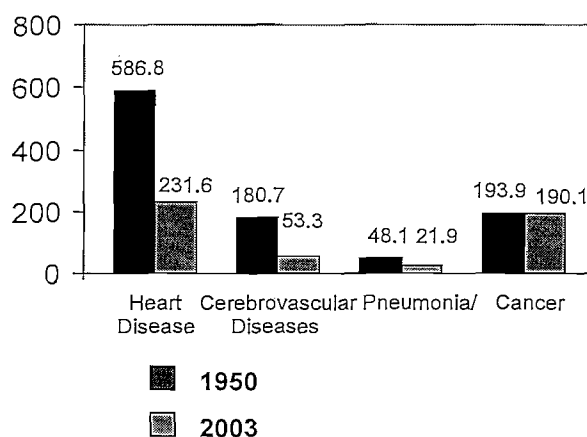


Figure 2.4 Change in the US death rates by cause, 1950 & 2003
(American Cancer Society, 2006)

2.3.4 The South African cancer situation

As has been discussed in 2.3.3, the incidence statistics of the population coverage in Africa is very poor, including the South African reporting and coverage of cancer incidence, mortality and prevalence. The acting manager of the National Health Laboratory Service, Patricia Kellet (2008), confirmed that the latest official statistics available from the National Cancer Registry is from the year 1998 and 1999. See section 2.3.5.2 for a detailed discussion on the problems with South Africa's National Cancer Registry.

In 1999 there were 84 diagnosing laboratories countrywide reporting to the National Cancer Registry, but this has decreased since then, due to smaller laboratories merging with larger laboratories (Mqoqi *et al.*, 2004:11). There were 120 515 new cancer cases reported in 1998 and 1999 combined, with the largest proportion of cases (40%) from Gauteng province (GP) (table 2.3) and the second largest proportion of cases (18.6%) from KwaZulu-Natal (KZN) (Mqoqi *et al.*, 2004:11). The figures presented in table 2.3 reflect the cancer management service provision in South Africa rather than the cancer cases in each province.

There is a great inequity between the public and private health sectors in South Africa. Inequities in resources between urban and rural areas, across and within provinces are a big challenge for the South African health system (Chetty, 2007:20).

It is estimated that only 20-25% of the South African population has regular access to the private health care system of South Africa (Palmer & Wolvardt, 1997:37). According to legislative updates (National Progressive Primary Health Care Network, 1999) on the Medical Scheme Act, 1998, over 60% of health care resources in South Africa are consumed by the private health care sector. An article reporting on health care in South Africa (SouthAfrica.info, 2008) states that a average of R59.36 was spent on medicine per person in the public sector of South Africa, opposed to the R800.29 spent on medicine per person in the private sector in the year 2000. This emphasises the great inequities between the private and public health care sectors in South Africa.

In table 2.3 the number of diagnosing laboratories, as well as the number of cancer cases diagnosed in the different provinces in South Africa is summarised. Although these statistics has not been updated since 1999 and there are many problems surrounding these figures (see paragraph 2.3.5.2), it still gives an indication of cancer incidence and the control of cancer in South Africa.

Table 2.3 Frequency distribution of cancer diagnosing laboratories and cancer diagnosed in 1998 and 1999, according to province (Mqoqi *et al.*, 2004: 11)

Province	Number of labs	Percentage of labs	Number of cases	Percentage of cases
Eastern Cape	14	16.70	11 524	9.60
Free State	10	11.90	10 293	8.50
Gauteng	25	29.80	49 159	40.80
KwaZulu-Natal	11	13.10	22 452	18.60
Limpopo	1	1.20	330	0.30
Mpumalanga	3	3.60	1904	1.60
Northern Cape	2	2.40	1164	1.00
North-West	2	2.40	2138	1.80
Western Cape	16	19.00	21 551	17.90
Total	84	100.00	120 515	100.00

As has been said, the total burden of cancer by province in South Africa cannot be established from the available National Cancer Registry (NCR) data (Mqoqi *et al.*, 2004:11). Information on patient addresses is inaccurate and incomplete. Patients

from across provincial borders seek better treatment in better-resourced provinces, but tend to give local addresses rather than their home address. This was caused by the existing health policies governing provincial boundaries. According to Mqoqi and colleagues (2004:11) this problem can possibly be solved by launching population based cancer registries in all South African provinces.

Except for the lack of patient addresses in South Africa, further problems are also posed by poor communication, distance and ignorance especially in the less privileged communities (World Health Organisation, 1996:347).

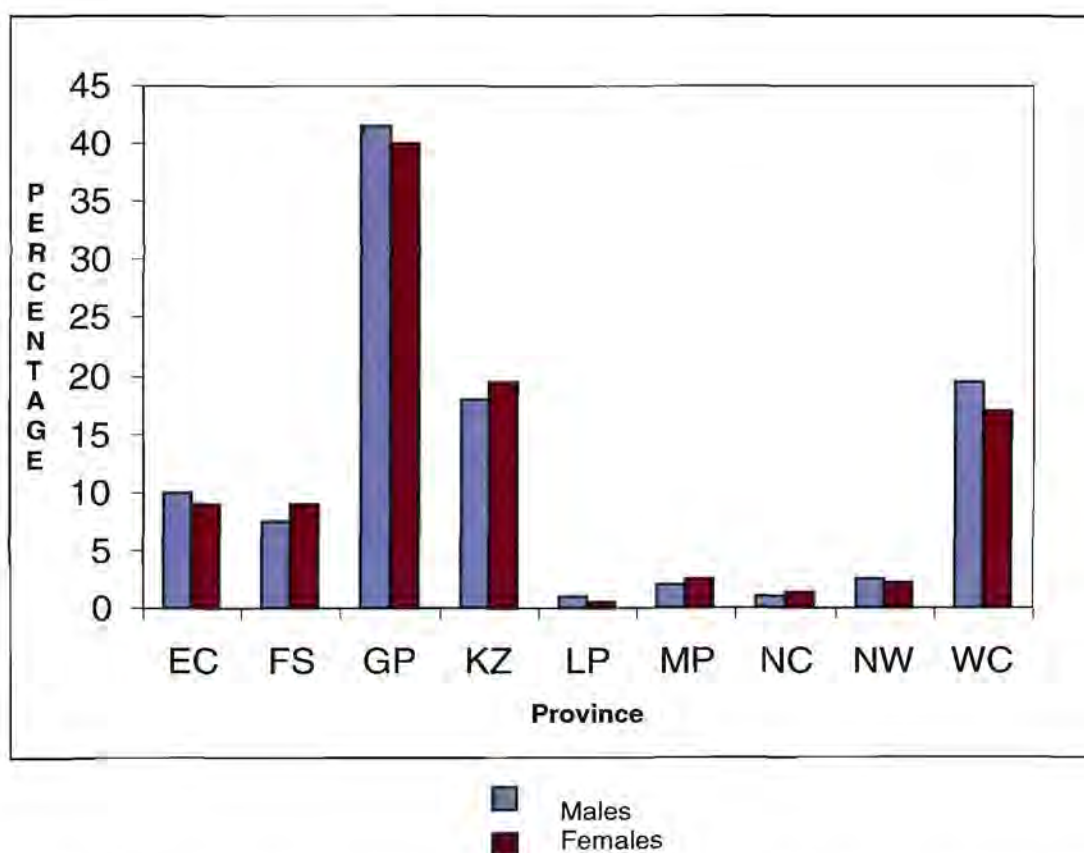


Figure 2.5 Percentage distribution of cancer cases by diagnosing province and sex, 1998 and 1999 combined (Mqoqi *et al.*, 2004:12)

Figure 2.5 shows the percentage distribution of cancer cases diagnosed in the 9 different provinces in South Africa. Gauteng had the highest percentage (40%) of cancer cases diagnosed in 1998 and 1999. There may exist different reasons for this distribution. As seen in table 2.3, Gauteng had the highest number of diagnosing facilities – therefore it was more accessible for people to be diagnosed. Furthermore,

according to Chetty (2007:16) the provinces in South Africa with the highest average per capita expenditure on public health care are Gauteng and the Western Cape. The average per capita expenditure for the Eastern Cape, Mpumalanga, Limpopo and the North West are considerably lower. Thus, inequalities in the financing of health care in the different provinces (Chetty, 2007:5) may also have an influence on the diagnosis of patients with cancer.

2.3.5 Cancer in the private health sector of South Africa

2.3.5.1 Introduction

In a verbal discussion with Dr. John L. Duminy (2007) of the Wilmed Park Oncology Centre in Klerksdorp, he explained that the five most prevalent cancers in his private practice are lung cancer, breast cancer, colorectal cancer, prostate cancer and lymphoma. However, this prevalence may differ from practice to practice, as the nature and scope of practice change.

According to the National Cancer Registry of South Africa (Mqoqi *et al.*, 2004:17), the top five cancers in South African males for 1998-1999 were prostate, lung, oesophagus, colorectal and bladder cancer. The Registry also stated that the incidence of breast, cervical, colorectal, oesophagus and uterus cancer was the most prevalent cancers in South African females in 1998-1999 (Mqoqi *et al.*, 2004:17). These statistics include both the private and public health sector of South Africa.

GLOBOCAN 2002, a project launched in 2002 by the International Agency for Research on Cancer, presents the estimates of the incidence, prevalence and mortality of 27 cancers for all countries of the world.

The statistics for South Africa used in GLOBOCAN 2002 was taken from the South Africa Cancer Registry 1996-1997 and scaled to incidence, using a percentage of Microscopically Verified cases observed in the United Kingdom, as is seen on the Cancer Incidence in Five Continents Vol. VIII – database (Parkin *et al.*, 2004). According to GLOBOCAN all estimated new cases and deaths in 2002 for both males and females in South Africa, is presented in figure 2.6. These figures will provide a clearer picture of the current prevalence and mortality of cancer in South Africa.

In the GLOBOCAN database, Parkin and colleagues (2004) state the top five cancers in South African males in 2002 (in descending order) as prostate cancer, lung cancer, oesophagus cancer, Kaposi sarcoma and cancer of the oral cavity. For

females it were cervical cancer, breast cancer, colorectal cancer, oesophagus cancer and Kaposi sarcoma. Although there are similarities between the findings of GLOBOCAN 2002, the South African National Cancer Registry and in Dr. Duminy's practice in South Africa – it is obvious that there is little structure and consistency in statistics about cancer in South Africa.

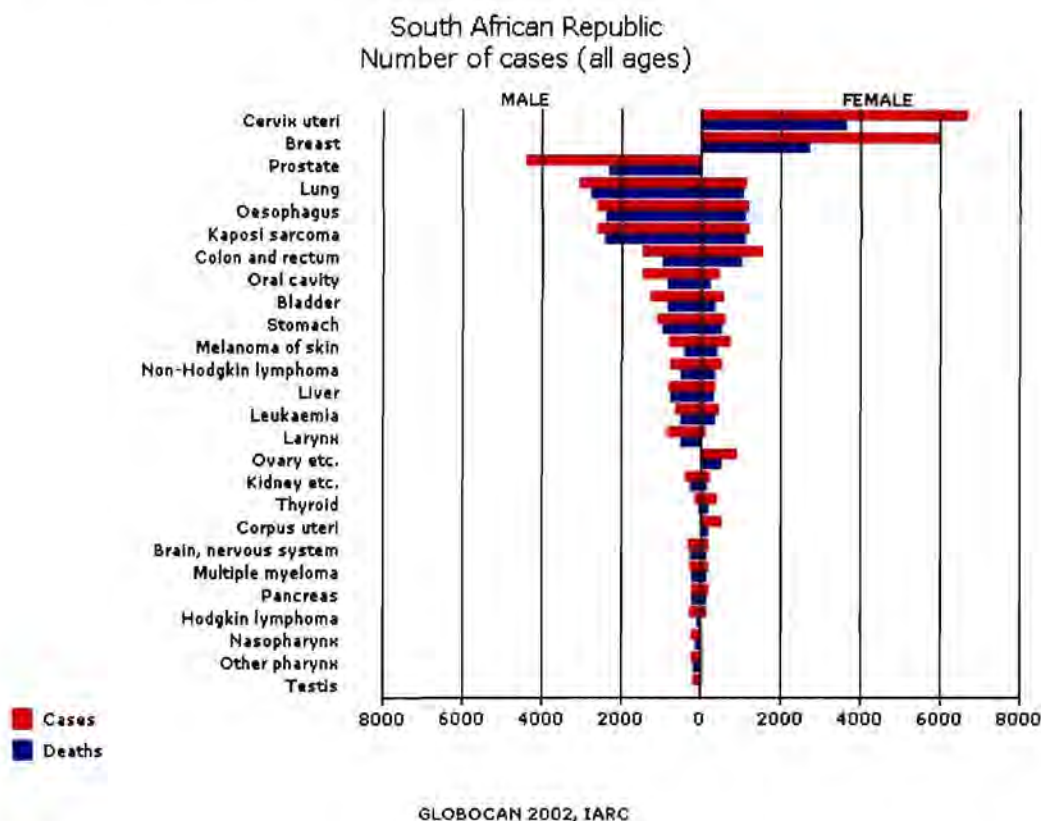


Figure 2.6 New cancer cases and deaths due to cancer in 2002
(Parkin *et al.*, 2004)

2.3.5.2 Problems with the South African Cancer Registry

According to a new organisation in South Africa, the Cancer Research Initiative of South Africa (CARISA, 2008:3), none of the existing South African cancer registries are mandated by law, this includes the National Cancer Registry, Transkei population based cancer registry and Elim Hospital registry. Thus, reporting of cancer cases is not regulated and is uncontrolled. In other countries cancer was made a reportable disease. This means that health facilities are required by law to report cancer to the cancer registry. This approach is being proposed for South Africa, and the decision is to be made by the Minister of Health (CARISA, 2008:3).

The National Cancer Registry is a division of the National Health Laboratory Services (NHLS) and provides epidemiological information for cancer surveillance in South Africa (NHLS, 2007). Although the National Cancer registry plays a major role in providing information on cancer in South Africa, there are many problems with this registry (Albrecht, 2006:12):

- *Last registry available issued in 1999*

For the past 9 years there have not been an update on the National Cancer Registry of South Africa and therefore no way to monitor the progress in the fight against cancer in South Africa.

- *No geographic data of South Africa*

There is no geographic data available to determine where cancer is most prevalent, that is where the cancer “hot spots” and “cold spots” in South Africa are. Incidence of cancer near nuclear and industrial facilities is non-existing and information about exposure to local carcinogens in different provinces and/or areas is limited. Overall, the cancer surveillance in South Africa is underdeveloped and urgently needs attention.

- *South African cancer incidence and mortality data do not harmonise*

The cancer incidence and mortality rates are presented in table 2.4. As explained previously (table 2.1 and 2.2), the age-standardised incidence rate (presented in table 2.4) is a summarised measure of a rate that a population would have had if it had a standard age structure. Standardisation is necessary when comparing several populations that differ with respect to age, because age is an important risk factor in cancer. The World Standardised incidence rate was also used here expressed per 100 000 persons.

Table 2.4 Top ten cancer sites in South Africa for 1999 and the comparison of male and female age-standardised incidence rate (ASR) values for incidence and mortality (Albrecht, 2006:11)

Cancer Site	Incidence			Mortality			Total cases
	MALES			FEMALES			
	Cases	I-ASR ¹	M – ASR ²	Cases	I-ASR	M-ASR	
Breast	-	-	-	5901	33	18	5901
Cervical	-	-	-	5203	29	19	5203
Prostate	3860	34	27	-	-	-	3860
Lung	1738	14	40	721	5	12	2459
Oesophagus	1540	11	25	909	6	11	2449
Colorectal	1245	10	10	1122	6	7	2367
Bladder	1005	8	9	395	2	2	1400
Stomach	775	6	11	442	3	5	1217
Non-HL ³	630	4	7	545	3	4	1175
Liver	360	2	12	215	1	5	575
TOTALS	11153			15453			26606

¹I-ASR: Incidence: Age-standardised incidence rate per 100 000 of the population

²M-ASR: Mortality: Age-standardised incidence rate per 100 000 of the population

³Non-HL: Non-Hodgkins Lymphoma

The highlighted areas in table 2.4 show the cases where the mortality age-standardised incidence rate (M-ASR) is higher than the incidence ASR (I-ASR) of the specific cancer. This includes all the cancers except prostate, breast and cervical cancer (Albrecht, 2006:11). The Burden of Disease Research Unit of the South African Medical Research Council (MRC) provided the mortality data for 2000 while the incidence data was taken from the National Cancer Registry (NCR) issued in 1999. This proves a huge underreporting of cancer cases in South Africa and may make the National Cancer Registry an untrustworthy source of data for many of the cancers in South Africa. The mortality data provided by the MRC is thus the only way to monitor cancer in South Africa (Albrecht, 2006:11).

In the summary report of the South African National Burden of Disease Study 2000: Estimates of Provincial Mortality (Bradshaw *et al.*, 2006:7) these cancers shown in figure 2.7 caused the most cancer deaths in the year 2000.

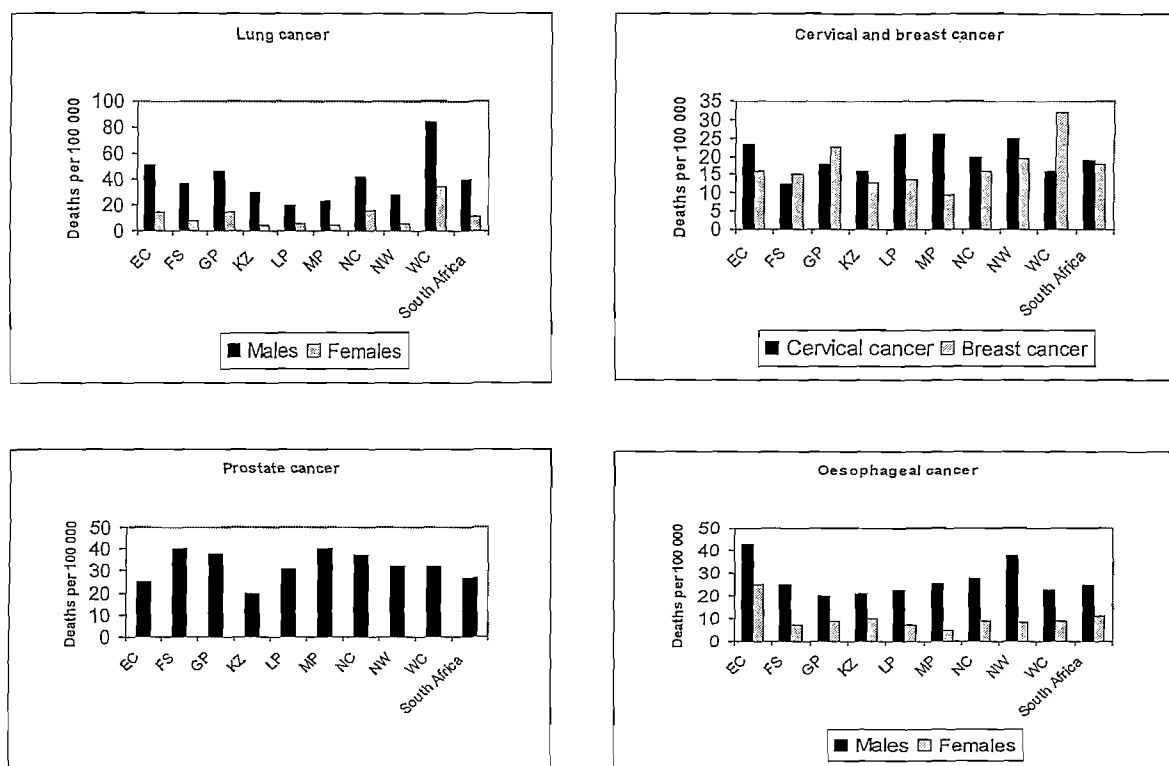


Figure 2.7 Provincial estimates of age-standardised death rates due to lung cancer, breast cancer, cervical cancer, prostate cancer and oesophageal cancer (Bradshaw *et al.*, 2006:7)

- *Poor histological diagnosis of lung, oesophageal and liver cancer*

Up to 50% of lung, oesophageal and liver cancer cases are not diagnosed histological due to late presentation, logistical insufficiencies or other reasons such as only making clinical diagnoses in order to reduce costs (Albrecht, 2006:12). Another explanation for incomplete incidence data could stem from the fact that only 50% of patients with cancer report the cases. Table 2.4 shows that the mortality ASR's of these three cancers are more than double the incidence rates. According to Albrecht (2006:12) the underreporting of cancer in South Africa can amount to 54 507 cases in 1999-2000. The National Cancer Registry reported that in 1999 the yearly incidence of new cancer patients in South Africa was 60 000, but when the

underreporting is brought into account; it could easily be closer to 114 000 new cancer patients per year (Albrecht, 2004:3).

- *Limited data for South African Cancer Progress Report*

According to Albrecht (2006:4) cancer in South Africa is only monitored by two criteria – cancer incidence (monitored by the National Health Laboratory Services) and mortality rate (monitored by the Medical Research Council). As seen above, the incidence rates of South Africa may be unreliable and thus of little use when monitoring the cancer control progress in South Africa. The only criteria that can be used are the cancer mortality rates of South Africa provided by the MRC.

In the United States of America state-based cancer registries is used to collect and analyse data about cancer cases and cancer deaths in each state. The National Program of Cancer Registries (NPCR) was implemented in 1992 and is administered by the Centres for Disease Control and Prevention (CDC). The NPCR, together with the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Programme collect data and statistics for the entire United States of America (CDC, 2007).

South Africa does not have a National Cancer Institute (NCI) or a National Program of Cancer registries (NPCR). There is no definite policy on cancer control in South Africa. This may explain the lack of correct data or a detailed Cancer Control Progress Report in South Africa (Albrecht, 2006:4).

2.4 TREATMENT OF CANCER

The first drug used in the treatment of cancer for its cytotoxic effects was nitrogen mustard, which was originally used in chemical warfare in the First World War. Soldiers exposed to this chemical was examined and it was found that those who died as a result of exposure to nitrogen mustard had no bone marrow while those who survived had a reduced white cell count (Calvert and McElwain, 1988). After researching this phenomenon, nitrogen mustard was first used in the treatment of leukaemia in 1941 and from thereon the interest in and understanding of cancer and the treatment thereof increased and is still increasing till this day (Calvert and McElwain, 1988).

New cancer treatment approaches introduced in the past four decades is currently playing a major role in the treatment of diseases that were previously either

untreatable or could only be treated locally with surgery or radiation (Chabner *et al.*, 2008:1,4)

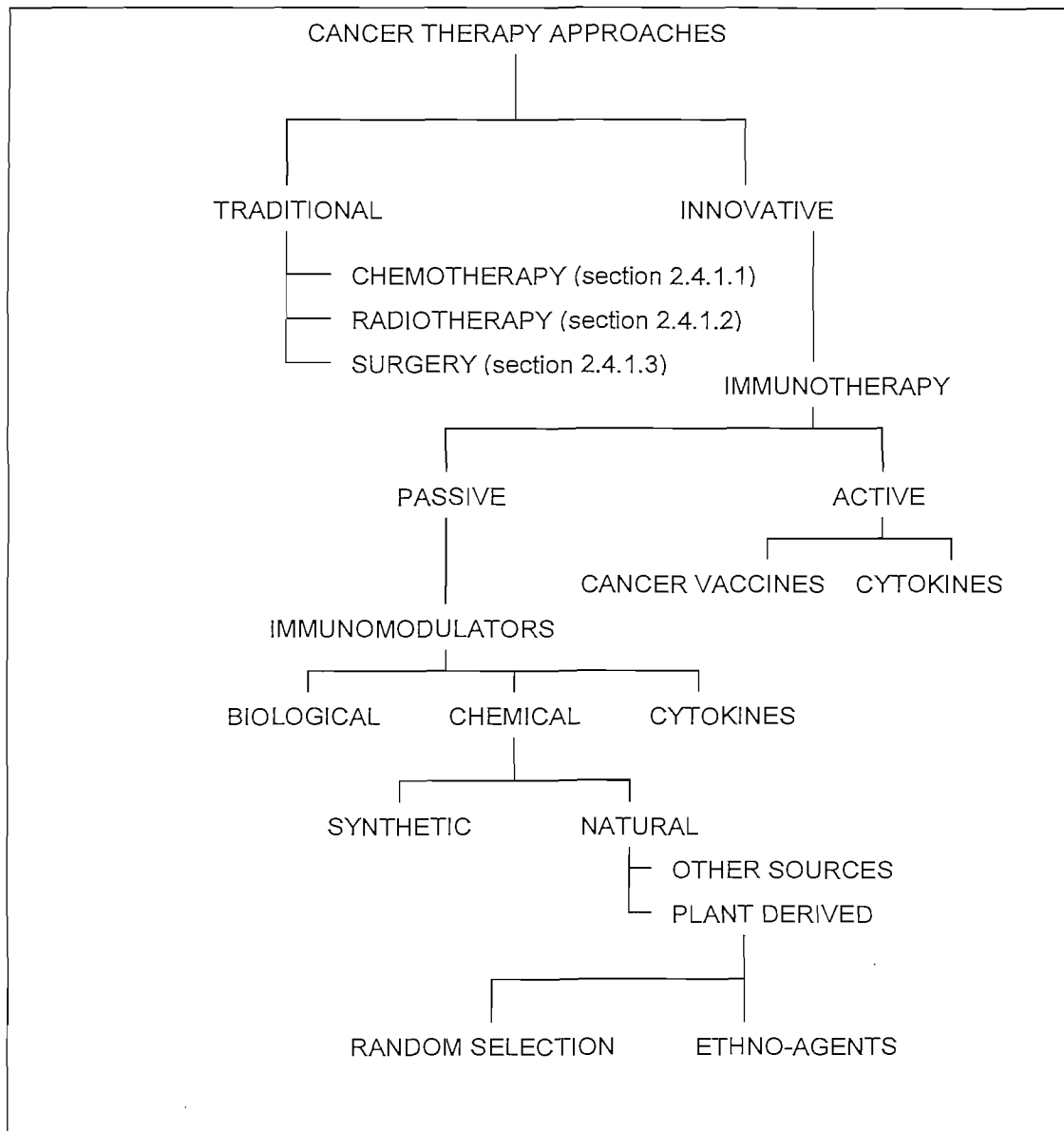


Figure 2.8 An overview of cancer therapy approaches (Diwanay *et al.*, 2004:480)

Figure 2.8 gives a schematic overview of cancer therapeutic approaches used. The traditional/conventional treatment of cancer includes chemotherapy, radiotherapy and surgery. These treatment options will be discussed in section 2.4.1. The novel and innovative treatment options include gene therapy, monoclonal antibodies, small

molecules and cancer vaccines. These new treatment approaches for cancer will be discussed in section 2.4.2.

The aim of treatment in patients with cancer is cure or, if this is not possible, effective palliation (Neal, 2005:92) to alleviate symptoms and prolong life. All normal cells as well as neoplastic cells in the body follow a specific cycle (Leon *et al.*, 1995:197). It is important to understand the kinetics of the cell cycle, in order to explain the mode of action, indications and scheduling of anticancer agents. A schematic summary of cell cycle kinetics is presented in figure 2.9 below (Chu & Sartorelli, 2004:901):

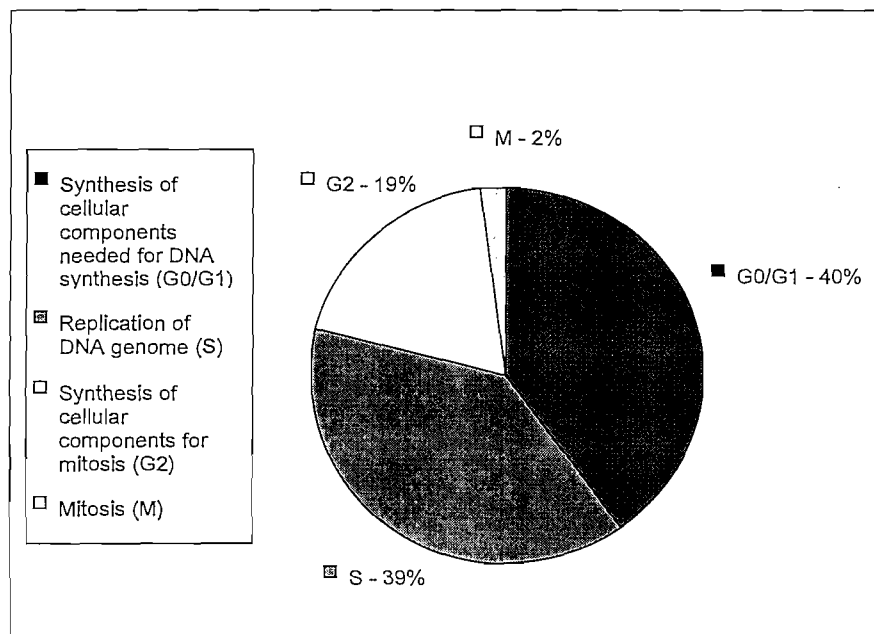


Figure 2.9 The cell cycle phases (Chu & Sartorelli, 2004:901)

- G0/G1-phase: Initial phase of the cell cycle (G0), where various enzymes required for cell function and DNA synthesis are produced. It is the rest period between cell divisions
- S-phase: DNA replication
- G2-phase: Further growth and protein synthesis
- M-phase: The mitotic phase of cell division comprising prophase, metaphase, anaphase and telophase.

The percentages given represent the approximate percentage of time spent in each phase by a typical malignant cell (Leon *et al.*, 1995:197). Anti-neoplastic agents fall into two specific groups: cell cycle specific drugs (CCS), which exert their action on cells passing through the cell cycle (phases G1 to phase M); and cell cycle non-specific drugs (CCNS), which act on cells irrespective of whether they are resting in G0-phase or passing through the cycle (Leon *et al.*, 1995:197).

Neoplasms with a high percentage of cells undergoing division are most susceptible to chemotherapy. Unfortunately, as mentioned before, these agents are also toxic to proliferating normal cells, especially in the bone marrow, gastrointestinal epithelium and hair follicles (Neal, 2005:92).

2.4.1 Conventional treatment of cancer

Conventional treatment has been described by the National Cancer Institute of the United States (2008a) as a "*currently accepted and widely used treatment for a certain type of disease, based on the results of past research*". The three main conventional or traditional methods of treating cancer are surgery, radiotherapy and chemotherapy.

2.4.1.1 Chemotherapy

According to Dorland's Illustrated Medical Dictionary (2003:345) chemotherapy is the treatment of a disease by chemical agents, originally applied to use as chemicals that affect the causative organism unfavourable, but that do not harm the patient.

In the book *Oncology for Health Care Professionals* (Leon *et al.*, 1995:197) chemotherapy is described as the use of chemical agents (drugs) in the treatment of malignant diseases. Chemotherapy may also be termed anti-neoplastic or cytotoxic (*kytos* – cell; *toxin* – poison) agents. Side effects of chemotherapy are discussed in the following section (2.4.1.1.1).

Cytotoxic agents (chemotherapy), have been used in (Luken & Middleton, 1995:78):

- Effecting a cure in some cancers, e.g. choriocarcenoma and Burkitt's lymphoma;
- Reducing tumour size before surgery and/or radiotherapy;
- Eliminating remaining disease after surgery and/or radiotherapy;

- Treatment for patient after a relapse;
- Palliation of advanced disease;
- Development of new treatments.

2.4.1.1.1 Adverse effects of chemotherapy

In malignant tumours a higher proportion of the component cells is undergoing division than in normal proliferating tissues (Neal, 2005:92), thus the selectivity of cytotoxic drugs is higher for malignant cells. Even so, anti-neoplastic drugs negatively affect all rapidly dividing cells in the body. Table 2.5 gives a summary of the adverse effects of chemotherapy.

Table 2.5 Summary of the adverse effects of antineoplastic agents

(Leon *et al.*, 1995:199)

Acute effects (occur shortly after administration)	Anorexia; nausea and vomiting; allergic reactions e.g. skin rashes, pruritus, erythema; local irritations, e.g. vesicant effects on the skin and mucous membranes; thrombophlebitis with IV therapy; fever, headache, hypotension; malaise and weakness.
Delayed effects (occur weeks or days after administration)	Bone marrow depression (BMD), with leukopenia, anaemia, thrombocytopenia and bleeding.
Immunosuppressant effects	Side effects involving antibodies and cell-mediated immunity. As a result of these effects, potentially life-threatening infections and haemorrhage may occur.
Gastrointestinal tract effects	Stomatitis, mouth ulceration, oesophagitis, abdominal pain, haemorrhage, diarrhoea, intestinal ulceration and perforation.
Long-term effects (becomes evident years after treatment)	Suppression of ovarian or testicular function, resulting in amenorrhoea or inhibition of spermatogenesis; gynecomastia; teratogenicity; mutagenicity and development of secondary carcinomas.

2.4.1.2 Radiotherapy

X-rays were first discovered by a German physicist named Wilhelm Conrad Rontgen in 1895 (Delfino & Day, 2006:12). Since then it has been recognized as an exiting discovery in medicine and still plays an important role in cancer treatment. Naturally Henri Becquerel, a physicist performing research on the properties of uranium, first discovered occurring radiation. He established that uranium was a naturally radioactive substance (Green & Kinghorn, 1995:113-4). In the years to follow, the

use of both x-rays and radioactive substances developed and a greater understanding as to how radiation actually works was obtained (Green & Kinghorn, 1995:114).

2.4.1.2.1 The mode of action of radiotherapy

Radiotherapy involves the use of ionizing radiation to destroy cancer cells and shrink tumours. It is also called radiation therapy, x-ray therapy or irradiation (National Cancer Institute, 2004:1). Radiotherapy penetrates the tissue of the body, destroying the cells within the tissue. The target of radiation in cancer is the genetic structure of the cells in the patient's body. Because cancer cells divide faster than normal cells, the damage done by radiotherapy is mainly performed on the cancer cells (Vachani, 2006:1). Unfortunately, like chemotherapy, other fast dividing cells in the body are also damaged - such as bone marrow, skin, hair follicles and gastrointestinal tract epithelium. Some of the side effects of radiation are similar to those of chemotherapy because the same cells are damaged in both processes (Green & Kinghorn, 1995:115-7).

2.4.1.2.2 Uses of radiotherapy in cancer

Radiotherapy can be used in the treatment of a variety of solid tumours (breast, cervical, lung, prostate, etc.) and the radiation dose depends on factors such as the type of cancer and site of the tumour (National Cancer Institute, 2004:2). There are mainly three types of radiation therapies (National Cancer Institute, 2004:2):

- External radiotherapy - A beam of radiation is directed from outside the body
- Internal radiotherapy - A source of radioactivity is surgically placed inside the
body, in the vicinity of the tumour.
- Systemic radiation therapy - Unsealed radioactive materials spread
throughout the body.

Radiotherapy can be used in combination with chemotherapy and/or surgery, or as a single therapy. If radiotherapy is used alone, it must be curative and destroy all the bodily tumour cells (Engel-Hills, 1995:184). There are a few guidelines to decide whether or not a patient can receive radiotherapy as a single treatment:

- The tumour must be sensitive to radiation.

- The tumour must be defined with little or no doubt.
- Metastatic spread must not have occurred.
- It must be possible to deliver a high dose to the tumour without too much risk to the surrounding normal tissue (Engel-Hills, 1995:184).

Radiotherapy in combination with either chemotherapy and/or surgery are considered in the following circumstances:

- Pre-operative radiation therapy

The patient is given a course of radiation before surgery in order to reduce the size of the tumour and make curative surgery a bigger possibility (Engel-Hills, 1995:184).

- Post-operative radiation therapy

After the first surgery, further surgery is too big a risk in some patients. Therefore radiation is given after surgery when there is residual tumour, which can cause recurrence. Post-operative radiation can also be given to an area beyond the local site as part of curative treatment (Engel-Hills, 1995:185).

- Radiation therapy and chemotherapy

Radiation can be given before or after chemotherapy. If radiation is given before chemotherapy the aim is to treat the primary tumour site and the chemotherapy then treats the residual disease and/or metastases.

Usually radiation is given with or after chemotherapy. The chemotherapy then reduces the tumour mass and the radiation is used on a smaller area (Engel-Hills, 1995:185).

- Surgery, radiation therapy and chemotherapy

Some cancer patients are treated with all three treatment options.

2.4.1.3 Surgery

Surgery is the oldest and most widely used form for treating cancer (Topping, 1995:146). In 80-85% of curable cancers surgery is the treatment of choice. The other two conventional methods for treating cancer, chemotherapy and radiotherapy, was only discovered and developed later on in the 19th century (Brainers & Jaftha, 1995:173). Although surgery is an effective form of treatment, it is often not effective alone, unless all the tumour and affected lymph nodes can be removed as a whole

and/or the cancer is confined to its primary site. Surgery is usually part of a treatment plan (Topping, 1995:147-8)

2.4.1.3.1 Uses of surgery in cancer

According to Jaftha and Brainers (1995:173) surgery can be divided into five categories:

- **Definitive surgery**

This surgery is performed to define the diagnosis and the spread of the cancer.

- **Staging surgery**

In order to decide on further treatment and to make a prognosis it is important to establish in which stage the cancer are.

- **Curative surgery**

If it is possible to remove all tumour and lymph nodes, curative surgery is performed. By doing this, the patient is placed in remission.

- **Palliative surgery**

Surgery can also be performed to make the patient more comfortable and enhance the quality of life of the patient.

- **Combination surgery**

This surgery includes two or more of the above options.

2.4.2 New treatment approaches

Although traditional treatment options like surgery, radiation and chemotherapy is still used, it is often unsuccessful in treating some cancers (Mulherkar, 2001:556). A new development to control cancer by the modulation of the patient's immunity provides an alternative to conventional chemotherapy. Improving immunity and avoiding undesired immune reactions is the key element of immunotherapy in cancer (Diwanay et al., 2004:479).

In the book, *The Economics of Cancer Care* (Bosanquet & Sikora, 2006a:7,123), the authors stated that over the last 5 years there has been a change in the approach to cancer medicine. The search for new cytotoxic drugs has been replaced by exploring drugs acting on defined molecular mechanisms. According to Sikora and Bosanquet

(2006a:7,123), there will be an observable shift in the types of agents used in the systemic treatment of cancer over the next 10 years. In future, cancer patients will receive drugs that are directly targeted at their lesions, a treatment that will be more selective and less toxic. The aim and ideal of the new strategy for cancer treatment is to convert cancer into a chronic, controllable illness comparable to diabetes today (Bosanquet & Sikora, 2006a: 7,123).

There have been a dramatic increase in the development of new molecular therapies and cancer drug development is entering a significant new phase. Reasons for the increase include (Sikora, 2002: 951):

- Sequencing and bioinformatics
- Expression vectors for target production
- Predictive ability of three-dimensional structural biology
- Platform approach to drug discovery
- Huge increase in number of targets. The potential timeline for the introduction of new technology to the marketplace is showed in figure 2.10. According to Sikora (2002:951) the crucial years are predicted to be 2005-2010:

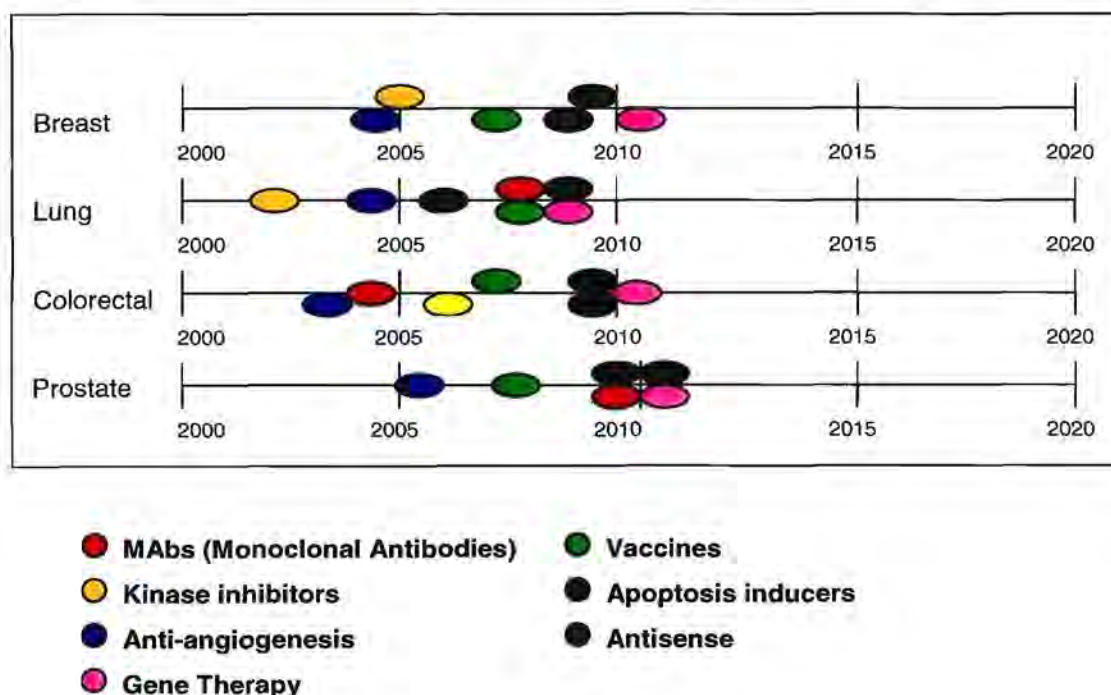


Figure 2.10 Predicted new drug application (NDA) dates with the US Food and Drug Administration for novel cancer drugs (Sikora, 2002:951).

The four major approaches in developing these new therapies for cancer, according to Karol Sikora (2006:10) are:

- gene therapy
- monoclonal antibodies
- small molecules
- vaccines

2.4.2.1 Gene therapy

Gene therapy can be described as the treatment of a disease by introducing genetic material (genes) into a cell (Parliamentary Office of Science and Technology, 2005:1). The core of gene therapy is the replacement of a defective gene with a normal gene in the patient's body (Mulherkar, 2001:555). Cancer is now generally accepted to be a genetic disease, and therefore the therapy approach to cancer has changed and evolved. Cancer may be the result of damage to the DNA caused by carcinogens or even spontaneously during DNA replication. Therefore these mutated genes are the targets of gene therapy (Mulherkar, 2001:555-558).

Gene therapy has various uses – it can be used alone or as an adjuvant to other treatment options. According to Mulherkar (2001:555-558) the different approaches for gene therapy being examined are:

- Targeting genetic lesions in tumour cells
- Immunomodulation by gene therapy
- Genetically modified tumour vaccines in gene therapy
- 'Suicide' gene therapy
- Apoptosis-inducing genes
- Blocking angiogenesis
- Combination of gene therapy with other treatment options

Table 2.6 Strategies used in gene therapy for cancer (in preclinical or clinical trials) (Mulherkar, 2001:557)

Strategy for gene therapy	Targeted gene/therapeutic gene	Type of cancer
Anti-sense molecules	<i>K-ras</i> <i>bcr-abl</i> <i>bcl-2</i>	Small cell lung carcinoma (SCLC) Chronic myelogenous leukaemia (CML) Non-Hodgkins lymphoma
Augmentation of immune response	<i>Co-stimulatory</i> <i>HLA-B7</i> <i>CD-80</i>	Head/neck cancer, childhood acute lymphoblastic leukaemia
Immunomodulation	<i>Cytokine genes such as IL-2, IL-4, IL-12, GM-CSF</i>	Various solid tumours
Prodrug activation	<i>Herpes simplex thymidine kinase gene</i> <i>Cytosine deaminase</i>	- Brain tumour, ovarian cancer, liver cancer, head/neck cancer, breast cancer. - Head/neck cancer, hepatocellular carcinoma.
Induction of apoptosis	<i>p53</i> <i>BAX</i> <i>hREC2</i> <i>Caspase-8</i>	SCLC, head/neck cancer, ovarian carcinoma, brain tumour, non-SCLC
DNA vaccines	<i>IL-12, IFN-γ (interferon-γ)</i>	
Genetic radio-isotope	<i>Sodium/iodide symporter</i>	Solid tumours
Inhibition of angiogenesis	<i>Angiostatin, Endostatin</i>	Solid tumours
Chemo-protection of bone marrow	<i>MDR-1</i>	Ovarian cancer
Oncolytic virus	<i>(kills cells carrying p53 mutations specifically)</i>	Head/neck cancer

- K-ras: The K-ras oncogene resides on chromosome 12p12, and encodes a 21-kD protein (p21ras) involved in the G-protein signal transduction pathway, modulating cellular proliferation and differentiation (Veripath Oncodiagnostics, 2008).
- Bcr-abl: Bcr-Abl, is a constitutively active protein-tyrosine kinase that is highly expressed in chronic myelogenous leukaemia and in acute myeloid leukaemia cells (Mukhopadhyay et al., 2002: 30622).

- Bcl-2: B cell lymphoma gene-2 proteins are associated with membranes and membrane activity forms part of a complex system of signalling that controls apoptosis (Emory University, 2008).
- Co-stimulatory-HLA-B7: Human histocompatibility human leukocyte antigen (HLA) surface antigen encoded by the b-locus on chromosome 6 (Centre for cancer education, 1998a).
- CD80: CC80 is expressed on activated B-cells and gamma-interferon-stimulated monocytes (Centre for cancer education, 1998b).
- IL-2, IL-4, IL-12: Interleukin-2; Interleukin-4; Interleukin-12
- GM-CSF: Granulocyte-macrophage colony-stimulating factor. It is a cytokine that is a type of hematopoietic (blood-forming) agent. (also called granulocyte-macrophage colony-stimulating factor and sargramostim) (National Cancer Institute, 2008b)
- P53: p53 is a nuclear phosphoprotein, which acts as a tumour suppressor. The gene for p53 is located on the short arm of chromosome 17 at 17p13 (NLM, 2008)
- BAX: BAX is the 192-amino acid, 21-kDa protein, which is ubiquitously distributed in normal tissues and acts as a tumour suppressor (Godlewski *et al.*, 2001:1).
- hREC2: is a putative member of the RAD51/52 family of double strand break repair enzymes, which play a key role in DNA recombination (Ingraham *et al.*, 1999:56).
- Caspase-8: Caspases are cysteine proteases that cleave substrates after a conserved aspartate residue and are known as the executioners of apoptosis (Goyal, 2001:905).
- MDR-1: Human *MDR1* is located on chromosomal region 7q21 (Bodor *et al.*, 2005:1).

2.4.2.2 Monoclonal antibodies

Monoclonal antibody therapy is widely used in the management and treatment of cancer including diagnosis, monitoring and treatment. The American Cancer Society (2008b) specifies mainly two types of monoclonal antibodies:

- Naked monoclonal antibodies – without any drug or radioactive material attached.
- Conjugated monoclonal antibodies – joined to a chemotherapy drug, radioactive particle, or a toxin.

Several monoclonal antibodies have been approved over the years for the treatment of different types of cancers:

**Table 2.7 Monoclonal antibodies approved for cancer treatment in America
(American Cancer Society, 2008b)**

Monoclonal antibody	Product	Cancer type	Year of approval
Rituximab	<i>Rituxan® (South Africa: Mabthera®)</i>	Non-Hodgkins lymphoma	1997
Trastuzumab	<i>Herceptin®</i>	Breast cancer	1998
Gemtuzumab ozogamicin**	<i>Mylotarg®</i>	Acute myelogenous leukaemia	2000
Alemtuzumab	<i>Campath® (South Africa: Mabcampath®)</i>	Chronic lymphocytic leukaemia	2001
Ibritumomab tiuxetan**	<i>Zevalin®</i>	Non-Hodgkins Lymphoma	2002
Tositumomab**	<i>Bexxar®</i>	Non-Hodgkins Lymphoma	2003
Cetuximab	<i>Erbix®</i>	Colorectal cancer Head and neck cancers	2004 2006
Bevacizumab	<i>Avastin®</i>	Colorectal Cancer NSCLC*	2004 2006
Panitumumab	<i>Vectibix®</i>	Colorectal cancer	2004

* Non-small cell lung cancer

** Conjugated monoclonal antibodies

2.4.2.3 Small molecules

Small molecules that are of importance in cancer are the protein tyrosine kinases. It has increased activity in neoplastic cells (Esteva, 2004:6). Several human epidermal growth factor receptor (HER) tyrosine kinase inhibitors are being investigated for different types of cancer (Esteva, 2004:6):

Table 2.8 HER tyrosine kinase (TK) inhibitors (Esteva, 2004:6)

Inhibitor	Selected tumour types
Gefitinib (Iressa®; AstraZeneca; Wilmington, DE)	Locally advanced or metastatic NSCLC*, head and neck, breast, ovarian, prostate, glioma, pancreatic, colorectal.
Erlotinib (Tarceva®; Genentech, Inc.; South San Francisco, CA)	NSCLC*, head and neck, breast, ovarian, prostate, pancreatic, colorectal, glioma.
EKB-569 (Wyeth-Ayerst Laboratories, Inc.; St. Davids, PA)	NSCLC*, breast, other ErbB**-dysregulated solid tumours.
CI-1033 (Pfizer Inc.; Groton, CT)	NSCLC*, breast, other ERbB-dysregulated solid tumours.
Lapatinab (GlaxoSmithKline; Research Triangle, NC)	ERbB-dysregulated solid tumours

* NSCLC: Non-Small Cell Lung Cancer

**ErbB: An epidermal growth factor receptor which is found on the surface of cells to which epidermal growth factor (EGF) binds (MedicineNet.com).

2.4.2.4 Vaccines

In contrast to the monoclonal antibodies, vaccines are considered to be an active form of immunotherapy because of their intrinsic immune response. Vaccines stimulate an immune response that can target the tumour antigens directly (Morse, 2008).

In February 2008, two new cervical cancer vaccines namely Gardisal® and Cervarix® was approved in by the Medicine Control Council (MCC) of South Africa. Both vaccines are currently only available in the private health care sector of South Africa and the cost of both vaccines amounts to more than R2100 for the three injections needed. Although these vaccines are seen as an effective way to prevent cervical cancer, the vaccines will need to be included in the government

immunisation programme in order to be accessible and affordable to all South Africans (CANSAs, 2008).

2.4.3 Cancer drugs used in this study

Because of the extensive spectrum and nature of individual cancer drugs (refer to section 3.2 for definition of cancer drug), this aspect will not be discussed in further detail in the literature study. The ATC classification system used to classify cancer drugs used in this study are presented in Appendix A and explained in section 1.2 as well as section 3.8.2.2. Cancer drugs complying with certain criteria with regard to aspects of cost, prevalence, cost prevalence index (CPI), age and/or gender will be discussed in further detail in Chapter 4.

2.5 FIVE COMMON CANCERS IN THE PRIVATE HEALTH SECTOR

Some of the most lethal and common cancers in the private health sector of South Africa will now be discussed. Data and statistics from the South African National Cancer Registry 1998-1999 were used due to lack of more recent data available.

2.5.1 Lung cancer

2.5.1.1 Definition and introduction

The lungs are a paired organ of respiration found in the chest cavity and enveloped by the pleura, with the primary purpose of taking up oxygen and eliminating carbon oxide (Dox *et al.*, 1985:254). Lung cancer is solid tumours that have been classified into four major cell types (Hamilton, 2003:629):

- Squamous cell carcinoma (<30% of all lung cancers)
- Adenocarcinoma (40%)
- Large cell carcinoma (15%)
- Small cell lung carcinoma (SCLC, or oat cell carcinoma) (20%).

For determining management strategy and overall prognosis, adenocarcinoma, squamous cell carcinoma, and large cell carcinoma are usually grouped together and referred to as non-small cell lung cancers (NSCLC) (Hamilton, 2003:629). Lung cancer can therefore be divided in two main subtypes, non-small cell cancer (75%-80%) and small cell cancer (20-25%) (Chu & Sartorelli, 2004:927). Lung cancer is not a single disease, but rather a collection of numerous diseases that are distinguished

by their existing cell type, the growth of the cells and the treatment for the specific "disease" (Oncolink, 2007).

2.5.1.2 Incidence and mortality

Lung cancer is the most frequently found cancer worldwide (Mqoqi *et al.*, 2004:36-37) representing 12.4% of all new cancers worldwide in 2002 and killing 1.18 million people (17.6% of all cancer deaths). Global cancer statistics shows that almost half (49.9%) of lung cancer cases occur in developing countries, such as South Africa (Parkin *et al.*, 2005:81). According to the South African National Burden of Disease Study it was the leading fatal cancer in South Africa in 2000 (Bradshaw *et al.*, 2006:7).

There were 3370 new lung cancer cases reported in South Africa in 1998 and 1999 combined (average of 6.3% of all new cancer cases) (Mqoqi *et al.*, 2004:36). Table 2.9 summaries the South African lung cancer statistics available.

2.5.1.3 Signs and symptoms

The most common initial signs and symptoms include persistent cough, dyspnea, chest pain, sputum production and hemoptysis (Hamilton, 2003:629). Other symptoms that may present in lung cancer are voice change, recurrent pneumonia or bronchitis (American Cancer Society, 2008c:13).

Table 2.9 Summarised statistics for lung cancer in South Africa, during 1998 and 1999 (Mqoqi *et al.*, 2004: 35).

Pop/Sex	N(Obs)	N(Adj)	Percent	Crude	ASR	Cumrisk	LR
FEMALES, 1998							
Asian	21	21	2.77	3.83	4.64	0.54	186
Black	311	321	40.98	1.87	2.92	0.35	286
Coloured	93	95	12.25	4.93	7.55	1.01	100
White	334	343	44.01	13.51	9.86	1.3	77
Total	759	780	100	3.54	4.95	0.62	162
MALES, 1998							
Asian	48	48	2.59	8.96	12.18	1.7	59
Black	1012	1066	55.04	6.49	12.07	1.49	68
Coloured	192	201	10.35	10.95	20.15	2.7	38
White	594	619	32.02	25.09	21.7	2.92	35
Total	1855	1934	100	9.11	15.18	1.93	52
FEMALES, 1999							
Asian	25	25	3.61	4.49	5.15	0.67	150
Black	219	229	31.6	1.3	1.98	0.23	435

Coloured	124	129	17.89	6.6	9.65	1.32	76
White	325	338	46.9	13.27	9.65	1.26	80
Total	693	721	100	3.27	4.58	0.59	170
MALES, 1999							
Asian	49	50	2.98	9.23	12.93	1.59	63
Black	797	842	48.42	5.01	9.28	1.16	87
Coloured	228	242	13.85	13.01	23.48	3.16	32
White	572	604	34.75	24.47	20.74	2.72	37
Total	1646	1738	100	8.19	13.98	1.76	57

N(Obs)	Number of cases observed
N(adj)	Observed cases adjusted for unknown population
Percent	Percentage of all site cancers
Crude	Number of cases/population per 100 000
ASR	Age-standardised incidence rate per 100 000 (World standard population)
Cumrisk	Cumulative lifetime incidence risk (0-74 years)
LR	Lifetime risk (0-74 years) of developing a cancer expressed as 1 in X number of people
<i>Please note:</i>	<i>Ranking excludes BCC, SCC of the skin, PSU and ill-defined sites</i>

2.5.1.4 Early detection

Only about 15% of lung cancer cases are found in the early stages, because lung cancer does not cause symptoms until the advanced stages of the disease (Health Alliance Cancer Services, 2006:1). Usually early lung cancer is found incidentally whilst patients are tested for other unrelated diseases like heart disease, pneumonia or other lung diseases (Health Alliance Cancer Services, 2006:1). Older methods to detect lung cancer such as chest x-rays, analysis of cells in sputum, and fiberoptic examination of the bronchial passages have limited value in reducing mortality. There are newer tests including molecular markers in sputum and low-dose spiral computed tomography (CT) scans available to detect lung cancer at an earlier stage (American Cancer Society, 2008c:14).

Spiral CT, a screening test, which was introduced in the 1990's, detects tumours under a centimetre in size, while standard chest x-rays only picks up tumours of about 1-2 cm in size. In 2002, a study was launched by the American National Cancer Institute to compare these two screening tests for diagnosing lung cancer

(American Cancer Society, 2008c:14). In February 2004, approximately 50 000 current or former smokers was participating in this study to assess whether lung cancer deaths can be reduced by using these screening tests (National Cancer Institute, 2008c). Results from this study are only expected by 2010 (American Cancer Society, 2008c:14), but to date no scientific evidence has shown whether screening and early detection of lung cancer with these tests actually reduces mortality or whether it only prolongs and improves life (National Cancer Institute, 2008c).

2.5.1.5 Risk factors

Exposure to carcinogens (especially tobacco smoke) causes chronic inflammation and lead to genetic and cytologic changes. Eventually lung carcinoma arises from the epithelial cells of the lungs (Hamilton, 2003:629). According to the American Cancer Society (2008c:14) cigarette smoking is by far the biggest and most important risk factor for lung cancer. This risk also increases with the quantity and duration of cigarette consumption.

2.5.2 Breast cancer

2.5.2.1 Definition and introduction

The breast is a glandular structure, consisting of 9-20 glands forming wedge-shaped lobes that converge on the nipple. The glands are autonomous, made up of numerous lobules with no anastomoses (Cohen, 1995: 45-47). The breasts are embryological modified sweat glands and therefore appendages of the skin. Major lymph drainage occurs towards the axilla. This lymph drainage is the most important route for the spread of breast cancer (Cohen, 1995: 45-47).

Staging of breast cancer is based on the size of the primary tumour (T1-4), presence and extent of lymph node involvement (N1-3), and presence or absence of distant metastases (M) (Hamilton, 2003:613). The staging is presented in table 2.11.

2.5.2.2 Incidence and mortality

Cancer of the breast comprises 18% of all cancers in woman, making it the leading malignancy in woman (Parton *et al.*, 2001:1528). An estimated 1.15 million new cases was recorded worldwide in 2002, thus ranking second overall when both sexes

are considered (Parkin *et al.*, 2005:84). The prognosis from breast cancer is relatively good with 4.4 million survivors up to 5 years following diagnosis, and therefore making breast cancer the most prevalent cancer in the world today (Parkin *et al.*, 2005:84).

In South Africa breast cancer was second of the leading cancers in 1998 and the leading cancer in 1999 (18.6% and 19.4% of all cancers respectively). A total of 11 507 cases were reported in the two years (1998&1999) (Mqoqi *et al.*, 2004:30). Statistics for breast cancer in South Africa is summarised in table 2.10.

2.5.2.3 Signs and symptoms

In 90% of woman, the initial sign of breast cancer is a painless lump that is typically solitary, unilateral, solid, hard, irregular, and non-mobile. Other common signs are pain and nipple changes, and more advanced cases present with prominent skin edema, redness, warmth and induration (Hamilton, 2003:613).

Table 2.10 Summarised statistics for breast cancer in South Africa, during 1998 and 1999 (Mqoqi *et al.*, 2004:30)

Pop/Sex	N(Obs)	N(Adj)	Percent	Crude	ASR	Cumrisk	LR
FEMALES, 1998							
Asian	214	223	4.01	40.62	45.26	5.57	18
Black	2103	2210	39.4	12.88	17.98	1.99	51
Coloured	609	638	11.41	33.12	45.21	5.33	19
White	2412	2533	45.19	99.73	76.04	8.62	12
Total	5338	5604	100	25.28	32.7	3.65	27
FEMALES, 1999							
Asian	244	258	4.37	46.38	49.62	5.84	18
Black	2186	2307	39.11	13.13	18.39	2.06	49
Coloured	691	730	12.36	37.35	49.77	5.79	18
White	2468	2606	44.16	102.35	76.46	8.7	12
Total	5589	5901	100	26.61	34.61	3.88	26

N(Obs)	Number of cases observed
N(adj)	Observed cases adjusted for unknown population
Percent	Percentage of all site cancers
Crude	Number of cases/population per 100 000
ASR	Age-standardised incidence rate per 100 000 (World standard population)
Cumrisk	Cumulative lifetime incidence risk (0-74 years)

LR Lifetime risk (0-74 years) of developing a cancer expressed as 1 in X number of people

Please note: *Ranking excludes BCC, SCC of the skin, PSU and ill-defined sites*

2.5.2.4 Early detection

Breast self-examination (BSE) is very important in the early detection of breast cancer and should be promoted and taught to every woman (Bryant, 1995:407). For woman between 20 and 30, clinical breast examinations (CBE) should be performed approximately every 3 years. Woman over the age of 40 should be examined every year and annual mammograms are also recommended from this age forward (American Cancer Society, 2007c:1). The different stages of breast cancer are explained in table 2.11.

Table 2.11 Staging of breast cancer (Bryant, 1995:405)

PRIMARY TUMOUR (T)	TX	Primary tumour cannot be assessed
	T0	No evidence of primary tumour
	TIS	Carcinoma <i>in situ</i> . Intraductal carcinoma, lobular carcinoma <i>in situ</i> , or Paget's disease of the nipple with no tumour.
	T1	Tumour 2 cm or less in greatest diameter T1a 0,5 cm or less in greatest dimension T1b More than 0,5 cm but no more than 1 cm in greatest dimension T1c More than 1 cm but no more than 2 cm in greatest dimension
	T2	Tumour more than 2 cm but no more than 5 cm in greatest dimension
	T3	Tumour more than 5 cm in greatest dimension
	T4	Tumour of any size with direct extension to chest wall or skin T4a Extension to chest wall T4b Oedema (including peau d'orange) or ulceration of the skin of breast or satellite nodules confined to same breast T4c Both T4a and T4b T4d Inflammatory carcinoma
LYMPH NODE (N)	NX	Regional nodes cannot be assessed
	N0	No regional lymph nodes metastasis
	N1	Metastasis to movable ipsilateral axillary lymph node(s)
	N2	Metastasis to ipsilateral axillary lymph node(s) fixed to one another or to other structures
	N3	Metastasis to ipsilateral and infra-/supra-clavicular internal mammary lymph node(s)
DISTANT METASTASIS (M)	MX	Presence of distant metastasis cannot be assessed
	M0	No distant metastasis

	M1	Distant metastasis (includes metastasis to ipsilateral supraclavicular lymph nodes)
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2.5.2.5 Risk factors

The evident worldwide risk factors for breast cancer are summarized in table 2.12. The relative risk and high-risk groups for the different risk factors are also shown.

Table 2.12 Established and probable worldwide risk factors for breast cancer (McPherson *et al.*, 2000:625)

Factor	Relative risk	High risk group
Age	>10	Elderly
Geographical location	5	Developed countries
Age at menarche	3	Menarche before age 11
Age at menopause	2	Menopause before age 54
Age at first full pregnancy	3	First child in early 40's
Family history	≥2	Breast cancer in first degree relative when young *
Previous benign disease	4-5	Atypical hyperplasia
Cancer in other breast	>4	
Socio-economic group	2	Groups I and II**
Diet	1.5	High intake of saturated fat
Body weight:		
• Premenopausal	0.7	Body mass index >35
• Postmenopausal	2	Body mass index >35
Alcohol consumption	1.3	Excessive intake
Exposure to ionising radiation	3	Abnormal exposure in young females after the age of 10
Taking exogenous hormones:		
• Oral contraceptives	1.24	Current use
• Hormone Replacement Therapy	1.35	Use for ≥10 years
• Diethylstilbestrol	2	Use during pregnancy

* First degree relative: Mother, daughter, sister;

Second degree relative: Grandmother, granddaughter, niece

** Group I: Elderly;

Group II: Persons in developed countries

2.5.3 Prostate cancer

2.5.3.1 Definition and introduction

The prostate gland forms part of the male reproductive system and consist of 30-50 glands and can be divided into three zones: the peripheral zone, transition zone and central zone (Cancerline, 2007). In an adult, the prostate is about the size of a walnut and surrounds the upper part of the urethra. The prostate secretes a milky, alkaline fluid into the urethra, which makes up 10-20% of the ejaculatory fluid. The precise function of the prostate is poorly understood but it is thought that it plays a role in preventing urinary infections and aiding fertilisation (Ahlering, 2008).

According to the Cancer Council of West Australia (2008) prostate cancer is the uncontrollable growth of cells in the prostate. This cancer may metastasize and spread to tissue near the prostate and other parts of the body like the bones (in more than 90% of cases spreading occurs in the bones), liver, lungs or lymph nodes (Swierzewski, 2007). Prostate cancer can often be detected at routine medical examinations when a rectal examination is performed. The risk of developing prostate cancer increases with age, more than 70% of men diagnosed with prostate cancer are over the age of 65 (Oncolink, 2007).

2.5.3.2 Incidence and mortality

Prostate cancer is one of the leading cancers in men worldwide (Mqoqi *et al.*, 2004:50). In 2002 there were 679,000 new cases of prostate cancer worldwide, making it the fifth most common cancer in the world and the second most common in men, comprising 11.7% of new cancer cases overall, with 19% in developed countries and 5.3% in developing countries (Parkin *et al.*, 2005:89).

The American Cancer Society (2006:18) estimated a total of 234,460 new prostate cancer cases in the US during 2006. Over the last 20 years incidence rates for prostate cancer have changed substantially: rapidly increasing from 1988 to 1992, declining sharply from 1992 to 1995, and increasing modestly since 1995 (Jemal *et al.*, 2007:47). The changes in the utilisation of prostate-specific antigen (PSA) blood testing could have played a big role in these trends. During the past decade, men younger than 65 were also screened with a PSA screening tool, explaining the moderate increase in incidence rates since 1995. The estimated mortality rate for 2007 in America was 27 350 deaths, making prostate cancer the second highest cause of cancer related deaths in men (Jemal *et al.*, 2007:47).

According to the National Cancer Registry of South Africa (Mqoqi *et al.*, 2004:50-51) prostate cancer had the highest incidence of cases in men during 1998 (4 171 cases reported) and 1999 (3 860 cases reported). This comprises 14% and 13% consecutively of all cancers reported in males. Prostate cancer is more common after the age of 55, with an ASR of 56 per 100 000 at ages 55-59, reaching a high of 455 per 100 000 at the age of 75 years and older. Prostate cancer was the cancer with the highest incidence in all population groups over the two years. White men comprised more than half of all prostate cancer cases (14% of cancers in white men) reported during this period and had the highest incidence rate, with one in 10 white men at risk of developing prostate cancer. The second highest incidence was observed in coloured men (10% of all prostate cancer cases). Prostate cancer in black men made up one third of all prostate cancers in this period, and the black men and Asian men had the lowest rates and risk (four times lower than in white men) (Mqoqi *et al.*, 2004:50-51), as seen in table 2.13.

2.5.3.3 Signs and symptoms

Early prostate cancer is usually asymptomatic (Van der Werf-Messing & Schroeder, 1982:478). Clinical presentations of prostate cancer include difficulty in initiating urinary flow, dribbling after passing urine, chronic backache, musculoskeletal aches and pains (Bailey & Pervan, 1995:462). These symptoms usually show that the disease has developed. Symptoms such as continual pain in the lower back, pelvis, or upper thighs, could be the presentation of benign conditions but may also indicate metastatic disease (American Cancer Society, 2006:18). Other non-specific signs of advanced disease are anaemia and weight loss (Hamilton, 2003:645).

2.5.3.4 Early detection

Beginning at age 50, every man at average risk should be offered a digital rectal examination and the PSA blood test (American Cancer Society, 2006:18). This test identifies a protein made by the prostate called prostate-specific antigen. Men with a medical history of prostate cancer and ethnic groups at high risk of developing prostate cancer should begin screening at age 45. The ideal would be that all men should be informed about the benefits and limitations of testing in order to make informed decisions (American Cancer Society, 2006:18).

Table 2.13 Summarised statistics for prostate cancer in South Africa, during 1998 and 1999 (Mqoqi *et al.*, 2004:50)

Pop/Sex	N(Obs)	N(Adj)	Percent	Crude	ASR	Cumrisk	LR
MALES, 1998							
Asian	61	64	1.54	11.95	20.41	2.2	46
Black	1360	1432	34.36	8.72	20.64	2.39	42
Coloured	375	396	9.47	21.58	47.14	6.17	17
White	2162	2277	54.62	92.31	78.51	10.35	10
Total	3958	4169	100	19.61	37.59	4.59	22
MALES, 1999							
Asian	55	59	1.52	10.89	18.34	2.6	39
Black	1143	1220	31.59	7.26	17.17	2.01	50
Coloured	386	410	10.67	22.04	47.98	5.43	19
White	2034	2169	56.22	87.86	74.38	10.05	10
Total	3618	3858	100	17.81	34.12	4.18	24

N(Obs)	Number of cases observed
N(adj)	Observed cases adjusted for unknown population
Percent	Percentage of all site cancers
Crude	Number of cases/population per 100 000
ASR	Age-standardised incidence rate per 100 000 (World standard population)
Cumrisk	Cumulative lifetime incidence risk (0-74 years)
LR	Lifetime risk (0-74 years) of developing a cancer expressed as 1 in X number of people
<i>Please note:</i>	<i>Ranking excludes BCC, SCC of the skin, PSU and ill-defined sites</i>

2.5.3.5 Risk factors

As has been said, the most important risk factor for developing prostate cancer is age. Prostate cancer is 130 times more likely to develop in a male in his seventies than a male in his forties (Prostate Cancer Foundation, 2004). Further factors include ethnicity, nationality, family history and diet. As previously mentioned, different races have different incidence and mortality rates, the reason for this is unclear. There also seems to be a genetic or inherited factor in prostate cancer. The risk for a man to develop prostate cancer doubles when a father or brother has prostate cancer (American Cancer Society, 2007b:5).

2.5.4 Colorectal cancer

2.5.4.1 Definition and introduction

Colorectal cancer is the term used for either cancer of the colon and/or the rectum because of the many similarities between the two cancers (American Cancer Society, 2007e). The colon and rectum form part of the digestive system. The colon has four sections: the ascending colon, transverse colon, descending colon and the sigmoid colon. The sigmoid colon then joins the final part of the digestive system, the rectum and the anus (University of Virginia Health System, 2007).

Adenocarcinomas (mucin-secreting) are the most common type of tumours in the colon and rectum. Other histological types of tumours found are lymphomas, leiomyosarcoma, and carcinoid tumours, especially in the appendix. The spread of the tumours are: 16% in the ascending colon, 6% in the transverse colon, 20% in the sigmoid colon, and 50% in the rectum (Bryce, 1995:444).

2.5.4.2 Incidence and mortality

It is estimated that 108 070 new colorectal cancer cases will be presented in America in 2008 (American Cancer Society, 2008c:12). Colorectal cancer is still the third most common cancer in both men and women, but the incidence rates have been decreasing since 1985, because of increased screening and polyp removal. The mortality rates have also declined with an average of 1.8% per year since 1985 (American Cancer Society, 2006:12).

A total of 1 171 and 1 245 colorectal cancer cases were reported in South Africa during 1998 and 1999 (Mqoqi *et al.*, 2003:25). As can be seen in table 2.14, colorectal cancer comprised an average of 3.7% and 3.4% of all cancers reported in men and women respectively over the two years, with a 60% greater risk for men than women to develop colorectal cancer in 1999. Table 2.14 also shows that colorectal cancer in white males and females had a higher incidence rate than any other race in South Africa, with more than 50% of all colorectal cancer cases reported in 1998 and 1999. Coloured men had a greater risk of developing colorectal cancer than Asian men in South Africa and the risk for black men were 9 times lower than that of white men. The incidence rates of colorectal cancer were the lowest in black females and the highest in white females of South Africa (Mqoqi *et al.*, 2003:25-26). This information and other statistics for colorectal cancer in South Africa is summarised in Table 2.14.

2.5.4.3 Signs and symptoms

The location of the tumour usually determines the signs and symptoms of colorectal cancer (Bryce, 1995:444). The general symptoms of a colonic carcinoma include nausea and vomiting, abdominal pain, anaemia, altered bowel habits, weight loss and anorexia. More specific symptoms distinguish between tumours of the right colon (unexplained iron-deficiency, GIT bleeding, seldom obstruction), left colon (passage of blood/mucus per rectum, often obstruction) and the rectum (frank bleeding, tenesmus) (Bryce, 1995:444-5).

2.5.4.4 Early detection

If colorectal cancer is detected in the early stages of the disease, the probability of excision and cure increases dramatically (Barkun & Flegel, 2007:545). People at average risk of developing colorectal cancer should begin regular screening from the age of 50 (National Institute of Health, 2007). A screening test that is economical and non-invasive is the faecal occult blood test (FOBT), it detects hidden blood in the stool. It is recommended that this screening test will be performed annually. Other more expensive methods to detect cancer in the colon or rectum include flexible sigmoidoscopy and colonoscopy. Further screening methods for colorectal cancer are under clinical evaluation at this time (National Institute of Health, 2007).

Table 2.14 Summarised statistics for colorectal cancer in South Africa, during 1998 and 1999 (Mqoqi et al., 2003:24)

Pop/Sex	N(Obs)	N(Adj)	Percent	Crude	ASR	Cumrisk	LR
FEMALES, 1998							
Asian	46	47	5.09	8.56	10.45	1.29	78
Black	226	240	25	1.4	2.04	0.22	455
Coloured	102	109	11.28	5.66	7.99	0.92	109
White	530	564	58.63	22.21	14.99	1.73	58
Total	904	960	100	4.33	5.83	0.65	154
MALES, 1998							
Asian	44	44	3.97	8.22	11.01	1.07	94
Black	271	287	24.48	1.75	3.02	0.31	323
Coloured	130	138	11.74	7.52	13.76	1.75	58
White	662	699	59.8	28.34	23.74	2.89	35
Total	1107	1168	100	5.51	9.44	1.09	92
FEMALES, 1999							
Asian	35	35	30.31	6.29	7.31	1.02	99
Black	268	284	25.31	1.62	2.31	0.26	385
Coloured	125	132	11.8	6.75	9.66	1.13	89
White	631	668	59.58	26.23	17.52	2.09	48
Total	1059	1119	100	4.96	6.61	0.77	131
MALES, 1999							
Asian	53	56	4.57	10.33	14.28	1.98	51
Black	278	301	23.97	1.79	2.96	0.35	286
Coloured	128	138	11.03	7.42	14.09	1.8	56
White	701	752	60.43	30.46	25.44	3.27	31
Total	1160	1247	100	5.74	9.74	1.21	83

N(Obs)	Number of cases observed
N(adj)	Observed cases adjusted for unknown population
Percent	Percentage of all site cancers
Crude	Number of cases/population per 100 000
ASR	Age-standardised incidence rate per 100 000 (World standard population)
Cumrisk	Cumulative lifetime incidence risk (0-74 years)
LR	Lifetime risk (0-74 years) of developing a cancer expressed as 1 in X number of people
<i>Please note:</i>	<i>Ranking excludes BCC, SCC of the skin, PSU and ill-defined sites</i>

2.5.4.5 Risk factors

There are a wide variety of risk factors linked with colorectal cancer including a diet high in animal fat (red or processed meat) or low in natural fibre (fruits and

vegetables), obesity, physical inactivity, smoking and heavy alcohol consumption (Bryce, 1995:444).

Genetic factors that increase the risk of developing colorectal cancer include a personal or family history of colorectal cancer and/or polyps or a personal history of inflammatory bowel disease. Inherited genetic mutations (FAP and HNPCC) also increase the risk of colorectal cancer. Age also plays a role in colorectal cancer, more than 90% of cases diagnosed are in persons over the age of 50 (American Cancer Society, 2006:12).

2.5.5 Lymphoma (Non-Hodgkins lymphoma and Hodgkins disease)

2.5.5.1 Definition and introduction

The lymphatic system is a network of organs, ducts, and nodes that are directly connected to the blood's circularly system, with the purpose of transporting lymph through the body (Simon & Cannistra, 2003:1). Lymphocytes, cells present in the lymphatic system, are involved in defending the body against infectious organisms. Other functions of the lymphatic system include the transportation of fats, proteins, and other substances collected from the body's tissue through the ducts. It also restores 60% of the fluid that leaks from the blood capillaries back into circulation. In the lymphatic system there is small structures called lymph nodes that contain lymph vessels, connective tissue and white blood cells. The average size of a lymph node varies from the size of a pinhead to a bean (Simon & Cannistra, 2003:1-2).

The disease, lymphoma, can be defined as a nodular diffuse malignancy starting in the lymphoid tissue of the body. The lymph nodes are usually the first structures affected, but any lymphoid or reticuloendothelial elements in the body can be affected (Pervan & Johnson, 1995:535).

Classification of the malignancy depends on the cell type, degree of differentiation and the pattern of growth. Thomas Hodgkins first identified lymphoma in 1832. This disease can be sub-divided into two main groups: Hodgkins disease (HD) and Non-Hodgkins lymphoma (NHL) (Pervan & Johnson, 1995:535). Table 2.15 presents a comparison between these two diseases.

Table 2.15 A comparison between Hodgkins disease and Non-Hodgkins lymphomas (Simon et al., 2005:6).

Characteristics	Hodgkins Disease (HD)	Non-Hodgkins Lymphoma (NHL)
Age and prevalence	Average age is 27.7 with two age peaks: - o Between 15 and 24 - o Lesser peak after the age of 55	Average age is about 67. NHL more common than HD.
Location	Most often both malignancies occur in the lymph nodes above the collarbone. In HD it is more likely to appear in the chest cavity between the lungs (mediastinum), especially in younger patients. Only about 15-20% of cases are found in areas below the diaphragm. In about 4% of cases HD occurs outside the nodes.	Most often both malignancies occur in the lymph nodes above the collarbone. In NHL it is more likely to appear in the nodes in the abdomen (mesenteric nodes). In less than 40% of the patients the disease occurs in the chest cavity. **Exception: lymphoblastic lymphoma first appears in the chest. In about 23% of patients NHL occurs outside the nodes. Slow-growing lymphomas are common in the liver and bone marrow.
Symptoms	HD is more likely to have systemic symptoms (fever, night sweats) at the time of diagnosis than NHL.	NHL is less likely to have systemic symptoms at the time of diagnosis (27%).
Progression	Less likely than NHL to be diagnosed in stage IV. HD progression is orderly, from one lymph node region to the next. This process may be slow, particularly in younger people, or very aggressive. It usually spreads downward from the initial site. If it spreads below the diaphragm it usually reaches the spleen first, then the disease may spread to the liver and bone marrow. If HD starts in the middle of the chest, it may spread outward to the chest wall and areas around the heart and lungs.	More likely than HD to be diagnosed in stage IV. The lymphomas are less predictable in their course than HD and they are more apt to spread.

2.5.5.2 Incidence and mortality

Estimated new cases of lymphoma globally for 2008 are 74 340, which includes 8 220 Hodgkins disease (HD) cases and 66 120 cases of non-Hodgkins lymphoma (NHL) (American Cancer society, 2008c:15). The incidence rates of HD have

decreased in men and slightly increased in women. In contrast, incidence rates of NHL have practically doubled in the last 30 years, one of the reasons being the pandemic spread of HIV and AIDS, resulting in AIDS-related NHL (American Cancer Society, 2008c:15).

The only statistics of lymphoma provided by South Africa's National Cancer Registry was those of non-Hodgkins lymphoma, which ranked 8th and 9th on the list of leading cancers in men and 9th on the list in women in 1998 and 1999 (Mqoqi *et al.*, 2004:41).

There were 1 266 and 1 175 new cases of NHL reported in 1998 and 1999 respectively. Compared to the other population groups white males had the highest NHL incidence rate (42% of all cases), coloured men the second highest rate and black men the lowest incidence rate in 1998 and 1999. White females also had the highest incidence rate (45% of all female NHL cases) and coloured woman the second highest incidence rate (Mqoqi *et al.*, 2004:41-2). Statistics of NHL is summarised in table 2.16.

2.5.5.3 Signs and symptoms

2.5.5.3.1 Hodgkins disease

Hodgkins disease usually presents with the following persistent symptoms (Lymphoma Research Foundation, 2007):

- Swollen lymph nodes (not always painful)
- Fever
- Night sweats
- Unexplained weight loss
- Lack of energy

Table 2.16 Summarised statistics for non-Hodgkins lymphoma in South Africa, during 1998 and 1999 (Mqoqi *et al.*, 2004:24)

Pop/Sex	N(Obs)	N(Adj)	Percent	Crude	ASR	Cumrisk	LR
FEMALES, 1998							
Asian	20	20	3.58	3.64	3.89	0.4	251
Black	248	258	44.44	1.5	1.98	0.23	435
Coloured	50	50	8.96	2.6	3.51	0.41	244
White	240	248	43.01	9.76	7.15	0.81	124
Total	558	576	100	2.61	3.31	0.37	270
MALES, 1998							
Asian	22	22	3.36	4.11	4.76	0.46	218
Black	291	305	44.43	1.86	2.55	0.25	401
Coloured	72	73	10.99	3.98	5.94	0.74	136
White	270	283	41.22	11.47	9.85	1.05	96
Total	655	683	100	3.24	4.51	0.49	206
FEMALES, 1999							
Asian	15	15	2.83	2.7	2.9	0.34	295
Black	212	216	40	1.23	1.53	0.15	667
Coloured	56	56	10.57	2.87	3.58	0.33	304
White	247	253	46.6	9.94	7.14	0.9	112
Total	530	626	100	2.41	3.01	0.34	297
MALES, 1999							
Asian	21	21	3.48	3.87	4.68	0.47	213
Black	262	273	43.45	1.62	2.22	0.22	455
Coloured	60	60	9.95	3.23	4.57	0.47	213
White	260	272	43.12	11.02	9.37	1.02	99
Total	603	626	100	2.91	4.06	0.43	234

N(Obs) Number of cases observed

N(adj) Observed cases adjusted for unknown population

Percent Percentage of all site cancers

Crude Number of cases/population per 100 000

ASR Age-standardised incidence rate per 100 000
(World standard population)

Cumrisk Cumulative lifetime incidence risk (0-74 years)

LR Lifetime risk (0-74 years) of developing a cancer expressed as
1 in X number of people

Please note: *Ranking excludes BCC, SCC of the skin, PSU and ill-defined sites*

Non-Hodgkins lymphoma

Non-Hodgkins lymphoma usually presents with the following persistent symptoms (Lymphoma Research Foundation,2007):

- Swollen lymph nodes (not always painful)
- Fever
- Night sweats
- Unexplained weight loss
- Lack of energy
- *Itching*
- *Chills*

2.5.5.4 Early detection

People with known risk factors for HD or NHL (such as HIV, infections, organ transplants) should visit their medical practitioner regularly for a medical check-up. Patients and their doctor should also be aware of the signs and symptoms of HD and NHL, and keep a close watch on their health (American Cancer Society, 2007a).

2.5.5.5 Risk factors

2.5.5.5.1 Hodgkins disease

The following factors can increase the risk of Hodgkins disease (Simon & Cannistra, 2003:2-3):

- **Gender** - HD is more common in males, but incidence rates in young woman has increased dramatically in the last few years.
- **Age** - The greatest risk for HD is at the ages between 10-30 years. Incidence rates in young people are increasing and have declined in elderly people.
- **Family factors** - Siblings of people suffering of HD have a three times greater risk than the general population. In about 5% of cases HD runs in the family, but studies also suggest that these cases can just as likely be due to environmental factors.

- **Epstein Barr Virus (EBV)** - People who have had infectious mononucleosis (caused by the EBV) is at greater risk of getting HD. EBV plays a role in roughly half of HD cases, mostly being elderly people. The virus is very common, but usually only causes a mild infection with no long-term significant effects.
- **Exposure to chemicals**
- **Other risk factors** - HIV-positive status, ulcerative colitis, Crohn's disease, people from small families, persons with higher education or living in developed countries

2.5.5.5.2 Non-Hodgkinslymphoma

Risk factors of Non-Hodgkins disease include (Simon et al., 2005:2-4):

- **Gender, age, and ethnicity** - Risk is higher in men than women and peaks between the ages of 45-60 for both sexes.
- **Lifestyle factors** - The risk for siblings of a NHL patient is two times higher than the general population. Although, studies suggest that these cases can just as likely be due to environmental factors.
- **Infections and disorders of the immune system** - Viruses or infections such as Epstein-Barr virus, gastritis, Human herpes virus, Borrelia Burgdorferi also plays a role in NHL. Immune system diseases increase the risk of NHL including HIV/AIDS, rheumatoid arthritis, Crohn's disease, and Sjogren's syndrome.
- **Industrial chemicals and other environmental risk factors**

2.6 OTHER RELEVANT CANCERS IN SOUTH AFRICA

It is difficult to determine the top cancers in South Africa because of various reasons:

- In South Africa there is such a wide spectrum of population groups, cultures, beliefs etc. When it comes to health care in South Africa, there is also a big gap between the underdeveloped areas and the developed areas. Therefore, in South Africa different cancers affect different people, depending on the quality of life, ethnic group etc (Albrect, 2006:36).
- Cancer is not a national priority in South Africa. There is exceptionally low funding from the Medical Research Council and other stakeholders

compared to international standards. There is also no Cancer Control Programme policy at the South African Department of Health and no National Cancer Institute (Albrecht, 2006:5).

- As been discussed previously in this chapter, the South African cancer data that is available is out of date (National Cancer Registry last issued in 1999) and inadequate.

In table 2.17 several of the reference sources of cancer data available in South Africa is summarized, and is also compared to data sources of America (USA) and to the global incidence of cancer:

Table 2.17 Comparison between different cancer statistics sources

SOUTH AFRICA								
Reference	Year (statistics)	Incidence/deaths	Sex	Rankings				
				1	2	3	4	5
Mqoqi <i>et al.</i> , 2004:17	1998-1999	Incidence	Females	Breast	Cervical	Colorectal	Oesophagus	Uterus
			Males	Prostate	Lung	Oesophagus	Colorectal	Bladder
Parkin <i>et al.</i> , 2004	2000	Incidence	Females	Cervical	Breast	Colorectal	Oesophagus	Kaposi sarcoma
			Males	Prostate	Lung	Oesophagus	Kaposi sarcoma	Oral cavity
South African Medical Research Council	2000	Deaths	<i>Overall</i>	Lung	Oesophagus	Cervical	Breast	Liver
AMERICA								
Brown <i>et al.</i> , 2001:93.	1997	Incidence	<i>Overall</i>	Prostate	Breast	Lung	Colorectal	Corpus and uterus
		Deaths		Prostate	Breast	Lung	Colorectal	Urinary bladder
American Cancer Society. <i>Cancer Facts and Figures</i> , 2006.	2006	Incidence	Females	Breast	Lung	Colorectal	Uterine corpus	Non-Hodgkin lymphoma
			Males	Prostate	Lung	Colorectal	Urinary bladder	Melanoma of the skin
		Deaths	Females	Lung	Breast	Colorectal	Pancreas	Ovary
			Males	Lung	Colorectal	Prostate	Pancreas	Leukaemia
Jemai <i>et al.</i> , 2007:47.	2007	Incidence	Females	Breast	Lung	Colorectal	Uterine corpus	Non-Hodgkin lymphoma
			Males	Prostate	Lung	Colorectal	Bladder	Non-Hodgkin lymphoma
		Deaths	Females	Lung	Breast	Colorectal	Pancreas	Ovary
			Males	Lung	Prostate	Colorectal	Pancreas	Leukaemia
GLOBAL RATES								
Mathers & Boschi-Pinto, 2000:3.	2000	Incidence	<i>Overall</i>	Lung	Stomach	Liver	Colorectal	Breast
Parkin <i>et al.</i> , 2005:78.	2002	Incidence	Females	Breast	Cervical	Colorectal	Lung	Stomach
			Males	Lung	Prostate	Stomach	Colorectal	Liver
		Deaths	Females	Breast	Lung	Cervical	Stomach	Colorectal
			Males	Lung	Stomach	Liver	Colorectal	Oesophagus
WHO, 2003:4	2003	Incidence	<i>Overall</i>	Lung	Breast	Colorectal	Stomach	Liver

2.7 MANAGED CARE AND CANCER

2.7.1 Definition of Managed Care

In a South African perspective, managed care can be seen as a diverse range of healthcare organisational approaches with three main purposes: controlling cost; improving access; and assuring higher levels of quality of care provided to those covered by medical schemes (Council of Medical Schemes, 2003:1)

According to the Medical Schemes Act, No 131 of 1998 (1998:1) managed care is “*a clinical and financial risk assessment and management of health care, with the view to facilitating appropriateness and cost-effectiveness of relevant health care services within the constraints of what is affordable, through the use of rule-based and clinical management-based programmes*”.

The Council for Medical Schemes endeavour to deliver managed health care provision and financing, which is:

- Affordable
- Accessible
- High quality care

These services should be focused on the emotional, physical, social and spiritual needs of patients while maintaining confidentiality and personal integrity (Council for Medical Schemes, 2003:19).

2.7.2 Types of managed health care plans

In the last decade, managed health care plans have evolved in such a manner that at present it is difficult to correctly distinguish between the various types (Wagner & Kongstvedt, 2007:20-22). When managed care started out, health maintenance organizations (HMOs), preferred provider organization (PPOs) and the conventional range of indemnity health insurance were distinct and evenly exclusive products and methods for providing health care coverage. Today it is sometimes difficult to distinguish between an insurance company or a managed health care organization (MCO). There are no definite features or borders between the different managed care organizations (MCOs) but each MCO has distinguishing features that sets it apart from the rest (Wagner & Kongstvedt, 2007:20-22).

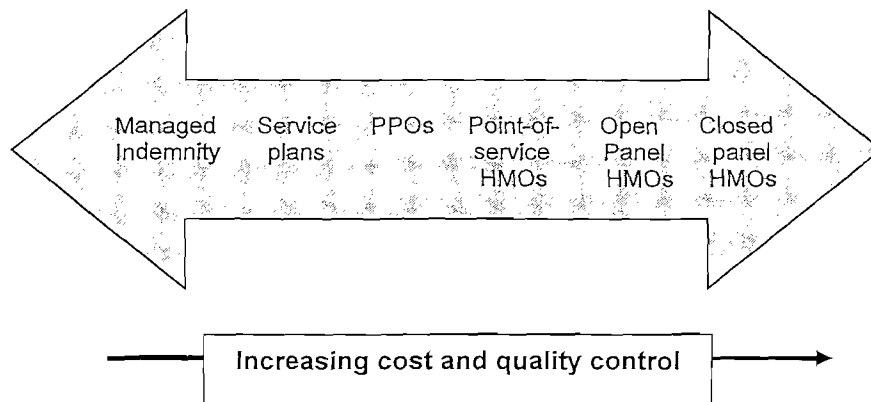


Figure 2.11 Continuum of managed care (Wagner & Kongstvedt, 2007:22)

2.7.2.1 Indemnity insurance

- Indemnity health insurance indemnifies the beneficiary from financial costs associated with health care.
- Indemnity insurance is relatively rare nowadays because of rising health care costs.
- Different managed care approaches is applied when indemnity insurance is used (Wagner & Kongstvedt, 2007:23).
- Indemnity insurance allows the beneficiary to choose any physician and hospital nationwide, while other plans such as preferred provider organizations (PPOs) or point-of-service plans (POS) provide a list of network physicians and hospitals for their members (Wright, 2008:1).

2.7.2.2 Service plans

- Service plans contracts directly with providers (hospitals, doctors etc.)
- The contract of the provider stipulates that the plan will pay them directly, and they may only bill the patient (member) for co-insurance, co-payments, or deductibles.
- As long as a member (beneficiary) receives services from a contracted provider, the provider cannot bill the patient for charges denied by the plan.
- The plan determines the maximum fee that will be paid for all procedures/services and the appropriate payments to hospitals.

- Service Plans also came under fire because of rising health costs.
- Service Plans often form part of another offering (e.g. Preferred Provider Organisations) (Wagner & Kongstvedt, 2007:23).

2.7.2.3 Preferred provider organisations (PPOs)

Preferred Provider Organisations can be defined and explained by the following features:

- Provider network
 - PPOs contracts with selected providers in a region to supply health services for covered individuals.
 - Most PPOs contract directly with hospitals, physicians, and other diagnostic facilities
 - The reason for the selection of specific providers varies between their cost efficiency, community reputation or scope of services.
- Negotiated payment rates
 - PPOs usually simply inform the physician or professional provider of what payment rates will be. The physician or provider can agree to these rates or not agree in which case they do not become a PPO provider. Negotiating payment rates sometimes take place, but it is not common.
 - PPOs endeavour to provide hospitals with payment rates that include some forms of discount. This includes payments based on diagnosis-related groups, fixed fee schedules and other charges.
 - Bundled pricing arrangements for certain services are also used in some PPOs. Examples of this are normal delivery, open-heart surgery and some types of oncology.
- Utilisation management
 - Implementing utilisation management programmes sometimes controls utilisation and cost of health services provided by PPOs.
 - These programmes are used to supervise the use of health service provided and to manage the cost thereof (Wagner & Kongstvedt, 2007:24-5).

➤ Consumer choice

- Beneficiaries are allowed to use non-PPO providers when they need health services. When using a non-PPO provider, higher levels of co-insurance or deductibles apply to the services provided (Wagner & Kongstvedt, 2007:24-5).

2.7.2.4 Exclusive provider organizations (EPOs)

- Exclusive Provider Organisations (EPOs) is comparable to PPOs in their organisation and purpose.
- EPOs differ from PPOs because their beneficiaries are required to receive all their covered health care services from providers that is part of that specific EPO.
- Employers that is focused on cost saving chooses EPOs. This is not a popular choice because of the restrictions of this plan (Wagner & Kongstvedt, 2007:25).

2.7.2.5 Point-of-service plans (POS)

- The essence of Point-of-service plans is a combination of Health Maintenance Organisations with indemnity coverage or service plans. These plans were implemented mainly to provide care outside of the Health Maintenance Organisation.
- There are mainly two ways in which POS plans are executed:
 - Primary Care Preferred Provider Organizations
 - Point-of-Service Health Maintenance Organizations (Wagner & Kongstvedt, 2007:26)

2.7.2.6 Health maintenance organizations (HMOs)

- HMOs are responsible for the financing and delivery of a broad range of wide-ranging health services to registered people.
- HMOs can be seen as a combination of a health insurer and a health care delivery system.
- Thus, HMOs are responsible to ensure access to health care services and the provision of quality and appropriate health services to their members.
- There are five commonly recognized models of HMOs:
 - Staff model
 - Group Model
 - Network Model
 - Independent (individual) Practice Association Model
 - Direct Contract Model (Wagner & Kongstvedt, 2007:28-32).

2.7.2.7 Self-insured and Experience-rated health maintenance

Self-insured benefit option - The HMO covers administrative services and profit as well as variable payments. These payments are based on the real or acquired expenses made by the HMO for health services. The HMO receives a fixed monthly payment from the employer involved for the service they provide. At the end of a specific period, there is a settlement process where either the HMO makes a payment to the employer or the employer to the HMO (Wagner & Kongstvedt, 2007:33).

Experience-rated benefit option - As with traditional premium-based plans, the HMO receives monthly premium payments. There is also a settlement period where the employer receives a portion (or all) of the actual cost of its company/group to determine the final premium rate. The variations in payments and possible refunds are calculated and then paid to either the HMO or the employer (Wagner & Kongstvedt, 2007:34).

2.7.3 Oncology managed health care organisation

The South African Oncology Consortium (SAOC) is a registered managed health care organisation. This company was established with the objective of assisting in cost-effective and appropriate oncology treatment in South Africa (SAOC, 2007).

The SAOC developed oncology treatment guidelines, which are used by many medical schemes in South Africa. These guidelines include chemotherapy and radiation treatment regimens, which is customized and adjusted to meet each individual's financial situation and medical needs (SAOC, 2007). These tiered oncology treatment guidelines is divided into three tiers:

- Tier 1 - This is the equivalent of the Prescribed Minimum Benefits (PMB).
- Tier 2 - This provides the standard of care.
- Tier 3 - Referral Tier (peer review).

The SAOC includes 140 participating oncologists and is represented in every oncology centre in South Africa (SAOC, 2007). Members of professional associations such as oncologists and medical staff represent this company:

- The South African Society of Radiation and Clinical Oncologists (SASCRO)
- The South African Society of Medical Oncologists (SASMO)
- The South African Society of Haematologists (SASH)

The set of treatment guidelines as well as the strict application of participation criteria for SAOC members ensure that the standard of cancer care in the private oncology sector of South Africa compares with the best international standards (SAOC, 2007).

2.8 MEDICAL SCHEMES IN SOUTH AFRICA

In 2008, there were 121 registered medical schemes in South Africa of which 38 was "open" medical schemes while the remaining 83 was "restricted" medical schemes (Council of Medical Schemes, 2008a). An open medical scheme is accessible to all members of the public while a restricted/closed medical scheme is limited to employees, a specific profession, association or union (Selfmed, 2008).

A list of the registered open medical schemes in South Africa is presented in table 2.18.

**Table 2.18 Registered open medical schemes in South Africa
(Council of Medical Schemes, 2008a)**

SCHEME NAME	YEAR REGISTERED
Bestmed Medical Scheme	1971
Bonitas Medical Fund	1982
Cape Medical Plan	1971
Community Medical Aid Scheme (Commed)	1995
Compcare Wellness Medical Scheme	1978
Discovery Health Medical Scheme	1971
Fedhealth Medical Scheme	1969
Fishing industry Medical Scheme (Fish-Med)	1969
Gen-Health Medical Scheme	1996
Genesis Medical Scheme	1995
Good Hope Medical Aid Society	1976
Hosmed Medical Aid Scheme	1988
Humanity Medical Scheme	1995
Ingwe Health Plan	1998
Keyhealth	1968
Liberty health Medical Scheme	1998
Medicover	1994
Medihelp	1969
Medimed Medical Scheme	1980
Medshield Medical Scheme	1968
Momentum Health	1971
National Independent Medical Aid Society (NIMAS)	1971
Openplan Medical Scheme	1996
Oxygen Medical Scheme	1971
Pathfinder Medical scheme	2001
Pharos Medical Plan	1994
Pro Sano Medical Scheme	1976
Protea Medical Aid Society	1969
Purehealth Medical Scheme	1969
Renaissance Health Medical Scheme	2001
Resolution Health Medical Scheme	1998
Selfmed Medical Scheme	1974
Sizwe Medical Fund	1978
Spectramed	1971
Suremed Health	1976
Telemed	1970
Thebemed	2002
Topmed Medical Scheme	1972

2.8.1 Prescribed minimum benefits

Prescribed Minimum Benefits (PMB) was developed to ensure all medical scheme members access to certain minimum health services. PMB is a defined set of benefits that ensure every medical scheme member of continuous care to improve their health and well-being and affordable healthcare, regardless of the medical scheme and benefit option they have selected (Council for Medical Schemes, 2008b).

According to the Council for Medical Schemes (2008b), PMB ensures that medical schemes covers the costs related to the diagnosis, treatment and care of:

- **Any emergency medical condition**, which is indicated by the sudden and, at the time, unexpected onset of a health condition that requires immediate medical treatment and/or an operation.
- **A limited set of 270 medical conditions** (defined in Annexure A of the Medical Scheme Act 131 of 1998)
- **25 chronic conditions** (defined in the Chronic Disease List).

The 270 limited set of conditions listed in the Prescribed Minimum Benefits (PMB) is provided in Annexure A of the Medical Scheme Act 131 of 1998 (South Africa, 1998). These conditions can be divided into 15 broad categories:

- Brain and nervous system
- Eye
- Ear, nose, mouth and throat
- Respiratory system
- Heart and vasculature (blood vessels)
- Gastro-intestinal system
- Liver, pancreas and spleen
- Musculoskeletal system (muscles and bones); Trauma NOS
- Skin and breast
- Endocrine, metabolic and nutritional
- Urinary and male genital system
- Female reproductive system

- Pregnancy and childbirth
- Haematological, infectious and miscellaneous systemic conditions
- Mental illness

The different conditions are divided under these 15 categories and further divided into diagnosis and treatment pairs, for example:

CODE: 950A

DIAGNOSIS: Benign and malignant brain tumours, treatable.

TREATMENT: Medical and surgical management, which includes radiation therapy.

The chronic disease list (CDL) of South Africa specifies 25 chronic conditions. CDL conditions have minimum standards for treatment and these must be covered by medical schemes. All doctor consultations and tests related to the condition must also be covered by medical schemes (Council of Medical Schemes, 2008b). Cancer is not included on this chronic disease list.

The fully descriptive list of prescribed minimum benefits is presented in the Regulations to the Medical Scheme Act Annexure A (South Africa, 1998).

2.8.2 Cancer and medical schemes

In this section the oncology treatment programmes and management of three registered medical schemes in South Africa will be discussed. This discussion is only for example purposes and not necessarily representative of all the oncology treatment options available in South Africa.

2.8.2.1 Discovery Health medical scheme

The following information was obtained from the official website for Discovery Health (www.discovery.co.za).

- Discovery Health has an oncology programme for all members who have been diagnosed with cancer.
- The programme includes approval for treatment, prioritised payment for related claims, hospital authorisations for cancer-related admissions and counselling

- Discovery Health will only pay for medicine (and treatments) if it is registered with the South African Medicines Control Council.
- The designated service provider for oncology is any specialist who is registered with the South African Oncology Consortium. Discovery Health's guidelines for cancer treatment are based on those of the South African Oncology Consortium – ensuring that members with cancer receive the most appropriate treatment.
- Funding for biological medicines - The Executive and Comprehensive plans, available at Discovery Health, have access to specific high cost speciality medicine through a clearly defined medicine benefit. This is called the Speciality Medication Benefit and this benefit covers certain medicine:

- Avastin®	- Alimta®
- Herceptin®	- Zevalin®
- Velcade®	- Mylotarg®

The two plans covering these high cost speciality medicine has different payment details:

- Executive Plan: Up to an annual limit of R400 000 (member co-payment/levy of 20%).
- Comprehensive Plan: Up to an annual limit of R200 000 (member co-payment/levy of 20%).
- In 2006, a number of breast cancer patients sued Discovery Health because the medical scheme refused pay for recommended Herceptin® treatment, because of the high cost of this cancer drug (Macharia, 2006). The case was settled in March 2006 and the treatment guidelines, issued by the South African Oncology Consortium, for the provision of Herceptin® by Discovery (Kahn, 2006) is presented below.

The treatment guidelines for Herceptin®:

- The member needs to meet specific clinical entry criteria and a positive fluorescence in situ hybridization (FISH) analysis.
- Members with early stage breast cancer (adjuvant treatment) can be funded for these regimens, as presented in table 2.19.

Table 2.19 Discovery Health regimen options for early breast cancer treatment (Discovery Health medical Scheme, 2008)

REGIMEN	PLANS	FUNDING POLICY
FinHer (Finland Herceptin) <i>9 week treatment</i>	All Plan types except KeyCare	Fund in full as per the FinHer 9 week trail
HerA (Herceptin Adjuvant) <i>12 month treatment</i>	Only for Executive and Comprehensive Plans	Fund through the Speciality Medicine Benefit – 80% of the costs up to the annual limit as per the 12 month Hera study

- Treatment of metastatic breast cancer with Herceptin® will be reviewed by Discovery Health and approved in line with the clinical protocols for members (all plans except KeyCare).
- There are 13 different benefit option/scheme options available from Discovery Health. These plans are divided into lower income plans, hospital cover plans, hospital cover and day-to-day benefits and top end cover plans. The comprehensive and executive plan options fall under the top end cover plans.

2.8.2.2 Liberty Health medical scheme

The following information was obtained from the official website for Liberty Health (www.liberty.co.za).

- Liberty Health Medical Scheme has an Oncology Disease Management programme for all members who have been diagnosed with cancer as well as extensive oncology benefits.
- Access by members to the oncology benefit is authorised by Liberty Health's Oncology Disease Management team.
- This team consists of a number of health care professionals who work with the treating doctor. This ensures that the treatment provided is cost-effective and clinically appropriate.

- The Oncology Disease Management team further relies on:
 - A number of oncologists and haematologists from the private, public and academic sector.
 - Cancer guidelines and protocols, which are frequently updated with new treatments and products.
- There are 8 different scheme options available from Liberty Health. These are Platinum Complete, Gold Complete, Platinum Plus, Gold Plus, Platinum Focus, Gold Focus, Silver Corporate Network, and Silver Focus.
- All these benefit options offer oncology benefits such as chemotherapy, radiotherapy, consultations, pathology, surgery and hospitalisation etc.

2.8.2.3 Medihelp medical scheme

The following information was obtained from the official website for Medihelp medical Scheme (www.medihelp.co.za).

- There are 6 different scheme options available from Medihelp Medical Scheme. These are Medihelp Plus, Dimention elite, Dimention Prime 1, 2 and 3 and Necessé.
- Five of Medihelp Medical scheme's benefit options offer oncology benefits. These benefit options are Medihelp Plus, Dimention Elite and Dimention Prime 1, 2 and 3.
- The preferred provider of oncology services (cancer treatment) for Medihelp, must be any specialist who is registered with the South African Oncology Consortium (SAOC).
- All oncology treatments are pre-registered and pre-authorised by Medihelp.
- Every benefit option available from Medihelp offers a different cancer management programme.

2.9 PHARMACOECONOMICS

2.9.1 Objectives of pharmacoeconomic studies

Pharmacoeconomics seen in its simplest means is basically the improvement of efficiency in the health care system (Larson, 2001:1). Efficiency can be defined as using resources (inputs) in a way that generates the greatest possible benefit (output). A system that is inefficient is not using the available resources to the greatest benefit (output) possible (Larson, 2001:1). The essence of pharmacoeconomics is that society, especially modern society, seeks to maximize the total aggregate health benefits gained, no matter what level of resources is used (Weinstein & Stason, 1977:717). The objective of economic evaluations is to ensure that available resources are used in the best possible way to generate the best benefit for the decision-making jurisdiction involved (Larson, 2001:1).

In cancer management, pharmacoeconomics plays a major role in determining the most appropriate pharmacotherapy for cancer patients. Pharmacoeconomic studies prove to be of value at every stage of cancer care – this includes screening, prevention, treatment, complications, palliation and end-of-life care (Goldspiel, 2000).

It is also vital to know that the pharmacoeconomics of cancer differs somewhat from the economic studies performed on other diseases. Cancer pharmacoeconomics must be more focused on the quality-of-life of the cancer patients and not just the analysis of different drugs and the costs involved (Amber, 2000:1204).

2.9.2 Pharmacoeconomics defined

Pharmacoeconomics is the identification, measurement and comparison of the costs and consequences of health care products and services (Bootman *et al.*, 1991:4). The costs can be seen as the resources consumed to perform an activity or implement a decision, and consequences being the outcomes, positive or negative, of that action or decision (Larson, 2001:4).

Costs can thus be defined as a specific therapy's overall effect on health care resources. These costs include (Larson, 2001:4):

- Resources used in producing the therapy itself, this includes the drug product, the supplies and personnel time consumed in preparation, administration and monitoring.
- Health care resources used in treating the side effects of the therapy.

- If an illness is prevented by therapy, the avoided costs (resources saved).
- If a diagnostic or referral process is involved, the costs that result from information obtained (e.g. information or recommendation from a pharmacist) are included.
- If life is extended by the therapy, the costs of health care services consumed during the additional years of life should be included.

Consequences/outcomes of a health decision can be expressed/studied in two ways:

- Effectiveness: Refers to the objective of the therapy or service. It is usually measured in “years of life saved” (i.e. the number of lives saved multiplied by the average remaining life expectancy of the patients). A clinical indicator can also be used as the measure of effectiveness, if it includes all the important outcomes.
- Utility: Adjusts length of life for its quality. Utility values are preferences for health states, ranging from 0 (death) to 1 (normal health). When utility is multiplied by years of life, the result is quality-adjusted life-years, QALYs (Larson, 2001:4).

Pharmacoeconomics can thus be described as a social science concerned with the impact of pharmaceutical products and services on individuals, health systems and society, as well as the description and analysis of the costs thereof (Wertheimer & Chaney, 2003).

2.9.3 Pharmacoeconomic methodologies

The main pharmacoeconomic methodologies will be discussed briefly, with emphasis on the analysis of cancer and cancer therapy.

2.9.3.1 Cost-Benefit Analysis (CBA)

A cost-benefit analysis is a clinical economic evaluation of the outcomes from a programme or intervention. The outcomes of the intervention or programme are measured by net benefits (net benefits = total benefits – total cost) or benefits-to-cost ratio (BCR = total benefits/total cost) (Carriere & Huang, 2001:21). The resources (costs) and the outcomes (benefits) of a cost-benefit analysis must be valued in the same units of lives (Kitz, 1991:103).

For example, the outcome/benefit of a specific cancer therapy may be the lives that are saved by that therapy. Then the cost/resource of that analysis is effectively the value (monetary) attached to those lives (Kitz, 1991:103). It is very difficult to place a monetary value on intangible outcomes of health care and in particular the value of a life. Therefore, true cost-benefit analysis is not that easy to perform (Earle *et al.*, 1998:477).

There are two basic approaches for cost-benefit analysis, namely ratio approach and the net benefit approach.

- Ratio approach - The amount of benefits (outcomes) that can be realized per unit expenditure on a technology vs. a comparator.
- Net benefits approach - The absolute amount of money saved or lost due to a use of a technology vs. a comparator (United States National Library of Medicine, 2008).

The choice of the approach can affect findings of the analysis and depends on numerous factors:

- Must costs be limited to a certain level?
- Should the absolute level of benefits be maximized?
- Can the cost/benefit ratio be minimized without taking into account the absolute level of costs? (United States National Library of Medicine, 2008).

Basic formula for Cost-Benefit analysis (CB)

(United States National Library of Medicine, 2008)

1. CB, Ratio Approach:

$$\text{Cost benefit Ratio} = \frac{\$Cost_{(int)} - \$Cost_{(comp)}}{\$Benefit_{(int)} - \$Benefit_{(comp)}}$$

For example: "Cost-benefit ratio of 1.5"

2. CB, Net Benefit Approach:

$$\text{CB Net} = (\$ \text{Cost}_{(\text{Int})} - \$ \text{Cost}_{(\text{Comp})}) - (\$ \text{Benefit}_{(\text{Int})} - \$ \text{Benefit}_{(\text{Comp})})$$

For example: "Net cost of \$5 000"

****Int: Intervention; Comp: Comparator**

There have been several cost benefit studies done on cancer in the past. In 1999, a cost-benefit analysis of Interferon Alfa-2b in treatment of hairy cell leukaemia was done and published in the Journal of the National Cancer Institute (Ozer *et al.*, 1999). A randomized prospective cost-benefit analysis of a follow-up program in patients with breast cancer was done in 2007 and published in The Breast Journal (Oltra *et al.*, 2007:571-574). Another study was done to compare the cost-benefit of capecitabine versus 5-fluorouracil/leucovorin in the treatment of colorectal cancer in the Netherlands (Jansman *et al.*, 2004:579-589).

2.9.3.2 Cost-Effectiveness analysis (CEA)

Cost-effectiveness analysis is a specific type of economic analysis used to evaluate health care interventions quantitatively and objectively, based on a defined model (Centre for Prevention and Health Services, 2004:2). It is an analysis that assesses both the costs and the effects of a health intervention or strategy. The outcomes are measured in units of outcomes experienced, such as cases of disease prevented or years of life gained, while the costs or resources are measured in monetary units, as with a cost-benefit analysis (Health Economics, 2008).

Basic formula for Cost-Effectiveness analysis (CB)

(United States National Library of Medicine, 2008)

$$\text{Cost effectiveness Ratio} = \frac{\$ \text{Cost}_{(\text{Int})} - \$ \text{Cost}_{(\text{Comp})}}{\$ \text{Effect}_{(\text{Int})} - \$ \text{Effect}_{(\text{Comp})}}$$

For example: "\$45,000 per life-year saved" or "\$10 000 per lung cancer case averted"

Int: Intervention; Comp: Comparator

Several cost-effectiveness studies have been conducted on many types of cancer. Examples of such studies include a cost-effectiveness study on colorectal cancer screening published in the *Annals of Internal Medicine* (Pignone *et al.*, 2002:96-104). Another cost effectiveness study published in 2007 analysed the cost-effectiveness of switching to exemestane versus continuing with tamoxifen as adjuvant therapy for postmenopausal women with primary breast cancer (Risebrough *et al.*, 2007:499-508).

The differences between CEA and CBA are summarized in table 2.20 and the difference in the scope of the studies is illustrated in figure 2.12.

Table 2.20 A comparison between cost-effectiveness analysis and cost-benefit analysis (Mason, 2004:1).

Cost-effectiveness analysis	Cost-benefit analysis
Calculates the direct financial cost of reaching specific outcome/output levels and requires one other alternative for comparison.	Compares all benefits to all costs and doesn't need a comparison with another alternative. If the benefit/cost ratio exceeds 1, the program is socially valuable.
Usually prospective	Usually retrospective
Takes on a macro (societal) view	Takes on a micro view of programme activities, outputs, or outcomes.

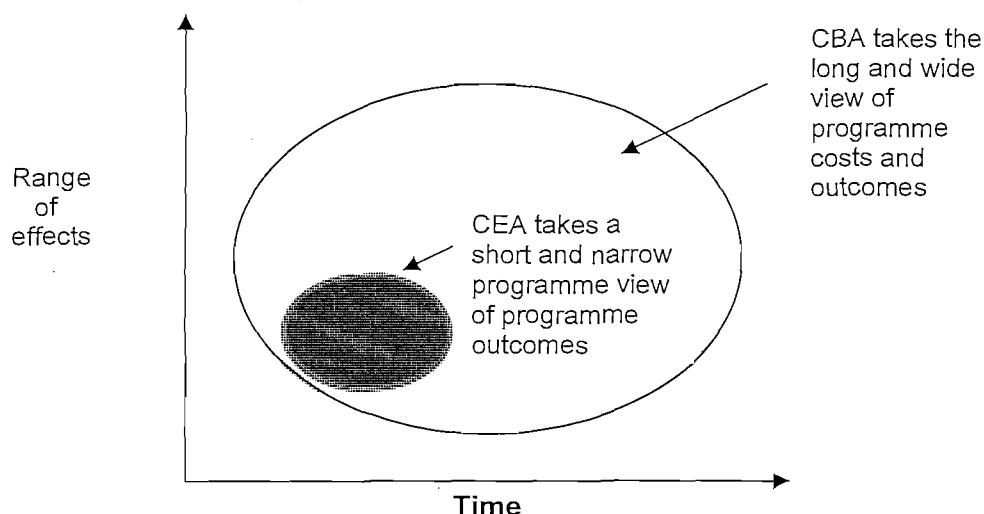


Figure 2.12 The scopes of cost-effectiveness analysis and cost-benefit analysis (Mason, 2004:2)

2.9.3.3 Cost-Minimisation Analysis (CMA)

Achieving to best possible outcomes that is both economical and effective is the main aim of all pharmacoeconomic analysis (Carriere & Huang, 2001:24). Cost-minimisation analysis (CMA) is used to compare different interventions and identify the least costly intervention. All the possible alternatives must have equal outcomes or consequences. A CMA is very similar to a CEA and also a CBA. The procedure followed in a CMA is comparable to the procedure of a CBA. CMA can also be regarded as a CEA where the outcomes from the interventions are the same (Carriere & Huang, 2001:24).

A cost-minimisation study was performed to analyse three regimens of chemotherapy (docetaxel-cisplatin; paclitaxel-cisplatin; paclitaxel-carboplatin) for advanced non-small-cell lung cancer. The results were published in 2002 in the journal *Lung Cancer* (Rubio-Terres *et al.*, 2002:81-89). Berges and co-workers (2007:135-146) performed another cost-minimisation study to compare different preparations of leuprolide acetate in the management of advanced prostate cancer.

In section 4.4.4 a cost-minimisation analysis was done on Tamoxifen to determine the potential cost saving when Nolvadex D 20mg tablets (original cancer drug) was

substituted by the generic cancer drug, Kessar 20mg tablets or Neophedan 20mg tablets.

2.9.3.4. Cost-Utility Analysis (CUA)

Every health care intervention may have some effect on the patient. The patient can either live longer (more life years) because of the intervention or live a healthier life (better quality). Quality adjusted life years can thus be defined as finding out how much quantity of life the patient is willing to give up in order to live a higher quality of life. Cost-Utility analysis is used to measure this effect, with the outcomes expressed in QALY (Brent, 2003:9).

Basic formula for Cost-Utility Analysis (CUA)

(United States National Library of Medicine, 2008)

$$\text{Cost Utility Ratio} = \frac{\$Cost_{(int)} - \$Cost_{(comparator)}}{\$Utile_{(intervention)} - \$Utile_{(comparator)}}$$

For example: "\$45 000 per life-year saved" or "\$10 000 per lung cancer case averted"

In the European Respiratory Journal, Dooks and co-workers (2006:895-901) published a cost-utility analysis of chemotherapy in symptomatic advanced non-small-cell lung cancer. In the study the single agent treatment with gemcitabine was compared with cisplatin-based chemotherapy. Outcomes such as symptom improvement and clinical benefits were important in this study because patients receiving treatment for advanced no-small-cell lung cancer generally has a short life expectancy. Although the least expensive treatment was the cisplatin-vindesine combination, gemcitabine proofed to be of more clinical benefit with an acceptable incremental cost-utility ratio (Dooks *et al.*, 2006:895-901). A cost-utility analysis was also performed on taxane therapy in patients with anthracycline-resistant metastatic breast cancer (Yee, 1997:11-15).

2.9.3.5 Cost-of-illness analysis (COI)

Many major diseases, including cancer, use the COI methodology to measure the burden of the specific disease (Brown *et al.*, 2001:98). Cost of illness is the losses, economic and otherwise, which originates in the disease. A cost of illness study estimates the overall economic burden of a disease such as cancer, and not just the treatment-related costs (Molinier *et al.*, 2006:651).

Steps in a cost of illness study include defining the disease studied, deciding on an epidemiological approach, the type of costs that will be assessed and the perspective of the study (Molinier *et al.*, 2006:652).

Costs included in a cost of illness study can be divided into three main categories (Brown & Fintor, 1995: 69):

- **Direct costs**

The expenditures for all medical procedures and services associated with treatment and care for the disease (Brown *et al.*, 2001:98).

- **Indirect costs/morbidity cost**

It is the cost of work time lost and loss of income because of disability of absence (Brown *et al.*, 2001:98). This includes costs incurred by family members or friends because of time spent caring for the patient, etc. (Brown & Fintor, 1995:70).

- **Psychosocial costs/ intangible costs**

These are the costs that are not reflected in the direct or indirect costs. This includes loss of a body part, loss of speech, impending death, pain and grief. Patients may also experience financial difficulties because of the illness. This combination of economic strain and psychological problems can be very devastating (Brown & Fintor, 1995:70).

According to Brown *et al.* (2001:98) there is another costly category in cancer. This is the mortality cost of the illness, which is measured as the lost income due to premature death.

Table 2.21 Cost of illness from cancer for the USA in 1990 (Brown *et al.*, 2001:99)

Type of cost	Amount (\$ millions)	Percent
Total	92, 126	100.00
Direct	27,458	28.60
Hospital care	17,935	
Physicians' services	6,613	
Nursing home services	1,333	
Drugs	1,068	
Other	509	
Morbidity	9,895	10.30
Mortality	58,773	61.10

The total cost of cancer in 1990 in the United States of America amounted to \$92 126 million dollars. Of these \$27 458 million are direct costs, which includes hospital care (\$17 935 million), physician services (\$6 613 million), nursing home services (\$1 333 million), cost of drugs (1 068 million) and other direct costs (509 million). The morbidity cost of cancer for 1990 in the USA was \$9 895 million dollars – this includes time lost at work for the patient as well as his family and loss of income as a result of the illness (Brown *et al.*, 2001:99). As seen in table 2.21, the loss of income due to premature death (mortality) as a result of cancer amounted to \$58 773 million dollars in 1990, which was 61.10% of all costs associated with cancer.

2.10 ECONOMICS OF CANCER

There is a great absence in the literature on the economics of cancer, although it urgently needs attention from the mainstream health economics field (Bosanquet & Sikora, 2006a:1).

Reasons for this include (Bosanquet & Sikora, 2006a:1-3):

- Long-term care and extended treatment is on the increase because of longer survival of patients. This increases the cost of cancer care.
- Cost of cancer therapies has risen dramatically with the constant entering of new and expensive drugs in chemotherapy and also in radiotherapy. In America, the cost of cancer therapies is 10 times more at present than it was in 1991.
- Cancer services are being renovated. The focus is better communication with patients, longer-term care programmes, more targeted therapies, more effective infrastructure and better staff skills.

- Diagnosing cancer at an early stage has saved many lives. There is a great need for development of effective strategies to detect more cancers at an early stage.

2.10.1 Cost of cancer treatment

The introduction of newer cancer drugs such as trastuzumab (Herceptin®) and oxaliplatin (Eloxatin®) is causing a steep upward trend in cost of cancer care (Niezen *et al.*, 2006:2887). The remarkable progress made in terms of the diagnosing, treating and screening of patients has led to this increase in expenditure of cancer (Meropol & Schulman, 2007:180).

In the cancer trends progress report of the National Cancer Institute of America (2007a:1), it is reported that the overall cost of treating cancer in America has increased by 75 percent between 1995 and 2004, and this may increase even faster in the future. Reasons for this is aging populations, greater frequency from better treatments and changes in cancer care – which in turn causes the number of cancer cases to increase (Bosanquet & Sikora, 2004:568).

As part of a Dutch policy to control the cost of hospital drugs, a list of expensive drugs was compiled. According to Niezen *et al.* (2006:2890) the costs of these 'expensive drugs' increased with 400% since 1999. In table 2.22 the drugs included in this Regulation Expensive Medicine are listed. Drugs of which the prognosis showed that it will consume at least 0,5% of the total pharmaceutical expenses of hospitals were included in the list (Niezen *et al.*, 2006:2890).

**Table 2.22 Drugs included on the regulation expensive medicines, March 2005
(Niezen *et al.*, 2006: 2890)**

*Docetaxel	Trastuzumab
Botulinetoxine	Irinotecan
Verteporfin	Immunoglobine IV
Doxorubicine liposomal	Paclitaxel
Vinorelbine	Infliximab
Bevacizumab	Rituximab
Pemetrexed	Oxaliplatin
Bortezomib	Gemcitabine

*Cancer treatment drugs in bold

2.10.2 Economic modelling of cancer care

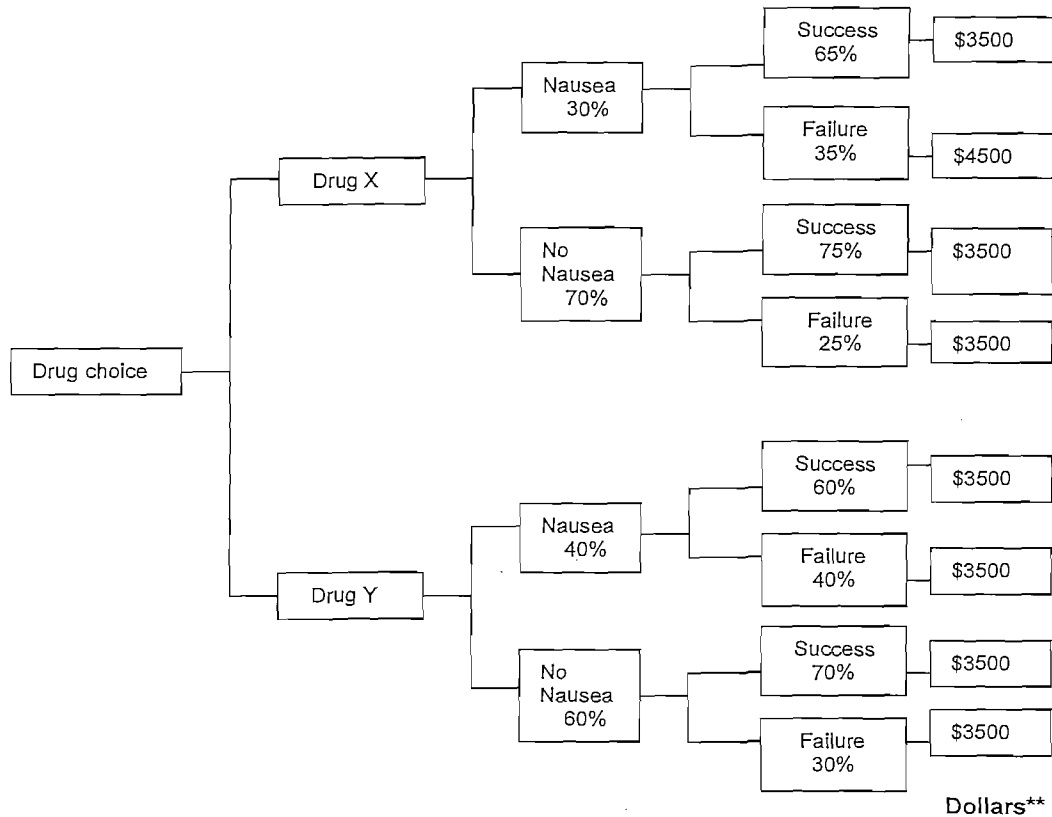
Economic modelling uses mathematical techniques and the other available information to evaluate different health care options such as different treatment regimens for cancer (Fourthhurdle, 2008). When the conditions, circumstances and consequences of a treatment decision are uncertain, economic modelling is used to describe and analyse these elements (Rheeder & Gordon, 2006:8).

Economic modelling brings together all available data on all the relevant factors such as effectiveness, costs, outcomes and alternative courses of action (Phillips, 2008:8). These models provide the framework for making health care decisions and bringing different data together. The main goal is to exclude irrelevant details and preserving the important features of the treatment that is being examined (Lidgren, 2007:16).

Two types of economic modelling, decision tree models and Markov models, will now be discussed.

2.10.2.1 Decision tree models

When a treatment has uncertain outcomes and decisions needs to be made, a decision tree can be used. A decision tree defines the available options for a certain situation and the possible outcomes are established. The optimal approach is identified by assigning values and probabilities to each intervention and outcome and calculating the value of each of these outcomes (Lidgren, 2007:17). An example of a decision tree for two cancer drugs is shown in figure 2.13.



** Dollar amounts represent the total cost of treatment, including drug cost, for the particular arm of the decision tree.

Figure 2.13 Decision tree for two cancer drugs (Rheeder & Gordon, 2006:9)

In figure 2.13 two chemotherapy drugs are presented, Drug X and Drug Y. Both of these drugs are effective in treating the given cancer. From the results in figure 2.13 the following can be seen:

- Drug X had a lower incidence of nausea than Drug Y; (30% vs. 40%)
- Drug X was somewhat more effective (higher success rate);
- BUT Drug X was also more expensive than Drug Y.

According to Rheeder & Gordon (2006:9), when the average cost was calculated, Drug X showed a lower average cost per patient treatment than Drug Y (\$3080 vs \$3124).

2.10.2.3 Markov models

Markov models are used in three situations:

- When a problem decision involves risk that is continuous over time.
- When the timing of events is important.
- When important events may happen more than once (Sonnenberg & Beck, 1993:322).

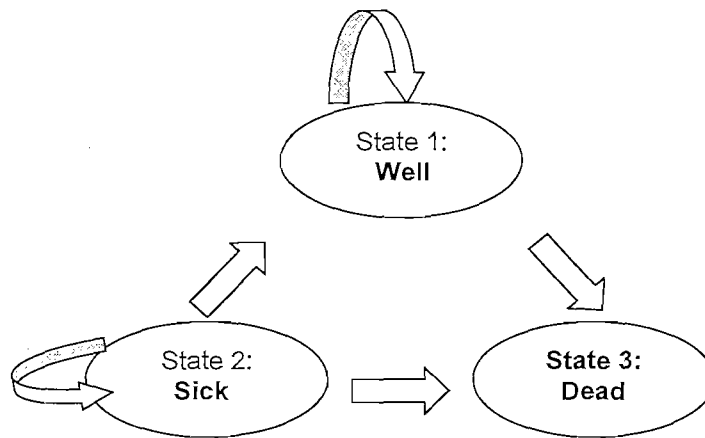


Figure 2.14 Markov model (Lidgren, 2007:17)

When a Markov model is used for a specific disease, such as cancer, the disease is divided into different states known as 'Markov states'. The different states form a Markov cycle with transition probabilities between the states. Movement between the states over a certain time period is possible. Long-term costs and outcomes associated with a disease and the particular intervention used can then be estimated (Briggs & Schulper, 1998:399). A simple Markov model is illustrated in figure 2.14.

Markov models are widely used in cancer studies. Examples of such studies include a study done on tumour progression in woman with a family history of breast cancer (Wu *et al.*, 2007:1-7) as well as a study estimating the costs and effectiveness of alternative strategies for cervical cancer screening (Maxwell *et al.*, 2002:740-748). In another study, a Markov model was also developed to determine the percentage of colorectal cancer cases, which are detected early or prevented due to screening (Haug & Brenner, 2005:422-428).

2.11 VALUE OF LIFE

It is very difficult to estimate the value of a person's life, because people attach importance to different abilities, services and belongings. Two methods to determine the value of a person's life will now be discussed (Brown & Fintor, 1995:71).

2.11.1 Human capital approach

The remaining lifetime earnings of the patient are estimated by using the age or gender specific average earnings and the expected productivity trends of that person (Brown & Fintor, 1995:71). Estimating the difference between the current age of the patient and the retirement age, determining the remaining working years, does this. The average income of the patient is then multiplied with the number of working years, which gives the remaining lifetime earnings of the involved patient (Brent, 2003:274). This approach is mainly focused on the economic productivity of the patient and places no value on human life or on any non-economical social relationships (Brown & Fintor, 1995:71).

2.11.2 Willingness-to-pay approach

The essence of the willingness-to-pay approach is that people differ in what they are willing to pay for something and what they will be willing to accept as compensation for not having something (Brent, 2003:300). Individuals are asked how much they would be willing to pay to avoid particular types of morbidity or risks of death (Brown & Fintor, 1995:71).

The willingness-to-pay approach is mostly used in cost-benefit analyses and is obtained mainly in two ways:

- Direct measurements: Patients are questioned about the amount they are willing to pay to reduce the risk of death or to improve quality of life. This indicates how much of other goods and services the patient is willing to give up (Gafni, 1991:1246).
- Indirect measurements: This method involves measurements such as wage-risk studies. This entails inferring from a person's behaviour what amount he/she is willing to pay for certain gains (Gafni, 1991:1246).

2.12 QUALITY OF LIFE

Quality of life can be defined and interpreted differently by all people on earth depending on their needs, goals and beliefs. The World Health Organisation (1997:1) defines quality of life as: “(an) individual’s perception of their position in life in the context of the culture and value system in which they live and in relation to their goals, expectations, standards and concerns. It is a broad-ranging concept affected in a complex way by the person’s physical health, psychological state, level of independence, social relationships, and their relationship to salient features in their environment.”

Quality of life (QOL) outcomes are difficult to measure and there is no universally appropriate QOL tool. The best ‘tool’ must be chosen for whatever aspect of life it is that needs to be measured (Brennan & Moynihan, 2005:38).

According to Brennan and Moynihan (2005:38-9) quality of life can be divided into seven different components:

- Physical concerns (pain and other symptoms)
- Functional ability (mobility, self-care, activity level, etc.)
- Family well-being
- Emotional well-being
- Treatment satisfaction
- Sexuality/intimacy (including body image)
- Social functioning

2.12.1 Relationship between the concepts of pharmacoeconomics and quality of life

When a patient receives treatment there are three different areas in which the outcomes of that specific therapy can be divided (Cramer & Spilker, 1998:10-1):

- **Clinical outcomes** - Usually measurable benefits such as changes in an individual patient’s signs and symptoms of the disease. The health outcomes in medicine are assessed under the subject of outcomes research.
- **Economic outcomes** - This entails the costs of the patient’s treatment. Factors playing a role are: who is paying for the treatment and what

limitations are being placed on the system because of economic factors. The health care costs are assessed under the subject of health economics.

- **Personal outcomes** - This is how the treatment affects the different areas and components of the specific patient's life. The patient assesses himself/herself in terms of his/her personal convictions and feelings.

The economics associated to quality of life are in many ways the same as the economic characteristics of most of the pharmacoeconomic methods, but also differs in many aspects. QOL economics can be seen as an independent division focusing on professional and work performance, but sometimes the direct costs and side effects must also be taken in account. Every patient's situation is different and therefore the overlap between pharmacoeconomics and quality of life assessments depends on the specific circumstances (Cramer & Spilker, 1998:11).

2.12.2 Health related quality of life assessment in cancer

Different instruments exist to determine, measure and assess the different aspects of the quality of life in cancer patients as well as other diseases.

2.12.2.1 The functional assessment of cancer therapy (FACT)

The functional assessment of cancer therapy (FACT) is a division of the FACIT (Functional Assessment of Chronic Illness Therapy) measurement system (Webster *et al.*, 2003:1). FACIT is a collection of health related quality of life (HRQOL) questionnaires aimed at chronic diseases such as cancer, HIV and multiple sclerosis. The FACT-G (Functional Assessment of Cancer Therapy – *General*) was the first questionnaire developed and is a 27-item compilation of general questions, which is divided into four primary QOL (quality of life) domains (Webster *et al.*, 2003:79):

- Physical well-being
- Social/Family well-being
- Emotional well-being
- Functional well-being

The FACT-G can be used for any tumour type but there is also subscales focusing on specific types of cancer. Each subscales has a unique name and acronym corresponding to the targeted issue, as seen in table 2.24 (FACIT, 2008).

Table 2.23 FACT Cancer specific measures (FACIT, 2008)

Acronym	Description
FACT – B	For patients with breast cancer
FACT – BI	For patients with bladder cancer
FACT – Br	For patients with brain cancer
FACT – C	For patients with colorectal cancer
FACT – CNS	For patients with cancer in the central nervous system
FACT – Cx	For patients with cancer of the cervix
FACT – E	For patients with oesophageal cancer
FACT – En	For patients with endometrial cancer
FACT – Ga	For patients with gastric cancer
FACT – H&N	For patients with head & neck cancer
FACT – Hep	For patients with hepatobiliary cancer (liver, bile duct & pancreas)
FACT – L	For patients with lung cancer
FACT – Leu	For patients with leukaemia
FACT – Lym	For patients with Lymphoma (NHL)
FACT – M	For patients with melanoma
FACT – O	For patients with ovarian cancer
FACT – P	For patients with prostate cancer
FACT – V	For patients with vulva cancer
Peds-FACT -BrS	Paediatric brain tumour survivors

2.12.2.2. The functional living index - cancer (FLIC)

The FLIC (Functional Living Index-Cancer) is a cancer-specific, functionally-orientated quality of life instrument (American Thoracic Society, 2007). This measurement instrument is used to evaluate all the areas that might be affected by the symptoms and treatment of cancer. It is a combination of many different questionnaires that is focused on one specific aspect of cancer and cancer treatment. The core of the Functional Living Index-Cancer is to measure the extent to which the normal function of a patient is affected by cancer and treatment thereof. The focus is thus not on the symptoms itself but if the symptoms disturbs normal living (Cramer & Spilker, 1998:11).

The FLIC is a 22-item questionnaire that is further divided into 5 categories (American Thoracic Society, 2007):

- Physical well-being and ability;
- Emotional state;
- Sociability;
- Family situation;
- Nausea (induced by cancer treatment).

2.12.2.3 European organisation for research on treatment for cancer

(EORTC).

The first questionnaire developed by the EORTC is called the EORTC Quality of Life Questionnaire-Core 36 (EORTC QLQ-36). This questionnaire was designed to be cancer specific, multidimensional, self-administrative and applicable across a range of cultural settings. This questionnaire has been adjusted to specific tumour sites and treatment modality of QOL dimension (European Organisation for Research and Treatment of Cancer, 2008).

TABLE 2.24 Different EORTC QOL questionnaires
(European organisation for research and treatment of cancer, 2008)

Acronym	Description
EORTC QLQ-LC13	Lung cancer
EORTC QLQ-BR23	Breast cancer
EORTC QLQ-H&N35	Head and Neck cancer
EORTC QLQ-OV28	Ovarian cancer
EORTC QLQ-OES18	Oesophageal cancer
EORTC QLQ-STO22	Gastric cancer
EORTC QLQ-MY20	Multiple Myeloma
EORTC QLQ-CX24	Cervical cancer

Two other questionnaires were also developed by the EORTC:

- Patient Satisfaction assessment form (EORTC IN-PATSAT32)
- A short form questionnaire for palliative care patients (EORTC QLQ-C15-PAL) (European Organization for Research and Treatment of Cancer, 2008).

2.12.2.4 Other quality of life (QOL) measurement instruments

There are numerous QOL measurement instruments available – some of these instruments are discussed below.

- **Schedule for the evaluation of individual quality of life (SEIQoL)**

SEIQoL is a 46-item interview questionnaire or self-administered questionnaire. It assesses the quality of life from an individual perspective in healthy or ill individuals. This questionnaire can be used in any disease including cancer (O'Boyle *et al.*, 2007).

- **Short form 36 (SF-36)**

The SF-36 is a 36-item multi-purpose, short-form health survey. It consists of an 8-scale profile concerned with functional health and wellbeing as well as psychometrical-based physical and mental health issues (Ware, 2003).

- **Life evaluation questionnaire (LEQ)**

The LEQ attempts to evaluate the patients' perspective when confronted with a disease such as cancer (Salmon *et al.*, 1996:755).

2.13 DRUG UTILISATION REVIEW

In this section an overview of drug utilisation review (DUR) will be given and the classification and types of DUR studies will be discussed briefly.

2.13.1 Definition of drug utilisation review (DUR)

In 1977 the WHO (2003:8) defined drug utilisation research as “the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences”. A drug utilisation review can also be defined as a qualitative and quantitative evaluation of prescription drug use, physician prescribing patterns, or patient drug utilisation to determine the appropriateness of the specific drug therapy (Wertheimer & Navarro, 1999:361).

According to Guo *et al.* (1995:1175), the key purpose of a drug utilisation study is reducing drug costs and controlling inappropriate prescribing. The WHO (2003:9) stated that the main aim of drug utilisation research is to facilitate the rationale use of drugs in every population. This can be done by prescribing well-documented drugs at an optimal dose with an affordable price, together with correct information about the drug given.

2.13.2 Classification of drug utilisation review

Drug utilisation research is classified as either a quantitative DUR review or a qualitative DUR review.

2.13.2.1 Quantitative drug utilisation review

In a quantitative drug utilisation study the data may be used to describe the current circumstances and the drug prescribing trends and drug usage in different levels of the health care system. The data used in this type of study is usually obtained from surveys or routinely collected data (WHO, 2003:20).

2.13.2.2 Qualitative drug utilisation review

In a qualitative study the appropriateness of drug utilisation are assessed through predetermined criteria. The quality, appropriateness and the medical necessity of the drugs prescribed can be compared (Lee & Bergman, 1994:380).

2.13.3 Types of drug utilisation studies

Drug utilisation reviews is done through either a prospective, retrospective or concurrent review process, which will be discussed below.

2.13.3.1 Retrospective drug utilisation studies

A retrospective DUR is performed following the dispensation of medicine and often after the patient has consumed the drugs under examination. One of the main aims of a retrospective DUR is to establish if there is any inappropriate or suboptimal drug use in order to prevent future costs and unfavourable outcomes. A retrospective DUR is of very little use for current patients but can be very valuable for future patients as well as for the person prescribing the drug (Fulda *et al.*, 2004:434).

Retrospective DUR is often used for analysing the use of high cost drugs like the new biological cancer drugs such as Herceptin®. According to Fulda *et al.* (2004:434) it is also very useful in comparing the use of classes of drugs or reviewing the lack of prescribing of particular classes of drugs to treat a given disease.

2.13.3.2 Prospective drug utilisation studies

Prospective DUR involves the evaluation of prescriptions before it is dispensed. This is done to identify problems such as drug-drug interventions, therapeutic duplication and other adverse effects of the prescribed drugs (Lyles *et al.*, 2001:75).

2.13.3.3 Concurrent drug utilisation studies

In a concurrent drug utilisation review the responsibility for review rests with the pharmacist and takes place during the period when patients and drug dispensers interact (Guo *et al.*, 1995:1175).

2.14 SUMMARY

Cancer is a devastating disease with a far-reaching effect that affects all people, rich or poor, educated or uneducated, black or white. According to Albrecht (2006:5) cancer is not getting enough attention or funding in South Africa. He also stated that the grade of cancer research in South Africa has reached a catastrophically low level and is in need of a major boost. Albrecht (2006:5) believes that this improvement will only come if people at all levels, from scientists to oncologists to the members of the public join together and support a proper cancer surveillance infrastructure and a Cancer Control Programme for South Africa.

New therapies that are being studied are exiting and life-saving developments for both patients and researchers. The cost associated with these therapies, or any cancer treatment is relatively high and therefore out of the reach for many cancer patients.

In this chapter cancer was defined and discussed with special reference to the situation of cancer internationally as well as in South Africa. The treatment of cancer was discussed as well as five common cancers in the private health care sector of South Africa.

This chapter also gave an overview of managed care, pharmacoeconomics and other aspects relating to cancer and treatment thereof. The importance of quality of life assessments was emphasized and also value of life issues such as methods of establishing willingness to pay was discussed briefly.

In chapter three the research objectives, study population, data source, database and data analysis of this empirical investigation will be discussed.

CHAPTER 3

Research methodology

3.1 INTRODUCTION

In this chapter the research objectives, study population, data source, database and data analysis of this empirical investigation will be discussed. The procedures followed in acquiring the relevant information and the subsequent analysis of the data will also be discussed.

3.2 DEFINITIONS

For the purpose of this study certain definitions were standardised:

- **Antineoplastic and immunomodulating agents:** All medication listed under the Anatomical Therapeutic Chemical classification code: L01 – L03 (refer to Appendix A). For the purpose of this study antineoplastic and immunomodulating agents are also referred to as:
 - ✓ cancer drugs *or*;
 - ✓ cancer medicine *or*;
 - ✓ cancer medicine items *or*;
 - ✓ cancer medicine treatment
- **Total population:** All the prescriptions or medicine items claimed through the database for the period 1 January 2005 to 31 December 2006. *Also referred to as total database.*
- **Total database:** See Total population
- **Study population:** All the cancer patient records used during this study, thus all prescriptions with one or more antineoplastic and immunomodulating agent(s). *Also referred to cancer database.*
- **Cancer database:** See Study population

- **Patient:** A person who received any medication on prescription or who have received pharmacist-initiated therapy during the period 1 January 2005 to 31 December 2006.
- **Cancer patient:** A person who received antineoplastic and/or immunomodulating medication on prescription during the period 1 January 2005 to 31 December 2006.
- **Prescription:** A physician's order for the preparation and administration of a drug or device for a patient. (Hospice Palliative Care Association SA, 2007).
All prescriptions used in this study may contain one or more medicine items.
- **Medicine item:** According to the Medicines and related substances Control Act (Act 101 of 1965) medicine items can be defined as “a substance intended for the use in the diagnosis, cure, mitigation, treatment, modification or prevention of disease, abnormal physical or mental state or the symptoms thereof in man”. For the purpose of this study, medicine items were used as a research instrument to measure and describe the prescribing patterns by means of the total number of medicine items claimed, as well as the average number of medicine items per prescription on both the total and cancer database.
- **Original medicine item (“O”):** Refer to section 3.8.3.3.
- **Generic medicine item (“Y”):** Refer to section 3.8.3.3.
- **No-generic medicine item (“N”):** Refer to section 3.8.3.3.

3.3 RESEARCH OBJECTIVES

The research objectives for this study are divided into general and specific objectives:

3.3.1 General objective

The general objective of this study was to investigate and review the drug prescribing patterns of antineoplastic and immunomodulating agents in a section of the private health care sector of South Africa by utilising a medicine claims database for a two-year period (2005 & 2006).

3.3.2 Specific research objectives

The research project consisted of two phases, the literature review and an empirical investigation.

3.3.2.1 Literature study

The specific objectives for this literature study were to:

- define cancer and put the disease in perspective, both globally and nationally;
- investigate the different cancer treatment approaches;
- describe different cancer types, in particular lung cancer, breast cancer, prostate cancer, colorectal cancer and lymphoma (Hodgkin's disease and non-Hodgkins lymphoma);
- define and describe the concepts: managed care, pharmacoeconomics and drug utilisation review;
- investigate the approach to cancer of some medical schemes in South Africa;
- determine the economics of cancer relative to treatment options; and
- investigate the methods used to evaluate and value the quality of life of cancer patients.

3.3.2.2 Empirical investigation

By using a medicine claims database in a section of the private health care sector of South Africa, the specific objectives for this empirical study were to:

- determine the prevalence, cost and usage patterns of antineoplastic and immunomodulating agents in comparison to medicine in general;
- analyse the prescribing patterns for the top twenty cancer medicine items according to highest total cost, highest average cost and highest prevalence
- determine the prevalence and cost associated with original, no-original and generic forms of cancer medicine items in the top twenty cancer medicine items according to highest total cost, highest average cost and highest prevalence;

- classification of cancer medicine items according to the different therapeutic, pharmacological and chemical subgroups;
- determine the prevalence and cost of cancer medicine items in the different therapeutic, pharmacological and chemical subgroups;
- determine the prevalence and cost of cancer agents associated with the different patient age groups;
- determine the prevalence and cost of cancer agents according to the gender of the patient;
- determine and analyse the prevalence and total cost of selected regimen therapy prescribed for five common types of cancer in the private health care sector of South Africa.

3.4 RESEARCH DESIGN AND METHODOLOGY

The aim of the study can be divided into two categories:

- the analysis, interpretation and reviewing of the drug utilisation of antineoplastic and immunomodulating agents;
- the analysis and investigation of the costs associated with the usage of antineoplastic and immunomodulating agents.

A retrospective drug utilisation study was done on data provided by a medicine claims database (refer to section 2.13.3.1 for a definition of retrospective drug utilisation study).

There were no experiments, e.g. clinical trials, done in this study. This research design can therefore be described as a non-experimental, retrospective quantitative research (refer to section 2.13.2.1 for a definition of a quantitative drug utilisation review).

The method used in the empirical investigation consisted of the following phases:

- The selection of the research design;
- the selection of the study population, using a medicine claims database (see section 4.6);
- the selection of the measuring instruments (see section 4.7.3);
- data application and data analysis (see section 4.7);

- reliability and validity of the research instruments (see section 4.8);
- the report and discussion of the results of the empirical investigation (chapter 4);
- the recommendations based on the results of the empirical investigation (chapter 5).

3.5 DATA SOURCE

The data used in this study were obtained from a medicine claims database, of a pharmacy benefit management company. Data were extracted for a period of 24 months, from 1 January 2005 to 31 December 2006.

3.6 DATABASE

The database consists of all prescriptions claimed through the medicine claims database, for the study period 1 January 2005 to 31 December 2006.

The following fields were used in this study:

- The ATC code of the medicine product (see section 3.8.2.2)
- the National Approved Product Pricing Index (NAPPI) code of the dispensed product (see section 3.8.2.4)
- The description (active ingredient & trade name) of the drug (see section 3.8.2.3)
- The prescription number
- The prescription date
- Indicator for the original, generic or no-generic product (refer to section 3.8.2.2)
- The quantity of the drug dispensed to the patient
- The dependant number of the patient/member
- Amount paid by the medical scheme
- Amount (levy) paid by the patient/member
- Total cost of medicine

- The gender of the patient
- The age of the patient (calculated from the birth date of the patient)

3.7 STUDY POPULATION

The total population consisted of all the prescriptions claimed through the pharmacy benefit management (PBM) used. The study population consisted of all the prescriptions for patients using antineoplastic and immunomodulating drugs during a two-year period starting on 1 January 2005 and ending 31 December 2006. A total of 17 568 712 prescriptions (2005 & 2006) were used for the analysis. For confidentiality purposes the names of the prescribing doctors, medical schemes as well as the names of the patients were not revealed.

The different strata were collected by following certain steps:

- Step 1: All the prescriptions on the prescription claims database were studied.
- Step 2: All the prescriptions containing antineoplastic and immunomodulating agents were withdrawn from the database.
- Step 3: The antineoplastic and immunomodulating agents “L” were classified according to the ATC codes (see section 1.2 and section 3.8.2.2).
- Step 4: The antineoplastic agents (L01) were classified according to active ingredient (see section 1.2).
- Step 5: The endocrine therapy agents (L02) were classified according to active ingredient (see section 1.2).
- Step 6: The immunomodulating agents (L03) were classified according to active ingredient (see section 1.2).

3.8 DATA ANALYSIS

Various instruments and statistical analysis were used in analysing the data. Different computer software programmes and classification systems were also applied in the analysis of the data.

3.8.1 Data analysis methods

The *Statistical Analysis System*® 9.1® was used to extract and analyse specific data from the database. *Microsoft Word XP*® and *Microsoft Excel XP*® were used for compiling tables and also to calculate certain statistical measures. Diagrams were also compiled as a guideline to assist with the analysis of the data.

3.8.2 Classification systems

The following classification systems were used during this study:

3.8.2.1 The MIMS classification system

The MIMS is a healthcare resource guide in which information such as the use, contra-indications, permitted/banned drugs in sport, treatment guidelines etc. for drugs is specified (Inseta, 2003:7). It classifies medicine according to its pharmacological action and is widely used in South Africa to determine the availability of alternative medicine, etc. Refer to Appendix D for a complete list of this classification (Snyman, 2007:11a). This classification system formed part of the criteria for extracting data via SAS 9.1® and classifying cancer drugs (SAS for Windows 9.1, 2001).

3.8.2.2 The ATC (Anatomical Therapeutic Chemical) classification

The Anatomical Therapeutic Chemical (ATC) classification system divides drugs into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties (WHO Collaborating Centre for Drug Statistics Methodology, 2008).

There are five different levels in which the drug groups are classified. The drugs are divided into fourteen main groups (1st level), with one pharmacological/therapeutic subgroup (2nd level). At level 3 and 4 the drugs are divided into chemical/pharmacological/therapeutic subgroups and level 5 is the chemical substance. The 2nd, 3rd and 4th levels are often used to identify pharmacological subgroups when that is considered more appropriate than therapeutic or chemical subgroups (WHO Collaborating Centre for Drug Statistics Methodology, 2008). As an example, the complete classification of *Mercaptopurine* illustrates the structure of the code:

L ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS

(1st level, anatomical main group)

L01 ANTINEOPLASTIC AGENTS

(2nd level, therapeutic subgroup)

L01B ANTIMETABOLITES

(3rd level, pharmacological subgroup)

L01BB PURINE ANALOGUES

(4th level, chemical subgroup)

L01BB02 MERCAPTOPURINE

(5th level, chemical substance)

3.8.2.3 Active ingredient classification

All the medicine items on the database were individually classified according to their active ingredient.

3.8.2.4 The NAPPI code

A NAPPI code is a unique identifier for a given product that enables the healthcare delivery chain. Ethical (non-surgical) NAPPI codes are allocated to pharmaceutical and other medicine products and surgical NAPPI codes are allocated to surgical appliances, medical appliances and consumables (Inseta, 2003:5).

NAPPI codes consist of a nine (9)-digit numeric character. The first six (6)-digits of the numeric character are unique for every product in certain strengths and forms but do not indicate the specific quantity or pack size of the product. The last three (3)-digits of the numeric character refer to a specific pack size of the relevant NAPPI product (Inseta, 2003:5). Also incorporated into the code is the product name, the manufacturer plus exclusions, etc. (Snyman, 2007:6a).

3.8.3 Measuring instruments

For the purpose of this study, the following were used as measuring instruments or criteria for data analysis:

3.8.3.1 Prevalence

The prevalence indicates the proportion of individuals in a population with a specific disease at a given time. Prevalence is a statistical concept referring to the number of cases of a disease that are present in a particular population at a given time (MedicineNet, 2008). In the Mediscor Medicines Review 2006 (Bester & Hammann, 2007:4) prevalence is defined as *"the portion of beneficiaries that claimed or the number of utilising beneficiaries expressed as a percentage of the total number beneficiaries in the population."*

According to the World Cancer Report cancer rates are set to rise by 50% to 15 million new cases in the year 2020 (World Health Organisation, 2007). The American Cancer Society estimated that in 2008, 565 180 Americans would die of cancer, this adds up to more than 1500 deaths per day. A further 1 437 180 new cancer cases were expected to be diagnosed in 2008 in America (American Cancer Society, 2008c:1).

Considering the abovementioned statistics (also refer to chapter 2), the usage of prevalence as a measuring instrument is an important element of this study.

3.8.3.2 Cost

As explained in paragraph 3.5.2, the cost of cancer care has increased dramatically over the past 10 years (National Cancer Institute, 2007:1). The introduction of newer cancer drugs such as Herceptin®, Eloxatin®, etc. and other changes in cancer care led to this increase in expenditure (Niezen *et al.*, 2006:2887).

Therefore, cancer drugs are key candidates in studies concerning cost-effectiveness. Costs of cancer drugs were used in this study as a measuring instrument and criteria for data analysis to emphasise the importance of the costs of cancer care.

3.8.3.3 Original, generic and no-generic drugs

Original medicine items are drugs that are manufactured and patented and are unique in terms of active ingredient and/or dosage and/or dosage forms. The Trade-

Related aspects of Intellectual Property Rights (TRIPS) was introduced in 1995 to protect manufacturers, to prevent disclosure of an original drug's composition and to exclude other manufacturers from developing, using and/or selling the product for a minimum of 20 years. This agreement was enforced to ensure that manufacturers will invest in drug research, development and marketing and to protect companies' profit margins (Media Resource Desk, 2008). For the purpose of this study, these drugs will be defined as "original medicine items" (refer to section 3.2) and are thus original drugs that were used in spite of generic medicine items available.

When a patent on a specific drug expires or is waived, other companies can make that drug generically. A generic drug is a copy of the original drug with the same active ingredients as the original drug. The generic drug is sold using a different brand name than the one under which the drug was initially manufactured (Media Resource Desk, 2008). For the purpose of this study, these medicine items will be defined as "generic medicine items" (refer to section 3.2).

According to an article by BioPortfolio Ltd. (1997-2008), generic cancer drugs accounted for less than 10% of all generic sales up to the year 2000. This, however is changing radically in the 21st century because a lot of cancer drugs is losing its patent protection in the near future.

Other drugs relevant for this study are drugs with no generic substitution. These are drugs that are either still under patent protection or for which no generic substitution has been developed after the patent protection has expired. For the purpose of this study, these medicine items will be defined as "no-generic medicine items" (refer to section 3.2).

There is a relative cost difference between original, generic and no-generic drugs and therefore they were used as measuring instruments in data analysis.

3.8.4 Statistical analysis

For the purpose of this empirical investigation, the following descriptive statistics and calculations were used:

3.8.4.1 Average value (mean)

The average value (mean) of a set of observations is the sum of all values making up the set of observations divided by the total number of observations in the set. (Banerjee, 2003:3). The formula can be illustrated as follows:

$$\text{Average value} = \frac{\text{Sum of all values in set}}{\text{Number of observations}}$$

3.8.4.2 Standard Deviation

Banerjee (2003:5) defines the standard deviation as the square root of the variance (see definition in section 4.7.4.4), which is expressed in the same unit as the average value. It measures the spread of the data around the average value and is a measure of variability.

When a small standard deviation is present it indicates that the values are grouped around the average value. A large standard deviation is an indication that the values are widely spread out around the average value (Banerjee, 2003:5).

3.8.4.3 Percentages

The use of percentages is a way of expressing ratios in terms of whole numbers. A ratio or fraction is converted to a percentage by multiplying by 100 and adding a percentage sign % (Weisstein, 2008).

3.8.4.4 Range/variance (r)

The range of a set of observations is calculated by subtracting the smallest value from the largest value in a set of observations (Campbell & Machin, 1990:43).

3.8.4.5 Effect sizes (d-values)

An effect size is the difference between two average values (means) divided by the standard deviation of the two values (Talheimer & Cook, 2002:3).

$$d = \frac{X_t - X_c}{S_{\max}}$$

Where:

- d = effect size
- X_t = average cost of treatment (mean)
- X_c = average cost of comparison treatment (mean)
- S_{max} = maximum standard deviation.

The following guidelines can be used to evaluate d-values (Steyn, 1999:3):

- <0.2 = small effect with no significant practical difference
- ≥ 0.5 and <0.8 = medium effect, which is observable and may be significant
- ≥ 0.8 = large effect, which is significant and of practical importance.

3.8.4.6 Cost prevalence index (CPI)

The cost prevalence index are defined as follows by Serfontein (1989:180):

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

The cost prevalence index is used to indicate the relationship between the amount of medicine items and the total medicine cost.

The cost prevalence index can thus serve as an indicator of the relative expensiveness of cancer drugs. The following analysis can be used for the purpose of this study:

- Cost prevalence index: < 1 = relatively inexpensive therapy.
- Cost prevalence index: 1 = there is a equilibrium between cost and prevalence of the therapy.
- Cost prevalence index: > 1 = relatively expensive therapy.

3.8.4.7 Potential cost saving

Potential cost savings may be calculated to determine the cost of medicine that could be saved if the price of the innovator (original) medicine item were replaced with the price of an equivalent generic medicine item (Van der Westhuizen *et al.*, 2008).

Cost savings can be calculated as follows (Van der Westhuizen *et al.*, 2008):

$$\text{Cost saving} = \text{Total cost}_o - (\text{Average cost}_g \times n_o)$$

Where:

- Total cost_o = the total cost of the original product on the specific database
- Average cost_g = the average cost of the least-or the most expensive generic equivalent; and
- N_o = number of original products on the specific database.

This calculation was used in section 4.4.4 to determine the potential cost saving when substituting Nolvadex D 20mg tablets® with more inexpensive generic products (Kessar 20mg tablets® and Neophedan 20mg tablets®).

3.9 RELIABILITY AND VALIDITY OF THE RESEARCH INSTRUMENTS

The central database of a Pharmacy Benefit Management company was used to acquire the data for this study. No manipulation of the data by the researcher was possible because the data were obtained directly from the central database.

The research was carried out from the standpoint that all data acquired from the central database were accurate and correct. This is a limitation of the study (see chapter 5).

Permission to conduct the study was granted by the PBM's administrator as well as by the NWU Ethical Committee. The ethical permission was granted by the NWU for the study "Investigation of medicine usage patterns in a section of the private health care sector utilizing data from a Pharmaceutical Benefit Management (PBM) Company in South Africa" and the ethical committee awarded the study with the following number of permission: NWU-0046-08-S5.

3.10 SUMMARY

In this chapter the empirical investigation was discussed. The research objectives, study population, data source, database and data analysis of this empirical investigation were described. This discussion also included the procedures followed in acquiring the relevant information and the subsequent analysis of the data.

The results of the empirical investigation will be reported on and discussed in chapter 4.

CHAPTER 4

Results and discussion

4.1 INTRODUCTION

In Chapter 4 the results of the empirical investigation will be reported and discussed. The results are for the period 1 January 2005 until December 2006 and were obtained from the medicine claims database of a pharmacy benefit management company.

4.1.1 Presentation of results

The results of the empirical study will focus on the **cost** and **prevalence** of medicine in general with specific reference to *antineoplastic and immunomodulating agents* (L01 –L03) (refer to section 1.2 and section 3.2). The cancer medicine items that were identified from the medicine claims database during 2005-2006 are summarised according to the ATC (anatomical, therapeutic, chemical) classification (refer to Appendix A). Discussion of these cancer drugs will be based on this classification.

Basic diagrams have been developed to explain the analysis of the empirical investigation during the period 2005-2006. The diagrams are presented on the following two pages:

Diagram 4.1 Illustration of general analysis of database

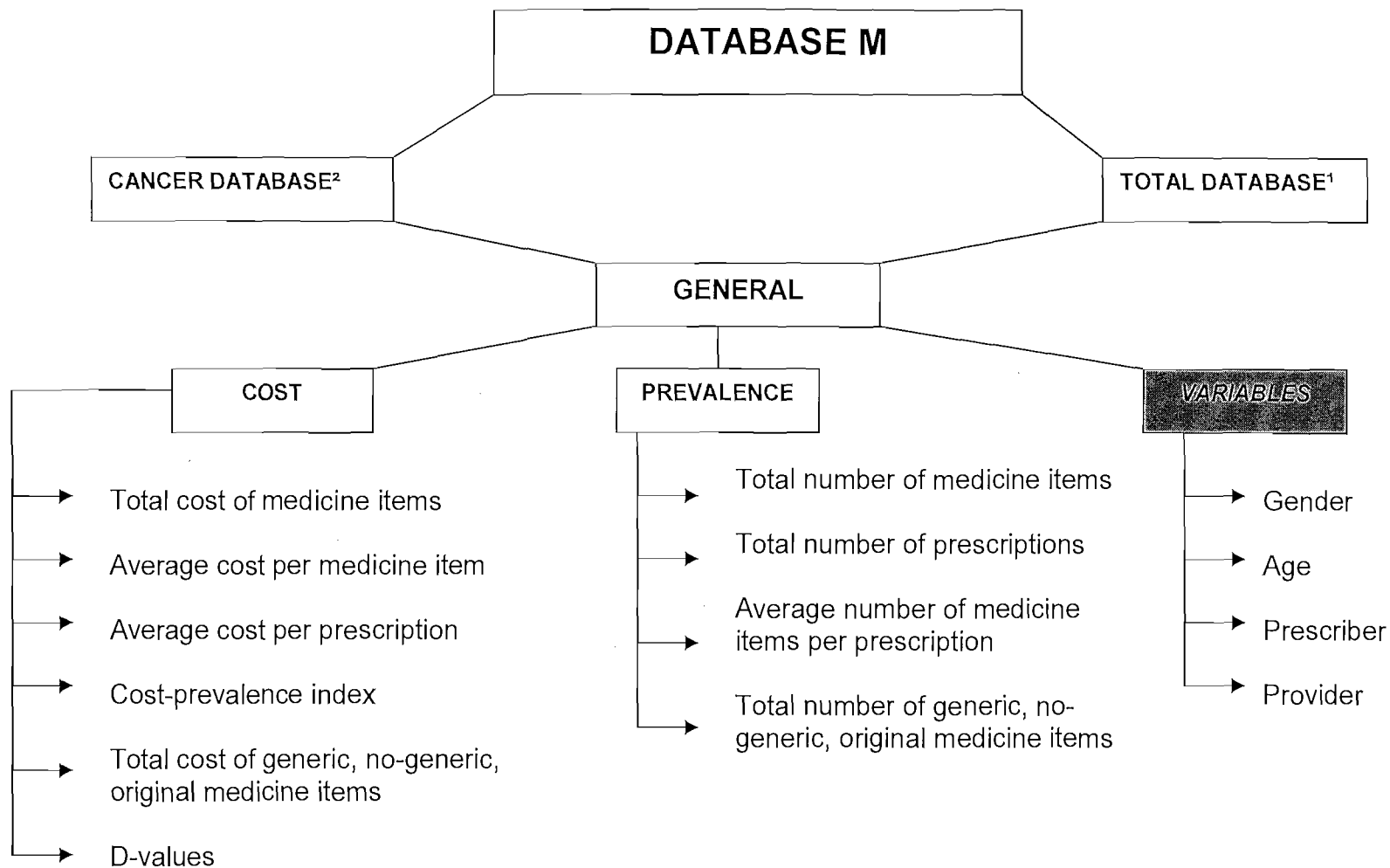
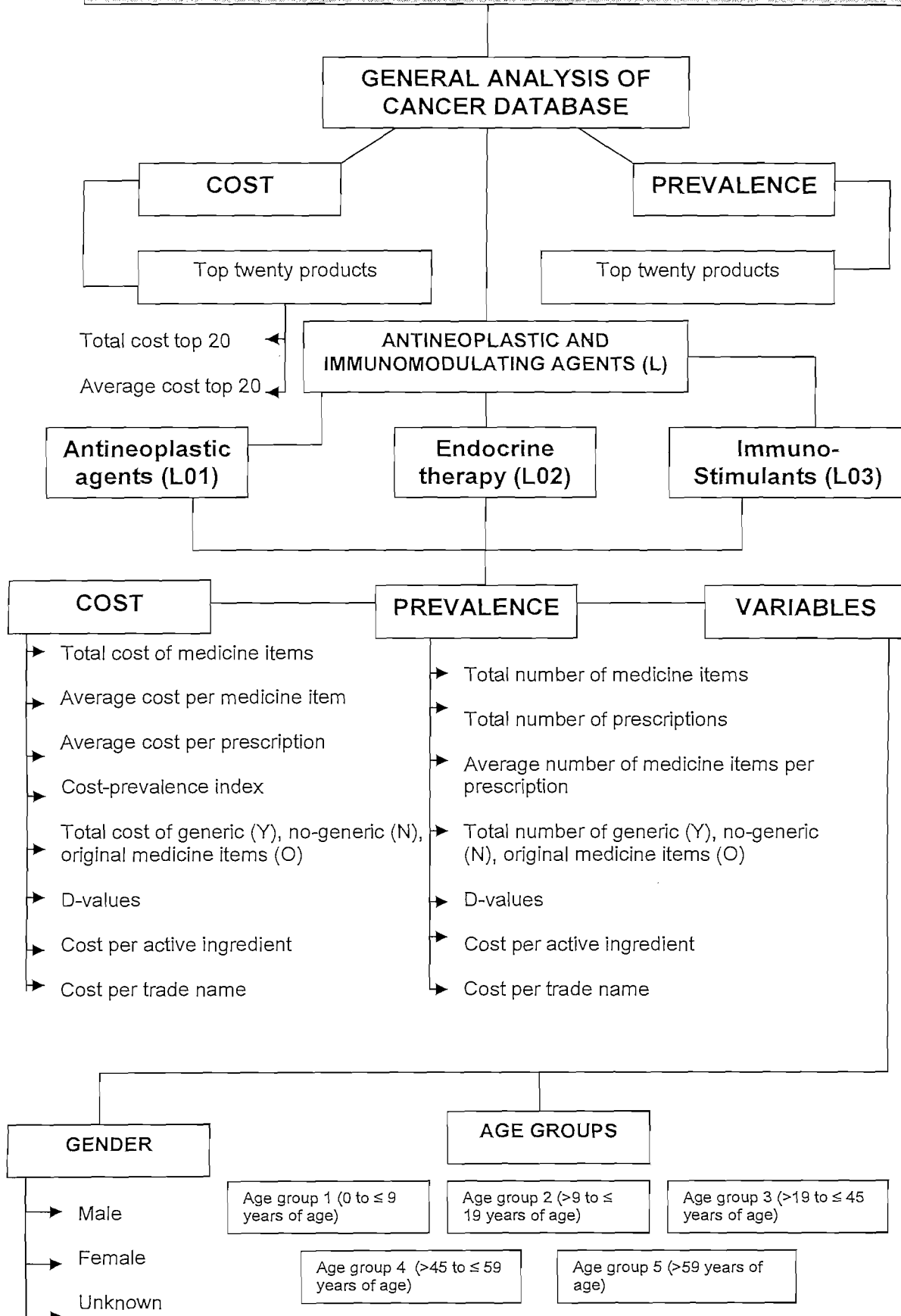
¹ Refer to definition of total database in section 3.2² Refer to definition of cancer database in section 3.2

Diagram 4.2 Illustration of the compilation of the cancer database

4.1.2 Points to take note of in the interpretation of data and tables

- Generic indicator (GI) is an indication of whether the cancer product is an original cancer medicine item ("O"), generic cancer medicine items ("Y") or a no-generic medicine item ("N") (refer to section 3.8.3.3 for definitions). This abbreviation (GI) is used in some tables throughout this chapter.
- The abbreviation "Prev." that is used in some tables, figures and diagrams stands for "prevalence". This indicates the number of cancer medicine items claimed.
- Due to technical matters some of the tables' font size differs from the font size in the text.
- The prevalence and cost percentages presented in table 4.26 – table 4.29 is a percentage of the total number of medicine items in that specific age group and the total cost of cancer medicine items in that specific age group.
- Reference to "cancer patients" refers to patients receiving one or more medicine item classified as antineoplastic and immunomodulating agents (L) (see diagram 4.2). Also see section 3.2 for the definition of a cancer patient.
- Due to technical reasons age groups are presented as numerical groups (1,2,3,4,5) in some tables, whilst in other tables the age of the patients in the different age groups are specifically classified (e.g: age group 1: 0 to $\leq$ 9 years of age).
- Treatment periods e.g. weekly or monthly as well as dosages were not included in the cost calculations of the data. This is a limitation to this study (refer to section 5.3).
- Treatment outcomes fall outside the scope of this study. This is a limitation to this study (refer to section 5.3).
- The birth dates and gender of all patients were not allocated in all cases and therefore the totals of all tables where age and gender are indicated will not correlate.
- Refer to section 3.2 for definitions of "prescription" and "medicine item".
- The average cost per medicine item for specific trade names/active ingredients was calculated as it were prescribed without further analysis regarding the average number of capsules/tablets/vials prescribed. This is also seen as a limitation of this study (refer to section 5.3).

- It is important to note that calculations were based on the ATC classification of antineoplastic and immunomodulating agents - “L” and not the related cancer or other treatments. Therefore, the average cost calculations are not related to any specific cancer or related treatment, nor could it be applied to a specific practice or consultation situation or the severity of the cancer.
- Refer to section 3.2 for the synonyms of “cancer medicine item”.
- The complete references of the sources used to indicate the possible indications of the different cancer medicine are presented in the bibliography.

4.2 MEDICINE ON THE DATABASE

The results of the general medicine utilisation patterns and the comparison of the usage of cancer medicine items with medicine in general will now be discussed.

4.2.1 General medicine utilisation patterns

The analysis will be divided into prevalence and cost of medicine items; both on the total database as well as on the cancer database (refer to diagram 4.1).

The *total number of patients* (refer to definition of patient in section 3.2) and the *total number of cancer patients* (refer to the definition of cancer patient in section 3.2) on the database will be considered in all discussions. In 2005, a total of 1 218 358 patients were recorded on the *total database*. Of these, 10 023 (0.82%) were cancer patients. The *number of cancer patients* increased with 516 from 2005 to 2006 to 10 539 cancer patients on the medicine claims database, which was 0.84% of all patients on the *total database* (n=1 259 099). The *number of patients on the total database* increased with 3.24% (n=40 741) from 2005 to 2006 (refer to table 4.2). The *total number of cancer patients* on the medicine claims database increased with 0.02% from 2005 to 2006.

Table 4.1 Average number of prescriptions per patient per study year

Average number of prescriptions per patient per year		
	2005	2006
Total database*	6.98 ± 7.83	7.17 ± 8.05
Cancer database*	5.85 ± 4.93	6.16 ± 4.90

*Total number of prescriptions per year for total and cancer database presented in table 4.2

Cancer patients receiving twelve or less prescriptions containing one or more cancer medicine item comprised 91.02% and 90.57% of all cancer patients in 2005 and 2006 respectively. The average *number of prescriptions per cancer patient per year* was 5.85 ± 4.93 (2005) and 6.16 ± 4.90 (2006) (refer to table 4.1). This may be because cancer treatments are usually given for a period of 6 months or a year. It can therefore be deducted that cancer patients possibly received a prescription every two months. It may also be an indication of shorter periods of cancer treatments.

The average number of prescriptions per *patient (total database)* per year was 6.98 ± 7.83 and 7.17 ± 8.05 for 2005 and 2006 respectively with 80.74% and 79.65% of all patients on the *total database* claiming twelve or less prescription per year for 2005 and 2006 respectively (refer to table 4.1 and table 4.3).

Table 4.2 General medicine prescribing patterns for 2005 and 2006

	2005			2006		
	Total database (a)	Cancer database (b)	% (c)*	Total database	Cancer database	%*
Total number of prescriptions (N)	8 522 574	58 682	0.69	9 046 138	64 919	0.72
Total number of medicine items (N)	19 860 679	71 972	0.36	21 473 074	82 525	0.38
Total number of patients (N)	1 218 358	10 023	0.82	1 259 099	10 539	0.84
Average number of medicine items per prescription (N)	2.33±1.56	1.23±0.72		2.37±1.58	1.27±0.83	
Total cost of all medicine items (R)	1 893 376 921	75 736 630.77	4.00	2 046 944 383	108 675 842	5.31
Average cost per medicine item (R)	95.33±192.21	1052.31±1912.21		95.33±227.99	1316.88±2267.40	
Total number of medicine items with no generic ¹ (N)	8 501 370	24 499	0.29	8 133 997	29 665	0.36
Total cost of items with no generic (R)	1 191 350 141	64 395 147.61	5.41	1 183 914 105	93 664 505.13	7.91
Average cost per medicine item with no generic (R)	140.14±267.20	2628.48±2386.27		145.55±339.64	3157.41±2664.32	
Total number of generic medicine items ² (N)	8 492 741	17 273	0.20	10 024 315	18 766	0.19
Total cost of generic medicine items (R)	416 570 452	4 037 946.70	0.97	337 960 440	6 251 255.67	1.85
Average cost per generic item (R)	49.10±66.41	233.77±553.08		52.07±70.13	333.12±821.61	
Total number of original items ³ (N)	2 728 603	30 200	1.11	3 281 896	34 094	1.04
Total cost of original items (R)	273 454 160	7 303 536.46	2.67	521 923 204	8 760 081.45	1.68
Average cost per original item (R)	100.22±139.34	241.84±929.84		102.98±164.66	256.94±1 136.91	

*Percentage % (c) is determined by dividing b by a, and then multiplying it with 100.

¹ An original medicine item for which no generic medicine item exists (refer to section 3.2).

² A generic medicine item for an original medicine item (refer to section 3.2).

³ An original item with generic medicine item available (refer to section 3.2).

Table 4.3 Number of prescriptions per patient per year

Number of prescriptions per patient per year*	Prevalence percentage (%)			
	Total database		Cancer database	
	2005	2006	2005	2006
1	25.33	26.64	25.34	22.30
2	13.40	12.45	11.15	10.40
3	9.27	8.68	8.40	8.11
4	6.98	6.55	6.57	6.59
5	5.46	5.17	5.17	5.65
6	4.43	4.23	4.32	5.24
7	3.62	3.48	4.23	4.36
8	3.04	2.98	4.03	4.36
9	2.58	2.62	3.95	4.85
10	2.28	2.35	5.02	4.95
11	2.15	2.22	5.41	6.45
12	2.22	2.27	7.42	7.32
13	2.18	2.27	4.45	4.44
14	2.05	2.15	1.39	1.58
15	1.85	1.92	0.81	0.82

*Total number of prescriptions per year for total and cancer database presented in table 4.2

4.2.1.1 Prevalence of medicine items on the total and cancer database

During 2005 a total number of 8 522 574 prescriptions (N) were claimed through the total database, of which 58 682 prescriptions (0.69%) contained one or more cancer medicine item(s). In the following year 0.72% (n=64 919) of all prescriptions claimed (n=9 046 138) contained one or more cancer item(s). The total number of *medicine items* prescribed in each year respectively was 19 860 679 (2005) and 21 473 074 (2006) of which 71 972 (0.36%) and 82 525 (0.38%) respectively were *cancer medicine items* (refer to table 4.2).

From Table 4.2 the following calculations and deductions may also be made:

- ✓ There was an increase of 7.50% in the *total number of medicine items* (total database) claimed and a 0.02% increase in the *number of cancer medicine items* (cancer database) claimed between 2005 and 2006.
- ✓ Accordingly there was an increase in the *number of prescriptions* issued from 2005 to 2006 for both the total and cancer database (see table 4.2).
- ✓ The *total number of patients* also increased (refer to paragraph 4.2.1) and this may be part of the explanation of the increase in number of prescriptions and medicine items claimed (also see section 4.2.1.2 for a further discussion of the cost increase).

- **Original (innovator) medicine items (refer to section 3.2 for a definition)**
 - ✓ *Original medicine items* on the total database encompassed 13.74% and 15.28% of all medicine items in 2005 and 2006 respectively (calculated from table 4.2). *Original cancer medicine items* comprised 1.11% (2005) and 1.04% (2006) of all *original medicine items* on the total database (presented in table 4.2)
 - ✓ Of all *cancer medicine items* prescribed 42% (2005) and 41% (2006) were *original cancer medicine items* ("O").
 - ✓ The percentage of *original cancer medicine items* claimed in 2005 and 2006 respectively was 28% and 26% higher than the percentage of *original medicine items* on the *total database* claimed during both study years (also refer to figure 4.1).
- **Generic medicine items (refer to section 3.2 for a definition)**
 - ✓ *Generic medicine items* ("Y") on the total database encompassed 42.76% and 46.68% of all medicine items in 2005 and 2006 respectively (calculated from table 4.2). *Generic cancer medicine items* comprised 0.20% (2005) and 0.19% (2006) of all *generic medicine items* on the total database (presented in table 4.2).
 - ✓ Of all the *cancer medicine items* claimed, 24% (2005) and 23% (2006) were *generic cancer medicine items* ("Y").
 - ✓ As can be seen (also refer to figure 4.1), the total number of *generic medicine items* on the total database was relatively higher than the *generic cancer medicine items* claimed in the two study years.
- **No-generic medicine items (refer to section 3.2 for a definition)**
 - ✓ *No-generic medicine items* on the total database encompassed 42.81% and 37.88% of all medicine items in 2005 and 2006 respectively (calculated from table 4.2). *No-generic cancer medicine items* comprised 0.29% (2005) and 0.36% (2006) of all *original medicine items* on the total database (presented in table 4.2)
 - ✓ Of all *cancer medicine items* 34% (2005) and 36% (2006) were medicine items for which *no generic medicine item* were available ("N").

See figure 4.1 for percentage distribution of generic, no-generic and original medicine items for both the total database and the cancer database.

4.2.1.2 Cost of medicine items on the total and cancer database

The total cost of all medicine items claimed during 2005 amounted to R1 893 376 921, of which 4% (R75 736 630.77) was identified as cancer medicine items. In 2006, cancer medicine items constituted 5.31% (R108 675 842) of the total cost (R2 046 944 383) of all medicine items claimed.

Calculated from table 4.2, the total cost of all medicine items on the *total database* increased with 7.5% from 2005 to 2006. The percentage that cancer medicine items comprised of the total cost of all medicine items increased with 1.31% from 2005 to 2006. The number of patients as well as the increase in number of medicine items was taken in account with the percentage increase.

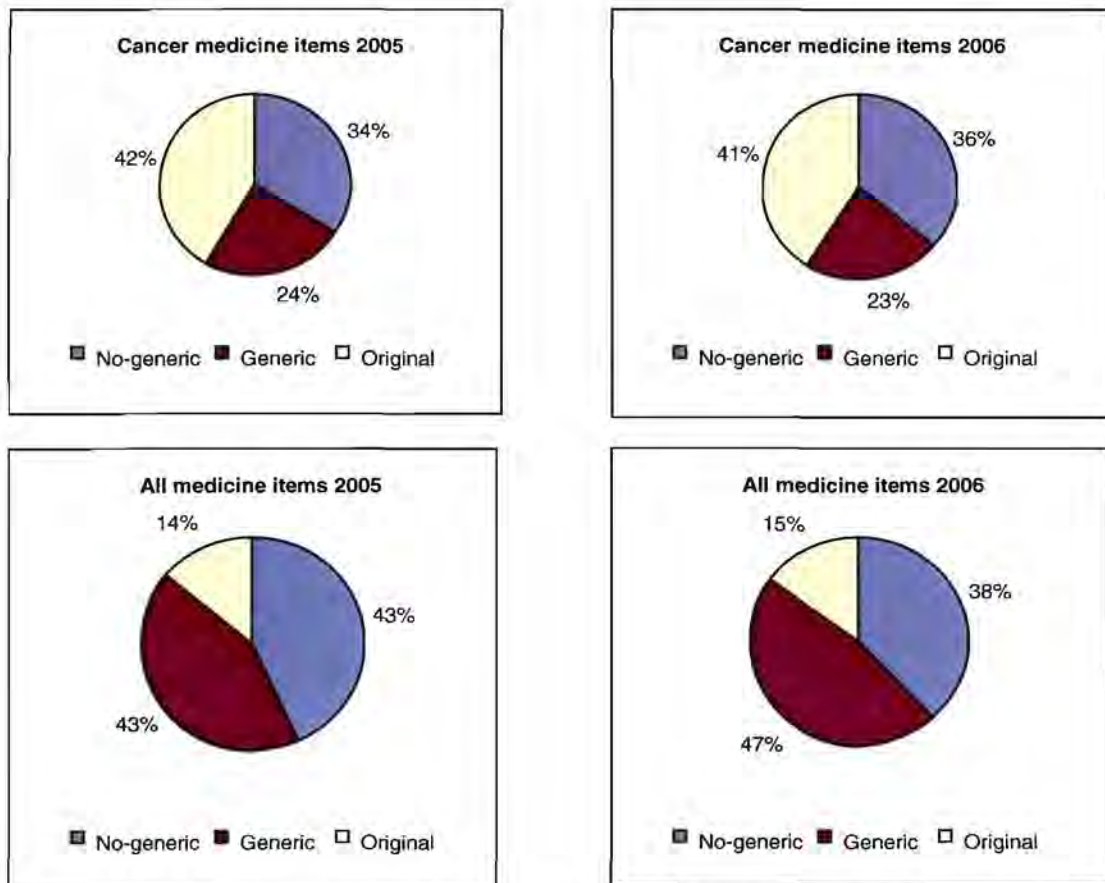


Figure 4.1 Prevalence percentage distribution of generic, no-generic and original medicine items for 2005 and 2006

The ratio cost per *cancer patient* per year for cancer medicine treatment was R7 556.28 and R10 311.78 for 2005 and 2006 respectively. This indicates an increase of 26.72% in ratio cost per patient between the two study years.

$$\text{Ratio cost per cancer patient per year} = \frac{\text{Total cost of cancer items claimed during study year}}{\text{Total number of cancer patients in study year}}$$

In the Medicines Review 2006 (Bester & Hammann, 2007:8) of a pharmacy benefit management company, the expenditure and utilisation illustrating the cost and usage patterns per therapeutic group during 2006 is summarised. In 2006 the group, cytostatics (cancer medicine items), ranked 7th moving up 7 positions from the 14th position in 2005. Cytostatics were in position 47 on the ranking list in 2004.

According to Bester and Hammann (2007:8) this considerable move in expenditure and utilisation of cancer medicine items is due to the introduction of the Single Exit Price (SEP) and the professional fee. This means that the oncologists treating patients no longer dispense oncology products but these expensive products are now dispensed by pharmacies. Because of this, the medicine claims database is now processing more claims for cancer medicine items. Thus, an increase in the usage of these relatively expensive cancer medicine items may not be the only factor playing a role in the increase in cost of cancer medicine items.

Original medicine items (total and cancer database) ("O")

- ✓ *Original medicine items* on the total database encompassed 14% and 26% of the total cost of all medicine items in 2005 and 2006 respectively (calculated from table 4.2). *Original cancer medicine items* comprised 2.67% (2005) and 1.68% (2006) of the total cost all *original medicine items* on the total database (presented in table 4.2)
- ✓ *Original cancer medicine items* comprised 10% of the total cost of *cancer medicine items* in 2005 and 8% in 2006. This is in contrast with the *number of original cancer medicine items* claimed, which was the highest in both study years (see section 4.2.1.1).
- ✓ In 2006, *original cancer medicine items* had the lowest average cost (R256.94 ± 1 136.91) of all cancer medicine items. Take note of the relatively high standard deviation, which is an indication of the possible wide range of cancer medicine prescription patterns and treatment periods.

Generic medicine items (total and cancer database) (“Y”)

- ✓ The total cost of *generic medicine items* on the *total database* comprised 22% (R416 570 452) in 2005 and 16% (R337 960 440) in 2006 of the total cost of all medicine items. *Generic cancer medicine items* comprised 0.97% and 1.85% of the total cost of all *generic medicine items* claimed on the total database in 2005 and 2006 respectively (refer to table 4.2).
- ✓ *Generic medicine items* on the *total database* also had the lowest average cost in 2005 (R49.10 ± 66.41) and in 2006 (R52.07 ± 70.13) and the lowest total cost of all medicine items in 2005 (refer to table 4.2).
- ✓ *Generic cancer medicine items* comprised only 5.00% of the total cost of *cancer medicine items* in 2005 and 6.00% in 2006 (calculated from table 4.2, also refer to figure 4.2).
- ✓ *Generic cancer medicine items* had the lowest average cost (R233.77 ± 553.08) and total cost (R 4 037 946.70) of all cancer medicine items in 2005. The average cost of *generic cancer medicine items* increased to R 333.12 ± 821.61 in 2006 (refer to table 4.2).

No-generic medicine items (total and cancer database) (“N”)

- ✓ The total cost of *no-generic medicine items* on the *total database* amounted to 63% (2005) and 58% (2006) of the total cost of all medicine items. *No-generic cancer medicine items* comprised 5.41% and 7.91% of the total cost of all *no-generic medicine items* claimed on the total database in 2005 and 2006 respectively (refer to table 4.2).
- ✓ *No-generic cancer medicine items* comprised 85% of the total cost of *cancer medicine items* in 2005 and 86% in 2006 (calculated from table 4.2, also refer to figure 4.2).
- ✓ The average cost of medicine items with no generic medicine items available was also the *highest* for both the *total database* and the study population (*cancer database*) (refer to table 4.2). See table 4.4 for the effect sizes (d-values) of these medicine items.
- ✓ No-generic drugs are either still under patent protection or no generic medicine item has been developed after the patent protection of the specific drug expired. The manufacturers of these drugs thus still have patent rights and therefore no-generic medicine items may be relatively more expensive

than generic or original medicine items (refer to section 3.2 and section 3.8.3.3).

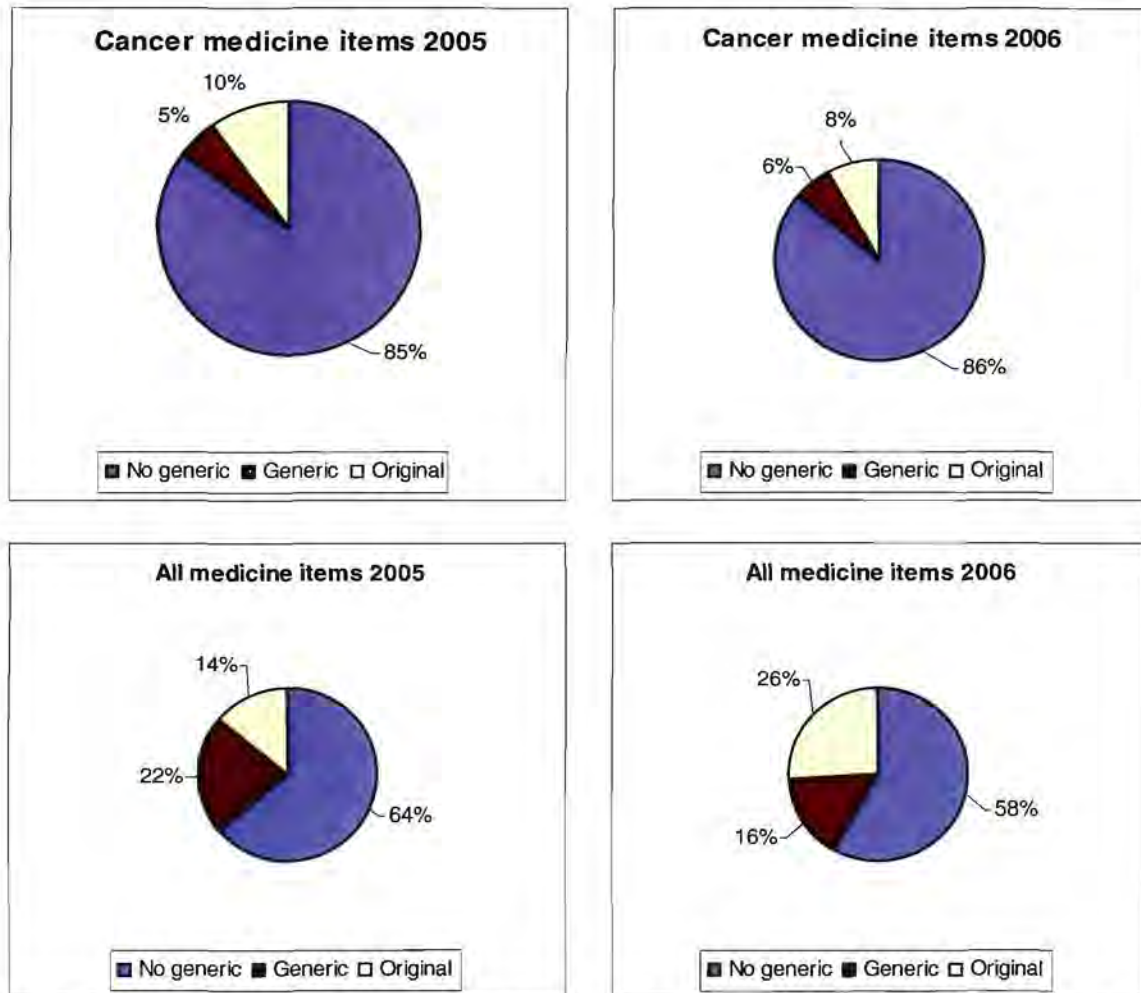


Figure 4.2 Cost percentage distribution of generic, no-generic and original medicine items for 2005 and 2006

The standard deviations of all the cancer drugs in the study period were relatively high which may indicate a relatively large patient variation in cancer medicine treatment. This may be because different cancers have a different treatment regimens and doses depend on the type of cancer, site of cancer, stage of the cancer, etc.

In table 4.4, the numerical values represent the following types of medicine items:

- 1 - *No-generic medicine items on the total database*
- 2 - *No-generic medicine items on the cancer database*
- 3 - *Original medicine items on the total database*
- 4 - *Original medicine items on the cancer database*

- 5 - *Generic medicine items on the total database*
- 6 - *Generic medicine items on the cancer database*

Table 4.4 Effect sizes (d-values) between the average costs of all medicine items and cancer medicine items according to type of medicine

2005						
	1	2	3	4	5	6
1		1.04		0.11		0.17
2						
3	0.15	1.06		0.15		0.24
4		1.00				
5	0.34	1.08	0.36	0.21		
6		1.00				0.33
2006						
	1	2	3	4	5	6
1		1.13		0.10		
2						
3	0.13	1.15		0.14		0.3
4		1.09				0.34
5	0.28	1.17	0.31	0.18		
6		1.06				

**Effect sizes calculated from average costs shown in table 4.2.*

***For the purpose of this study effect sizes (d-values) of 0.8 or higher will be assumed to have practical significance (refer to paragraph 3.8.4.5)*

Table 4.4 represents the effect sizes (d-values) of the average costs of cancer medicine items vs. the average cost of all medicine items, according to the type of medicine. This includes medicine *items with no generic substitution available, generic medicine items and original medicine items* for both the *total database* and the *cancer database*. For the purpose of this study, effect sizes (d-values) of 0.8 or higher will be assumed to have practical significance (refer to paragraph 3.8.4.5).

The d-values in table 4.4 indicate that *cancer medicine items with no generic product available* were relatively more expensive than all other medicine items, including *generic and original medicine items* on both the *total database* and the *cancer database*.

The effect sizes (d-value) between the *generic and original medicine items* on both the *total database* and the *cancer database* were also calculated for both study years, but there was no significant difference between the average costs of the different groups.

4.2.2 General medicine utilisation patterns according to different age groups

The analysis of the medicine utilisation pattern of the different age groups will be divided into prevalence of medicine items and cost of medicine items.

Table 4.5 is a summary of the prevalence and cost of medicine items on the total database as well as the cancer database according to the five age groups specified in this study. The different age groups are:

Age group 1: All patients on the database between 0 and ≤ 9 years of age.

Age group 2: All patients on the database between >9 and ≤ 19 years of age.

Age group 3: All patients on the database between >19 and ≤ 45 years of age.

Age group 4: All patients on the database between >45 and ≤ 59 years of age

Age group 5: All patients on the database of >59 years of age.

The number of patients in each age group, for both the *total database* and the *cancer database*, is indicated in table 4.5. The *cancer patients* comprised between 0.02% - 2.41% of all patients in every respective age group. Most patients on the *total database* were between the ages of 19-45 years (age group 3), comprising almost 38% of all patients on the *total database*, in both study years. Most cancer patients on the database were older than 59 years. The number of cancer patients has increased between 2005 and 2006 for age group 1, age group 4 and age group 5 but decreased in age group 2 and age group 3. The total number of cancer patients between the age of 9 and 19 years of age (age group 2) has decreased with 28 patients (0.02%) between 2005 and 2006 while the patients between the age of 19 and 45 years of age (age group 3) decreased with 13 patients (0.02%). The total number of cancer patients increased (total for all age groups) with 516 patients between 2005 and 2006 (refer to table 4.2 and section 4.2.1).

4.2.2.1 Prevalence of medicine items according to age groups on the total and cancer database

For both study years, *cancer medicine items* for each individual age group comprised less than 1% of all *medicine items* claimed in that specific age group (see table 4.5). The number of *cancer medicine items* claimed for persons between 0-9 years (age group 1) increased with 66.67% between 2005 and 2006 while it varied in the other age groups between 3% and 13%. See section 4.4 for further discussion of *cancer medicine items* claimed in each age group. The increase in *medicine items* claimed between 2005 and 2006, for the *total database*, varied between 4% and 11% for the

different age groups. Patients claimed the largest number of medicine items over the age of 59 years, for both the *total database* and the *cancer database*, during both study years (refer to table 4.5).

Table 4.5 Comparison of medicine items on the total database and the cancer database according to different age groups

	Description	2005			2006		
		Total database	Cancer database	%*	Total database	Cancer database	%*
1 (0 to ≤ 9 years of age)	Total number of medicine items (N)	1 600 919	162	0.01	1 668 287	270	0.02
	Average cost per item (R)	55.80±72.66	232.25±368.96		55.47±90.50	533.91± 974.96	
	Total cost of medicine items (R)	89 329 200.6	37 625	0.04	92 540 896.32	144 156.62	0.16
	Total number of patients (N)	158 450	30	0.02	155 133	31	0.02
2 (>9 to ≤ 19 years of age)	Total number of medicine items (N)	139 0573	1 280	0.09	1 499 217	1 322	0.09
	Average cost per item (R)	70.09±113.40	435.33±1149.69		69.48±124.47	595.83± 1 447.78	
	Total cost of medicine items (R)	97 470 392.52	557 219.23	0.57	104 158 833	787 684.99	0.76
	Total number of patients (N)	177 330	337	0.19	177 978	309	0.17
3 (>19 to ≤ 45 years of age)	Total number of medicine items (N)	5 933 729	12 496	0.21	6 377 057	13 652	0.21
	Average cost per item (R)	80.56±166.53	807.24±1 752.52		79.44±184.54	892.74±1 975.54	
	Total cost of medicine items (R)	478 014 067	10 087 227.87	2.11	506 572 755	12 187 675.82	2.41
	Total number of patients (N)	459 843	2 447	0.53	476 211	2 434	0.51
4 (>45 to ≤ 59 years of age)	Total number of medicine items (N)	4901485	20123	0.41	5447080	23323	0.43
	Average cost per item (R)	101.51±208.21	1 035.34 ±2 010.35		100.93±248.34	1 380.38 ± 2 422.06	
	Total cost of medicine items (R)	497 543 992	20 834 076.33	4.19	549 795 116	32 194 591.3	5.86
	Total number of patients (N)	253 018	2 669	1.05	269 586	2 913	1.08
5 (>59 years of age)	Total number of medicine items (N)	6 033 952	37 911	0.63	6 481 394	43 958	0.68
	Average cost per item (R)	121.15±230.83	1 166.43 ± 1 921.08		122.49±282.13	1 441.42 ± 2 272.79	
	Total cost of medicine items (R)	731 018 016	44 220 482.27	6.05	793 875 296	63 361 733.52	7.98
	Total number of patients (N)	198 547	4 726	2.38	210 030	5 052	2.41

*Cost percentage: The total cost of cancer medicine items in each age group divided with the total cost of all medicine items prescribed to the specific age group and multiplying it with 100.

*Prevalence percentage: The total number of cancer medicine items (prevalence) in each age group divided with the total number of all medicine items prescribed to the specific age group.

4.2.2.2 Cost of medicine items according to age groups

The **cost** percentages of *cancer medicine items* in each individual age group were relatively higher when compared to the **prevalence** percentage of *cancer medicine items* in each age group (refer to table 4.5). The cost percentages for the different

age groups varied between 0.04-6.05% for 2005 and between 0.16 to 7.98% in 2006 (refer to table 4.5).

Table 4.6 Cost prevalence index (CPI) for the different age groups on the total database and cancer database

AGE GROUP*	Cancer database		Total database	
	2005	2006	2005	2006
1	0.22	0.41	0.59	0.58
2	0.41	0.45	0.74	0.73
3	0.77	0.68	0.85	0.83
4	0.98	1.05	1.06	1.06
5	1.11	1.09	1.27	1.28

*see section 4.2.2 for age group classification

**CPI values calculated from table 4.5 and Table 4.2

For the purpose of this study, a cost prevalence index (CPI) values equal to or exceeding one is considered to have a relatively large cost percentage in comparison with the prevalence percentage (refer to paragraph 3.8.4.6). The CPIs printed in bold in table 4.6 (all CPIs in age group 5 and most CPIs in age group 4) is higher than one and medicine items claimed by the indicated age groups were thus relatively more expensive than medicine items claimed by patients in other age groups. These mainly included medicine items claimed by patients older than 59 years (both *total database* and *cancer database*) as well as patients between the ages of 45-59 years. The CPI for medicine items claimed by patients older than 59 on the total database was the highest (CPI=1.28), refer to table 4.6. The percentages used to calculate the CPI values was determined by dividing the number of medicine items/cost of medicine items in each age group (from table 4.5) through the total number of medicine items/cost of medicine items (from table 4.2). This percentage was used to calculate the CPI values presented in Table 4.6.

4.2.3 General medicine utilisation patterns according to gender.

The general analysis of the medicine utilisation patterns of female and male patients will be divided into *prevalence* of medicine items and *cost* of medicine items.

The total number of female and male patients is indicated in table 4.7. Female patients on the *total database* for 2005 amounted to 675 814 (55.47%) and for 2006 the total female patients were 698 477 (55.47%). Male patients on the total database amounted to 540 874 (44.39%) in 2005, and 559 535 (44.44%) male patients were

recorded in 2006. There were 1 670 (0.14%) and 1 087 (0.09%) patients which gender was not recorded on the database, in 2005 and 2006 respectively.

The number of *female cancer patients* comprised 1.05% (2005) and 1.06% (2006) of the total number of female patients on the *total database*. Female cancer patients comprised 70.49% and 69.93% of the total number of cancer patients of the *cancer database* in 2005 and 2006 respectively. This will be discussed in more detail in section 4.6.

Male cancer patients encompassed 0.55% and 0.57% of the total number of male patients on the *total database*, for 2005 and 2006 respectively. Male cancer patients comprised 29.43% (2005) and 30.02% (2006) of the total number of cancer patients on the *cancer database*. This will be discussed in more detail in section 4.6. Furthermore, there were 5 cancer patients in 2005 and 8 cancer patients in 2006 for which a gender was not allocated. Refer to section 4.6 for more detail about the number of cancer patients on the database.

Female cancer patients increased with 0.01% (n=305 patients) and the number of *male cancer patients* with 0.02% (n=214) from 2005 to 2006. The number of *female cancer patients* on the medicine claims database for both study years was almost 3 times higher than the number of *male cancer patients* on the medicine claims database for both years (refer to section 4.6 for more information). Female cancer patients comprised 1.05% (n=7 065) and 1.06% (n=7 370) in 2005 and 2006 respectively of all female patients on the total database. Male cancer patients comprised 0.55% (n=2 950) and 0.57% (n=3 164) in 2005 and 2006 respectively of all male patients on the total database.

This had an influence on the number of *cancer medicine items* claimed as well as *the total cost of cancer medicine items* for both male and female patients. It can be expected that the total cost of cancer medicine items for female cancer patients was much higher than those of male cancer patients (refer to section 4.2.3.2).

Table 4.7 General cancer medicine prescribing patterns according to gender

Gender	Description	2005			2006		
		Total database (a)	Cancer database (b)	%* (c)	Total database	Cancer database	%*
Female	Total number of medicine items (N)	11 974 255	51 491	0.43	12 924 812	58 007	0.5
	Average cost per medicine item (R)	94.26±185.03	813.48 ± 1 732.82		93.86±219.20	1 038.83 ± 2 088.57	
	Total cost of medicine items (R)	1 128 652 112	41 886 928.36	3.71	1 213 068 356	60 259 502.56	5
	Total number of patients	675 814	7 065	1.05	698 477	7 370	1.06
Male	Total number of medicine items (N)	7 870 112	20 445	0.26	8 537 499	24 495	0.3
	Average cost per medicine item (R)	96.98±202.27	1 653.83 ± 2 189.61		97.54±240.49	1 976.42 ± 2 524.19	
	Total cost of medicine items (R)	763 226 111	33 812 534.51	4.43	832 725 542	48 412 394.95	5.8
	Total number of patients	540 874	2 950	0.55	559 535	3 164	0.57

**Percentage % (c) is determined by dividing b by a, and then multiplying it with 100.

** Unknown prevalence: 16 312 items/2 757 patients (total database); 36 items/13 patients (cancer database)

4.2.3.1 Prevalence of cancer medicine items according to gender (refer to table 4.7)

The total number of medicine items claimed in 2005 by female patients comprises 60% (n=11 974 255) of all medicine items claimed whilst 40% (n=7 870 112) of all medicine items on the total database were claimed by male patients. In 2006, the total number of medicine items claimed by female patients comprised 60.19% (n=12 924 812) of all cancer medicine items claimed, whilst medicine items claimed by male patients comprised 39.76% (n=24 495) of all medicine items claimed. According to the medicine claims database, 16 312 medicine items (0.08%) in 2005 and 10 763 medicine items (0.05%) in 2006 of the total database could not be allocated to a specific gender member. Because this includes less than 0.1% of all the medicine items, it will be excluded in further discussions.

In 2005, cancer medicine items claimed by female cancer patients comprised 0.43% (n=51 491) of the total database while cancer medicine items claimed by male cancer patients comprised 0.26% (n=20 445). Cancer medicine items claimed by female cancer patients comprised 0.5% (n=58 007) of medicine items claimed in 2006, whilst cancer medicine items claimed by male cancer patients comprised 0.3% (n=24 495) of the total database. Refer to section 4.6.1 for more on the prevalence of cancer medicine items.

There were 69 cancer medicine items for both study years that could not be allocated to a specific gender member. It contains less than 0.1% of all cancer medicine items and therefore will be excluded from further discussion.

4.2.3.2 Cost of cancer medicine items according to gender (refer to table 4.7)

On the *total database*, medicine items claimed by *female patients* comprised 59.26% (R1128 652 112).and 59.26% (R1213 068 356) of the *total cost* of all medicine items claimed during 2005 and 2006 respectively. The remaining 40.31% (R763 226 111) and 40.68% (R832 725 542) of the *total cost* of medicine items are comprised by medicine items claimed by *male patients* for 2005 and 2006 respectively.

The *total cost* of all *cancer medicine items* claimed during 2005 to females was R 41 886 928.36, which represented 3.71% of all medicine items (total database) claimed by females. In 2006, cancer medicine items claimed by females amounted to R60 259 502.56, which represented 4.97% of all medicine items claimed during 2006. Refer to section 4.6.2 for more on the cost of cancer medicine items.

As seen in table 4.7, the total cost of cancer medicine items claimed by males in 2005 was R 33 812 534.51, which comprised 4.43% of all medicine items on the database. The total cost of cancer medicine items claimed by males in 2006 comprised 5.81% (R48 412 394.95). Refer to section 4.6.2 for more on the cost of cancer medicine items.

Table 4.8 Cost prevalence index (CPI) for cancer medicine items for male and female patients

GENDER	Cancer database		Total database	
	2005	2006	2005	2006
Females	0.78	0.76	1.00	0.98
Males	1.5	1.6	1.00	1.03

*CPI values calculated from table 4.7

**For the purpose of this study CPI values higher than one (1) will indicate relatively expensive treatment (refer to paragraph 3.8.4.6)

The results in table 4.8 reveal that cancer medicine items claimed by *male cancer patients* are relatively more expensive than for females. The CPI of cancer medicine items for female *cancer patients* was 0.76 and 0.78 for 2005 and 2006 respectively. This is lower than the CPI of cancer medicine items claimed by *male cancer patients*. This could be an indication that cancer medicine items claimed by male cancer patients may be more expensive than those claimed by female cancer patients. This aspect is discussed further in section 4.8.2. The CPIs of the total database shows that there is mostly equilibrium between the cost and prevalence medicine items for both males and female patients. The percentages used to calculate the CPI values was determined by dividing the number of medicine items/cost of medicine items in each gender (from table 4.7) through the total number of medicine items/cost of medicine items (from table 4.2). This percentage was used to calculate the CPI values presented in Table 4.8.

Table 4.9 Effect sizes (d-values) of the costs of cancer drugs according to different databases and gender

	2005		2006	
	Cancer database (Female)	Cancer database (Male)	Cancer database (Female)	Cancer database (Male)
Total database (Female)	0.4		0.5	
Total database (Male)		0.7		0.7
Cancer database (Female)		0.4		0.4

**Effect sizes (d-values) calculated from the average costs in table 4.7*

***For the purpose of this study effect sizes (d-values) of 0.8 or higher will be assumed to have practical significance (refer to paragraph 3.8.4.5)*

As discussed an effect size (d-value) of 0.8 or higher will be assumed to have practical significance (refer to paragraph 3.8.4.5). Because all of the effect sizes (d-values) calculated from table 4.7 were lower than 0.8, it can be concluded that there was no practical significant differences between the average costs of cancer medicine items claimed by female cancer patients and male cancer patients. This is also the case between cancer medicine items and all medicine items prescribed to females and males. However, trends to a higher d-value (0.7) of medicine items claimed by male cancer patients were encountered with male cancer patients.

4.2.4 Costs and co-payments per prescription

In this section the total cost per prescription, total scheme amount and patient levy for both the *total database* and the *cancer database* will be discussed (refer to table 4.10).

- **Medical scheme amount per prescription:** The percentage of the total cost per prescription, which was paid by the patient's individual medical scheme.
- **Patient levy per prescription:** The percentage of the total cost per prescription, which was paid by the patient himself/herself.

Table 4.10 Cost per prescription

	2005				
	Total cost per prescription (R) (a)	Medical scheme cost per prescription (R) (b)	%* (c)	Patient levy per prescription (b)	%* (c)
Total database					
Number of prescriptions (N)	8 522 574				
Average cost (R)	222.16±463.13	195.83±443.06		26.33±102.69	
Total cost (R)	1 893 376 921	1 668 952 860	88.15	224 424 061	11.85
Cancer database					
Number of prescriptions (N)	58 682				
Average cost (R)	1 290.63±3 618.97	1 254.07±3 581.89		36.55±479.69	
Total cost (R)	75 736 630.77	73 591 554.82	97.17	2 145 075.95	2.83
2006					
	Total cost per prescription (R) (a)	Medical scheme cost per prescription (R) (b)	%* (c)	Patient levy per prescription	%* (c)
Total database					
Number of prescriptions (N)	90 46138				
Average cost (R)	226.28±557.49	196.54±540.41		29.74±103.96	
Total cost (R)	2 046 944 383	1 777 954 851	86.86	268 989 532	13.14
Cancer database					
Number of prescriptions (N)	64 919				
Average cost (R)	1 674.02±4 587.37	1 645.81±4 571.58		28.22±325.74	
Total cost (R)	108 675 842	106 844 112	98.31	1 831 730	1.69

*Percentage % (c) is determined by dividing b by a, and then multiplying it with 100.

The average cost per prescription for the total database was R222.15 ± 463.13 in 2005 and R226.28 ± 557.49 in 2006. The average cost per prescription containing one or more cancer medicine item was R1 290.63 ± 3 618.97 in 2005 and R1 674.02 ± 4 587.37 in 2006. The effect sizes (d-values) between the average cost of medicine items on the total database and cancer medicine items was calculated but showed no practical significance (refer to section 3.8.4.5).

The cost per prescription covered by the medical schemes for all medicine items (*total database*) amounted to 88.15% (2005) and 86.86% (2006) of the total cost of all medicine items claimed, of which the total patient levies made up 11.85% and 13.14% for all medicine items (refer to table 4.10).

For the *cancer medicine items*, the medical schemes was responsible for more than 97% of the total cost of all cancer medicine items claimed for both study years. The patient was only responsible for 2.83% (2005) and 1.69% (2006) of the total cost of all cancer medicine items claimed (refer to table 4.10). Relatively low difference in the average levy cost (paid by patients) between cancer medicine items and medicine items on the total database were recorded. The average cost of the levy amount paid by patients ranged between R26.33±102.69 and R36.55±479.69.

4.3 TOP TWENTY CANCER PRODUCTS ACCORDING TO HIGHEST

TOTAL COST, HIGHEST AVERAGE COST AND HIGHEST PREVALENCE.

The top twenty cancer products for 2005 and 2006 according to cost and prevalence will now be discussed. The twenty cancer medicine items with the highest total cost (refer to table 4.11), the twenty medicine items with the highest average cost (refer to table 4.12) as well as the twenty cancer products which were most frequently claimed (refer to table 4.13), will be included in the discussion.

The following cancer products were identified from table 4.11 - 4.13 according to the specific criteria and will then be discussed:

- ✓ **Gleevec 100mg Capsules®** were identified because of its high total cost (refer to table 4.11).
- ✓ **Herceptin®** was identified because of the steep increase between 2005 and 2006 in both the prevalence and cost of Herceptin® (refer to table 4.11, 4.12, 4.13).
- ✓ **Mabthera 500mg vials®** were identified because of the difference in prevalence between 2005 and 2006 (refer to table 4.13).
- ✓ **Arimidex 1mg tablets®** were identified because of its relatively low cost prevalence index and relatively high total cost (refer to table 4.11 & table 4.13).
- ✓ **Eloxatin 100mg vials®** were identified because of its relatively low prevalence but relatively high average and total cost (refer to table 4.11 & table 4.12).
- ✓ **Methotrexate 2.5mg tablets®** were identified because of its high prevalence (refer to table 4.13).
- ✓ **Taxol 300mg/50ml injection/Taxol 100mg/vial injection®** was identified because of its high average cost in 2006 (refer to table 4.12).

Table 4.11 Top 20 cancer products ranked according to total cost

2005										2006									
Rank	Trade name ®	ATC code	GI	Prev. (N) *	Prev. % ¹	Average cost (R)	Total Cost (R) **	Cost % ²	CPI	Rank	Trade name ®	ATC code	GI	Prev. (N) *	Prev. % ¹	Average cost (R)	Total Cost (R) **	Cost % ²	CPI
1	Gleevec 100mg Cap.	L01XE01	N	1051	1.46	6 676.04±1 495.82	7016518.26	9.26	6.34	1	Herceptin	L01XC03	N	1 609	1.95	7063.74±2313.89	11365564.90	10.46	5.36
2	Gemzar 1000mg Inj.	L01BC05	N	850	1.18	5 209.82±1 643.76	4428343.39	5.85	4.95	2	Mabthera 500mg vial	L01XC02	N	1 188	1.44	6646.53±1983.34	7896082.68	7.27	5.05
3	Herceptin	L01XC03	N	629	0.87	6 787.62±1 686.08	4 269 416.08	5.64	6.45	3	Gleevec 400mg Tab	L01XE01	N	988	1.20	6862.11±1486.14	6779762.10	6.24	5.21
4	Taxotere 20mg/1.5ml Inj.	L01CD02	N	826	1.15	4 979.19 ± 1626.04	4112813.30	5.43	4.73	4	Gemzar 1000mg Inj.	L01BC05	N	1 075	1.30	5206.21±1564.86	5 596680.67	5.15	3.95
5	Taxotere 80mg Inj.	L01CD03	N	629	0.87	6 013.86± 1392.21	3782592.27	4.99	5.71	5	Taxotere 80mg Inj.	L01CD03	N	880	1.07	6028.42±1279.80	5 305005.78	4.88	4.58
6	Mabthera 500mg vial	L01XC02	N	649	0.90	5 582.51±2 713.76	3623047.29	4.78	5.31	6	Arimidex 1mg Tab.	L02BG03	N	4 016	4.87	1221.41±146.69	4903970.70	4.51	0.93
7	Arimidex 1mg Tab.	L02BG03	N	2724	3.78	1 232.03±178.45	3356062.09	4.43	1.17	7	Taxotere 20mg/1.5ml Inj.	L01CD02	N	849	1.03	4680.60±1514.10	3973833.21	3.66	3.55
8	Xeloda 500	L01BC06	N	1005	1.40	3 334.03±939.66	3350699.37	4.42	3.17	8	Mabthera 100mg vial	L01XC02	N	668	0.81	5553.84±1960.39	3709962.66	3.41	4.22
9	Zoladex-Depot 10.8mg Inj.	L02AE03	N	943	1.31	3 043.84±235.36	2870343.62	3.79	2.89	9	Temodal 100mg	L01AX03	N	568	0.69	6259.02±2215.20	3 555125.11	3.27	4.75
10	Taxol 100mg/vial Inj.	L01CD01	O	525	0.73	5 308.89±2 055.55	2787165.62	3.68	5.04	10	Xeloda 500	L01BC06	N	1 096	1.33	3 174.09±886.30	3478 800.00	3.20	2.41
11	Campto 5ml 20mg/ml Inj.	L01XX19	N	474	0.66	5 458.80±1 657.45	2587469.78	3.42	5.19	11	Zoladex-Depot 10.8mg Inj.	L02AE03	N	1 029	1.25	3 029.53±92.42	3117388.14	2.87	2.30
12	Casodex 150mg Tab.	L02AE03	N	668	0.93	3 324.31±245.04	2220641.41	2.93	3.16	12	Casodex 150mg Tab.	L02AE03	N	908	1.10	3 300.21±419.22	2996 594.55	2.76	2.51
13	Casodex 50mg Tab.	L02AE03	N	1376	1.91	1 551.58±290.22	2134970.55	2.82	1.47	13	Campto 5ml 20mg/ml Inj.	L01XX19	N	495	0.60	5658.37±2117.52	2 800 891.64	2.58	4.30
14	Mabthera 100mg vial	L01XC02	N	407	0.57	5 072.99±1 576.61	2064707.17	2.73	4.82	14	Taxol 100mg/vial Inj.	L01CD01	O	364	0.44	7066.53±2267.54	2 572 215.53	2.37	5.37
15	Temodal 100mg	L01AX03	N	297	0.41	4 966.74±2 185.75	1517822.83	2.00	4.86	15	Gleevec 100mg Cap.	L01XE01	N	320	0.39	6512.94±1354.92	2084140.40	1.92	4.95
16	Caelyx 20mg/10ml	L01DB01	O	317	0.44	4 693.72±991.27	1487909.88	1.96	4.46	16	Caelyx 20mg/10ml	L01DB01	O	310	0.38	6681.05±2405.26	2071126.39	1.91	5.07
17	Gemzar 200mg Inj.	L01BC05	N	520	0.72	2 649.09±1 488.29	1377526.5	1.82	2.52	17	Casodex 50mg Tab.	L02AE03	N	1 291	1.56	1 554.35±312.44	2006662.43	1.85	1.18
18	Lucrin Depot 11.25	L02AE02	N	421	0.58	3 221.91±175.78	1356424.79	1.79	3.06	18	Eloxatin 100mg IV	L01XA03	N	286	0.35	6405.73±1946.03	1832038.57	1.69	4.86
19	Navelbine 50mg Inj.	L01CA04	N	286	0.40	3 781.49±1 215.21	1081505.62	1.43	3.59	19	Gemzar 200mg Inj.	L01BC05	N	570	0.69	2907.12±1471.04	1 657057.32	1.52	2.21
20	Eloxatin 100mg IV	L01XA03	N	169	0.23	5 677.28±2 102.70	959460.57	1.27	5.40	20	Navelbine 50mg Inj.	L01CA04	N	350	0.42	3893.06±1261.92	1 362571.81	1.25	2.96
Total				13 958	19		5 379 7971	71		Total				18 859	23		79 065 475	73	

¹Prev. % was determined by dividing Prev. (N)* by the total number of cancer medicine items claimed in the specific study year (refer to table 4.2).

²Cost % was determined by dividing Total cost (R)** by the total cost of cancer medicine items claimed in the specific study year (refer to table 4.2).

Table 4.12 Top 20 cancer products ranked according to average cost

2005										2006									
Rank	Trade name ®	ATC code	GI	Prev. (N) *	Prev. % ¹	Average cost (R)	Total Cost (R) **	Cost % ²	CPI	Rank	Trade name ®	ATC code	GI	Prev. (N) *	Prev. % ¹	Average cost (R)	Total Cost (R) **	Cost % ²	CPI
1	P&U Cytarabine CSV 25ml	L01BC01	Y	2	0.00	8562.96±1774.70	17 125.92	0.02	8.14	1	Taxol 300mg/50ml Inj.	L01CD01	O	81	0.10	8746.48±1607.57	708465.02	0.65	6.64
2	Herceptin	L01XC03	N	629	0.87	6787.62±1686.08	4269416.08	5.64	6.45	2	Taxol 100mg/vial Inj.	L01CD01	O	364	0.44	7066.53±2267.54	2572215.53	2.37	5.37
3	Gleevec 100mg Cap.	L01XE01	N	1051	1.46	6676.04±1495.82	7016518.26	9.26	6.34	3	Herceptin	L01XC03	N	1 609	1.95	7063.74±2313.89	11365564.90	10.46	5.36
4	Avastin 400mg/16ml vial	L01XC07	N	77	0.11	6584.18±1461.97	506 981.67	0.67	6.26	4	Gleevec 400mg Tab	L01XE01	N	988	1.20	6862.11±1486.14	6779762.10	6.24	5.21
5	Taxotere 80mg Inj.	L01CD03	N	629	0.87	6013.66±1392.21	3782592.27	4.99	5.71	5	Avastin 100mg/4ml Inf.	L01XC07	N	83	0.10	6813.68±3290.78	565535.06	0.52	5.17
6	Avastin 100mg/4ml vial	L01XC07	N	96	0.13	5978.80±2196.55	506 981.67	0.67	5.02	6	Caelyx 20mg/10ml	L01DB01	O	310	0.38	6681.05±2405.26	2071126.39	1.91	5.07
7	Biolyse Paclitaxel for Inj. 5ml	L01CD01	Y	14	0.02	5750.44±1452.54	80 506.21	0.11	5.46	7	Avastin 400mg/16ml vial	L01XC07	N	194	0.24	6652.37±1138.32	1290559.01	1.19	5.05
8	Intron A HSA-free 10ml	L03AB05	N	6	0.01	5724.60±1604.11	34 347.58	0.05	5.44	8	Mabthera 500mg vial	L01XC02	N	1 188	1.44	6646.53±1983.34	7896082.68	7.27	5.05
9	Eloxatin 100mg IV	L02XA03	N	169	0.23	5677.28±2102.70	959 460.57	1.27	5.40	9	Gleevec 100mg Cap.	L01XE01	N	320	0.39	6512.94±1354.92	2084140.40	1.92	4.95
10	Mabthera 500mg vial	L01XC02	N	649	0.90	5582.51±2113.76	3623047.29	4.78	5.31	10	Eloxatin 100mg IV	L01XA03	N	286	0.35	6405.73±1946.03	1832038.57	1.69	4.86
11	Taxol 300mg/50ml Inj.	L01CD01	O	23	0.03	5553.65±1631.13	127 733.85	0.17	5.28	11	Temodal 100mg	L01AX03	N	568	0.69	6259.02±2215.20	3555125.11	3.27	4.75
12	Campto 5ml 20mg/ml Inj.	L01XX19	N	474	0.66	5458.80±1657.45	2 58746978	3.42	5.19	12	Eloxatin 100mg/20ml Inf	L01XA03	N	71	0.09	6188.21±1965.92	439363.22	0.40	4.70
13	Chiron IL-2 vial	L03AC01	N	113	0.16	5426.49±1509.36	613 193.92	0.81	5.16	13	Avastin 400mg/16ml Inf.	L01XC07	N	157	0.19	6130.75±2214.41	962528.06	0.89	4.66
14	Anzatax 150mg/25ml	L01CD01	Y	21	0.03	5315.36±2154.88	111 622.57	0.15	5.05	14	Eloxatin (sect 21) 100mg/20ml	L01XA03	N	182	0.22	6097.25±2112.90	1109700.00	1.02	4.63
15	Taxol 100mg/vial Inj.	L01CD01	O	525	0.73	5308.89±2055.55	2787165.62	3.68	5.04	15	Chiron IL-2 vial	L03AC01	N	187	0.23	6085.37±732.01	1137963.67	1.05	4.62
16	Gemzar 1000mg Inj.	L01BC05	N	850	1.18	5209.82±1643.76	4428343.39	5.85	4.95	16	Taxotere 80mg Inj.	L01CD03	N	880	1.07	6028.42±1279.80	5305005.78	4.88	4.58
17	Hycamtin Inf. 5ml	L01XX17	N	33	0.05	5205.80±2169.88	171 791.25	0.23	4.95	17	Biolyse Paclitaxel for Inj. 5ml	L01CD01	Y	43	0.05	5818.21±2829.87	250183.00	0.23	4.42
18	Temodal 100mg	L01AX03	N	297	0.41	5110.51±2042.17	1517822.83	2.00	4.86	18	Anzatax 150mg/25ml	L01CD01	Y	72	0.09	5730.13±1627.85	412569.27	0.38	4.35
19	Mabthera 100mg vial	L01XC02	N	407	0.57	5072.99±1576.61	2064707.17	2.73	4.82	19	Campto 5ml 20mg/ml Inj.	L01XX19	N	495	0.60	5658.37±2117.52	2800891.64	2.58	4.30
20	Taxotere 20mg/1.5ml Inj.	L01CD02	N	826	1.15	4979.19±1626.04	4 112 813.3	5.43	4.73	20	Roferon A 0.6ml penfill	L03AB04	N	55	0.07	5642.30±1411.39	310326.34	0.29	4.28
Total				6891	10		36 644 544	48		Total				8133	10		53449146	49	

¹Prev. % was determined by dividing Prev. (N)* by the total number of cancer medicine items claimed in the specific study year (refer to table 4.2).

²Cost % was determined by dividing Total cost (R)** by the total cost of cancer medicine items claimed in the specific study year (refer to table 4.2).

Table 4.13 Top 20 cancer products ranked according to prevalence

2005										2006									
Rank	Trade name ®	ATC code	GI	Prev. (N) ¹	Prev. % ¹	Average cost (R)	Total Cost (R) ²	Cost % ²	CPI	Rank	Trade name ®	ATC code	GI	Prev. (N) ¹	Prev. % ¹	Average cost (R)	Total Cost (R) ²	Cost % ²	CPI
1	Methotrexate 2.5mg Tab	L01BA01	O	23856	33.15	31.36±14.31	748132.75	0.99	0.03	1	Methotrexate 2.5mg Tab	L01BA01	O	26697	32.35	31.54±14.06	841923.49	0.77	0.02
2	Neophedan 20mg Tab.	L02BA01	Y	5535	7.69	146.09±18.53	819660.39	1.08	0.14	2	Neophedan 20mg Tab.	L02BA01	Y	5080	6.16	147.68±19.33	750227.29	0.69	0.11
3	Kessar 20mg Tab.	L02BA01	Y	5148	7.15	119.01±12.90	612677.12	0.81	0.11	3	Kessar 20mg Tab.	L02BA01	Y	4634	5.62	117.64±13.96	545158.74	0.50	0.09
4	Arimidex 1mg Tab.	L02BG03	N	2724	3.78	1232.03±178.45	3356062.09	4.43	1.17	4	Arimidex 1mg Tab.	L02BG03	N	4015	4.87	1221.41±146.69	4903970.70	4.51	0.93
5	Androcur 10mg Tab.	G03HA01	N	2683	3.73	246.70±65.47	661902.06	0.87	0.23	5	Androcur 10mg Tab.	G03HA01	N	2630	3.19	243.33±75.26	639953.05	0.59	0.18
6	Cipla Cyproterone acetate	G03HA01	Y	1675	2.33	184.39±154.14	308849.15	0.41	0.18	6	Herceptin	L01XC03	N	1609	1.95	7063.74±2313.89	11365564.90	10.46	5.36
7	Casodex 50mg Tab.	L02BB03	N	1376	1.91	1551.58±290.22	2134970.55	2.82	1.47	7	Cipla Cyproterone acetate	G03HA01	Y	1490	1.81	199.02±154.40	296537.12	0.27	0.15
8	Endoxan 1000mg Inj.	L01AA01	O	1089	1.51	105.81±44.95	115227.56	0.15	0.10	8	Endoxan 1000mg Inj.	L01AA01	O	1384	1.68	108.51±60.19	150178.89	0.14	0.08
9	Gleevec 100mg Cap.	L01XE01	N	1051	1.46	6676.04±1495.82	7016518.26	9.26	6.34	9	Abic Flurouracil 500mg/10ml	L01BC06	Y	1294	1.57	163.92±115.31	212117.32	0.20	0.12
10	Xeloda 500	L01BC06	N	1005	1.40	3334.03±939.66	3350699.37	4.42	3.17	10	Casodex 50mg Tab.	L02BB03	N	1291	1.56	1554.35±312.44	2006662.43	1.85	1.18
11	Zoladex-Depot 10.8mg Inj.	L02AE03	N	943	1.31	3043.84±235.36	2870343.62	3.79	2.89	11	Mabthera 500mg vial	L01XC02	N	1188	1.44	6646.53±1983.34	7896082.68	7.27	5.05
12	Abic Flurouracil 500mg/10ml	L01BC06	Y	919	1.28	118.46±93.72	108867.29	0.14	0.11	12	Xeloda 500	L01BC06	N	1096	1.33	3174.09±886.30	3478800.00	3.20	2.41
13	Hydrea 500mg Cap.	L01XX05	N	862	1.20	132.11±55.16	113876.91	0.15	0.13	13	Gemzar 1000mg Inj.	L01BC05	N	1075	1.30	5206.21±1564.86	5596680.67	5.15	3.95
14	Gemzar 1000mg Inj.	L01BC05	N	850	1.18	5209.82±1643.76	4428343.39	5.85	4.95	14	Zoladex-Depot 10.8mg Inj.	L02AE03	N	1029	1.25	3029.53±92.42	3117388.14	2.87	2.30
15	Taxotere 20mg/1.5ml Inj.	L01CD02	N	826	1.15	4979.19±1626.04	4112813.30	5.43	4.73	15	Gleevec 400mg Tab.	L01XE01	N	988	1.20	6862.11±1486.14	6779762.10	6.24	5.21
16	Fluoroblastin 500mg/10ml	L01BC06	O	740	1.03	171.87±127.98	127185.80	0.17	0.16	16	Hydrea 500mg Cap.	L01XX05	N	960	1.16	135.64±57.45	130217.24	0.12	0.10
17	Casodex 150mg Tab.	L02AE03	N	668	0.93	3324.31±245.04	2220641.41	2.93	3.16	17	Casodex 150mg Tab.	L02AE03	N	908	1.10	3300.21±419.22	2996594.55	2.76	2.51
18	Mabthera 500mg vial	L01XC02	N	649	0.90	5582.51±2713.76	3623047.29	4.78	5.31	18	Taxotere 80mg Inj.	L01CD03	N	880	1.07	6028.42±1279.80	5305005.78	4.88	4.58
19	Herceptin	L01XC03	N	629	0.87	6787.62±1686.08	4269416.08	5.64	6.45	19	Taxotere 20mg/1.5ml Inj.	L01CD02	N	849	1.03	4680.60±1514.10	3973833.21	3.66	3.55
20	Taxotere 80mg Inj.	L01CD02	N	629	0.87	6013.66±1392.21	3782592.27	4.99	5.71	20	Endoxan 200mg Inj.	L01AA01	O	711	0.86	64.11±41.27	45584.59	0.04	0.05
Total				53857	75		44781827	69		Total				59808	72		61032243	56	

¹Prev. % was determined by dividing Prev. (N)* by the total number of cancer medicine items claimed in the specific study year (refer to table 4.2).

²Cost % was determined by dividing Total cost (R)** by the total cost of cancer medicine items claimed in the specific study year (refer to table 4.2).

4.3.1. Gleevec 100mg Capsules®

- In 2005, Gleevec 100mg capsules® cancer products (n=1051) had the **highest total cost** (9.26%) of all the cancer products claimed through the medicine claims database (refer to table 4.11). In 2006, the total cost of Gleevec® 100mg Capsules decreased with 4.31% and comprised 4.95% (15th position on table 4.11) of the total cost of all cancer products on the database in 2006.
- In 2005, the average cost of Gleevec 100mg capsules® amounted to R6676.04 ± 1495.82 with a cost prevalence index (CPI) of 6.34, which is relatively high (refer to section 3.8.4.6). In 2006, the average cost of Gleevec 100mg capsules® decreased to R6512.94 ± 1354.92 with a CPI of 4.95 (refer to table 4.11 and table 4.12), which is still high and indicate that it is a relative expensive drug.
- The prevalence of Gleevec 100mg capsules® amounted to 1.46% of the total number of cancer products claimed in 2005 (refer to table 4.13). In 2006, the prevalence of Gleevec 100mg capsules® dropped with 1.07% to 0.39% of the total number of cancer products claimed. Gleevec 100mg capsules® were not included in the prevalence top twenty cancer products for 2006 (refer to table 4.13).
- The active ingredient in Gleevec 100mg Capsules® is imatinib. This is a protein-tyrosine kinase inhibitor (L01XE01 – refer to appendix A).
- Gleevec 100mg Capsules® (Imatinib) is used for the treatment of *newly diagnosed chronic myeloid leukaemia (CML) as well as CML in blast crisis, accelerated phase or in chronic phase* after failure of interferon-alpha therapy (Gibbon *et al.*, 2008; SAEPI, 2008; Sweetman, 2008).

4.3.2 Herceptin®

- In 2005, Herceptin® was claimed only 629 times (0.87% of all cancer medicine items), but had the **second highest average cost** (R6787.62 ± 1686.08) and a CPI of 6.45 (refer to table 4.12).
- The **average cost** of Herceptin® increased from R6 787.62 ± 1 686.08 in 2005 to R7 063.74 ± 2 313.89 in 2006 and the CPI remained high (5.36) and was **3rd highest** after Taxol 300mg/50ml Injection and Taxol 100mg/vial

Injection (see discussion of Taxol below) in the *average cost top 20* cancer products in 2006.

- In table 4.11, Herceptin® moved from the **3rd position** in 2005 to the **1st position** in 2006 with a **total cost** of R11 365 564.90. As calculated from table 4.12, the prevalence of Herceptin® increased with 1.08% (n=980) and the total cost of Herceptin® increased with 4.82% (R7 096 148.82) from 2005 to 2006.
- The active ingredient in Herceptin® is Trastuzumab, which is a monoclonal antibody specifically working on the human epidermal growth factor receptor 2 (HER2) (L01XC03 - refer to Appendix A).
- Herceptin® (Trastuzumab) is indicated for *metastatic breast cancer* in patients with tumours over expressing the human epidermal growth factor receptor 2 (HER2). It is also given in *early breast cancer* after surgery, chemotherapy, and radiotherapy (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008).
- See section 1.2 and section 2.10.1 for more information on Herceptin® and section 2.8.2.1 on how Discovery Health pays for Herceptin®.

4.3.3 Mabthera 500mg vial®

- Mabthera 500 mg vials® had the **6th highest total cost** (R3 623 047.29) in 2005 and were claimed 649 times, which accounts for 4.78% of the total cost of all cancer medicine items and 0.9% prevalence of all cancer medicine items claimed.
- In 2006, Mabthera 500mg vials® had the **2nd highest total cost** (refer to table 4.11), with 1 188 items claimed (represented 1.44% prevalence of all cancer medicine items) and a total cost of R7 896 082.68 (7.27% of total cost of all cancer medicine items). This means that the prevalence of Mabthera 500mg vials® increased with 0.54% (n=539) and the total cost of Mabthera 500mg vials® increased with 2.49% (R4 273 035) from 2005 to 2006.
- The *average cost* of Mabthera 500mg vials® was R5 582.51 ± 2 713.76 in 2005 and increased to R6 646.53 ± 1 983.34 in 2006. As seen in table 4.11 and table 4.12, the CPI of Mabthera 500mg vials® was 5.31 and 5.05 in 2005 and 2006 respectively.

- The active ingredient in Mabthera 500mg vials® is Rituximab, a chimeric monoclonal antibody to CD20 antigen (L01XC02 – refer to Appendix A).
- Mabthera 500mg vials® (Rituximab) is used in the treatment of *Non-Hodgkins lymphomas*. It can be used as mono-therapy in *relapsed or refractory low-grade or follicular lymphoma*, or as first-line treatment with combination therapy, such as CVP (cyclophosphamide, vincristine, and prednisolone) (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008).

4.3.4 Arimidex 1mg tablets®

- From table 4.13 it can be seen that Arimidex 1mg tablets® are the cancer products with the **4th highest prevalence** during 2005 (n=2 724) and 2006 (n=4 015).
- Arimidex 1mg tablets® are also included in the *total cost top twenty* cancer products (refer to table 4.11). Of all the cancer products included in the *total cost top twenty* cancer products, Arimidex 1mg tablets® had the **lowest average cost** for both 2005 (R1 232.03 ± 178.45) and 2006 (R1 221.41 ± 146.69).
- The CPI of Arimidex 1mg tablets® were 1.17 in 2005 and 0.93 in 2006. This is the **lowest CPI** included in the *total cost top twenty* cancer products. This CPI is still higher than 1.00 (refer to section 3.8.4.6) and therefore Arimidex 1mg tablets® is a relatively expensive drug.
- The active ingredient in Arimidex 1mg tablets® is anastrozole. Anastrozole is a potent and selective non-steroidal inhibitor of the aromatase (estrogen synthetase) system (L02BG03 – refer to Appendix A), which converts adrenal androgens to estrogens in peripheral tissue (Sweetman, 2008).
- Arimidex 1mg tablets® (anastrozole) are used in the treatment of *advanced or locally advanced breast cancer* and as adjuvant treatment in *early breast cancer* in postmenopausal woman (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008).

4.3.5 Eloxatin 100mg IV®

- Eloxatin 100mg IV® had the **lowest prevalence** of the *total cost top twenty* cancer products but still had relatively high total cost (refer to table 4.11),

during both study years. In 2005, the prevalence amounted to 169 (0.23% of all cancer medicine items) and to 286 during 2006 (0.35% of all cancer medicine items). Eloxatin 100mg IV® is thus not included in the *prevalence top twenty* cancer products.

- Even though Eloxatin 100mg IV® had the lowest prevalence of all the *total cost top twenty* cancer products (refer to table 4.12), the **average cost** of these cancer products was relatively high. Of all the items included in the *average cost top twenty* cancer products (refer to table 4.12), Eloxatin 100mg IV® had the **9th highest average cost** in 2005 (R5 677.28 ± 2 102.70) and the **10th highest average cost** in 2006 (R6 405.73 ± 1 946.03).
- The CPI of Eloxatin 100mg IV® were 5.40 in 2005 and 4.86 in 2006 which was relatively high and was therefore a relatively expensive drug (refer to section 3.8.4.6).
- Oxaliplatin is the active ingredient included in Eloxatin 100mg IV®. Oxaliplatin is a new generation platinum compound (L01XA03 – refer to Appendix A), related to cisplatin (L01XA01).
- Eloxatin 100mg vial® (oxaliplatin) is used in the treatment of *metastatic colorectal cancer*, together with fluorouracil and folinic acid. It is also used for adjuvant treatment of *stage III (DUKE C) colon cancer* (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008).

4.3.6 Methotrexate 2.5mg tablets®

- Methotrexate 2.5mg tablets® were claimed the most (**highest prevalence**) of *all cancer medicine items*, both in 2005 and 2006. Methotrexate 2.5mg tablets® alone comprised 33.15% (n=23 856) and 32.35% (n=26 697) respectively of *all cancer medicine items* claimed in 2005 and 2006. From table 4.13 it can be calculated that Methotrexate 2.5mg tablets® was claimed more than 4 times more often than the second most frequently claimed cancer medicine item, Neophedan 20mg tablets®.
- The *total cost* of Methotrexate 2.5mg tablets® accounted for less than 1% of the total cost of *all cancer medicine items* in both study years. In 2005, it comprised 0.99% (R748 132.75) and in 2006, 0.77% (R841 923.49) of the total cost of all cancer medicine items (refer to table 4.13).

- The CPI of Methotrexate 2.5mg tablets® was relatively low in 2005 (0.03) and in 2006 (0.02) and this indicates that Methotrexate 2.5mg tablets® is a relatively inexpensive drug (refer to section 3.8.4.6).
- Methotrexate 2.5mg tablets® had a *relatively low average cost* compared to other cancer products. In 2005, the average cost per medicine item for Methotrexate 2.5mg tablets® was R31.36 ± 14.31 and in 2006 it was R31.54 ± 14.06 (refer to table 4.13).
- Methotrexate 2.5mg tablets® are *original cancer products*.
- The active ingredient included in Methotrexate 2.5mg tablets® is methotrexate. Methotrexate, a folic acid analogue, is an anti-metabolite (L01BA01 – refer to Appendix A).
- Methotrexate is used:
 - in the management and treatment of *acute lymphoblastic leukaemia*;
 - as part of curative regimens of *choriocarcinoma* and other *gestational trophoblastic tumours*;
 - as adjuvant therapy of *osteosarcoma and breast cancer*;
 - in a wide variety of neoplasms including tumours of the *head, neck, breast and bone* (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008).

Please note: Methotrexate is also used in other diseases such as *rheumatoid arthritis, asthma and in severe and refractory psoriasis* (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). The medicine claims database used for this study did not distinguish between different diagnoses (ICD10 diagnosis not complete). This could be part of the explanation of the high prevalence of Methotrexate 2.5mg tablets® on the database. This is seen as a limitation for this study (see section 5.3). According to Duminy (2008), the usage of methotrexate for cancer treatment is mostly limited to intravenous usage.

4.3.7 Taxol 300mg/50ml injection® / Taxol 100mg/vial injection®

- In 2005, Taxol 300mg/50ml® had the **11th highest average cost** (R5 553.65 ± 1 631.13) of *all cancer medicine items*. In 2006, the average cost of Taxol 300mg/50ml® injection increased and had the **highest average cost** (R8 746.48 ± 1 607.57) of *all cancer medicine items* claimed through the medicine claims database. This was a relatively large increase between 2005 and 2006, with a *d-value* of 1.9 between the average costs of these medicine items (refer to table 4.12).
- In 2005, the Taxol 100mg/vial® injection had the **15th highest average cost** (R5 308.89 ± 2 055.55) of *all cancer medicine items* claimed. In 2006, the average cost of the Taxol 100mg/vial® injection increased and had the **2nd highest average cost** (R7 066.53 ± 2 267.54) of *all cancer medicine items* claimed through the medicine claims database (refer to table 4.12). This was also a practical significant increase with a *d-value* of 0.9 between the average costs of the medicine items during the two study years.
- In 2005, the Taxol 300mg/50ml® Injection comprised 0.03% (n=23) of *all cancer medicine items* claimed while in 2006, it comprised 0.10% (n=81) of *all cancer medicine items* claimed. It was thus not included in the *prevalence top twenty* cancer products (refer to table 4.13).
- Taxol 100mg/vial® injections comprised 0.73% (n=525) of *all cancer medicine items* claimed in 2005, while in 2006 the **prevalence** of Taxol 100mg/vial® injections decreased with 0.29% to 0.44% (n=364) of *all cancer medicine items* claimed. It was also not included in the *prevalence top twenty* cancer products (refer to table 4.13).
- The Taxol 300mg/50ml® injection was not included in cancer products according to the total cost (refer to table 4.11). This is because of the low prevalence of Taxol 300mg/50ml® injections (refer to table 4.13). The **total cost** of the Taxol 300mg/50ml injection® amounted to 0.17% (R127 733.85) of all cancer medicine items in 2005 and 0.65% (R2 572 215.53) of all cancer medicine items in 2006.
- The Taxol 100mg/vial® injection was included in the *total cost top twenty* (refer to table 4.11) for both 2005 and 2006. The **total cost** of the Taxol 100mg/vial® injection amounted to 3.68% (R2 787 165.62) of all cancer

medicine items in 2005 and 2.37% (R2 572 215.53) of all cancer medicine items in 2006.

- Taxol 300mg/vial® injections and Taxol 100mg/vial® injections are original medicine items.
- The active ingredient of the Taxol 300mg/50ml® and Taxol 100mg/vial® injection is paclitaxel. These medicine items are indicated for:
 - palliative treatment of stage 3 or 4 *advanced local carcinoma of the ovary* after surgical resection, in combination with cisplatin/carboplatin;
 - palliative management of *metastatic carcinoma of the ovary* after failure of first line or subsequent chemotherapy;
 - treatment of *metastatic carcinoma of the breast* after failure of a combination chemotherapy or relapse within 6 months of adjuvant chemotherapy;
 - palliative treatment of *advanced non-small cell lung cancer* in patients who are not candidates for potentially curative surgery and/or radiation (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008).

4.3.8 P&U Cytarabine CSV 25ml®

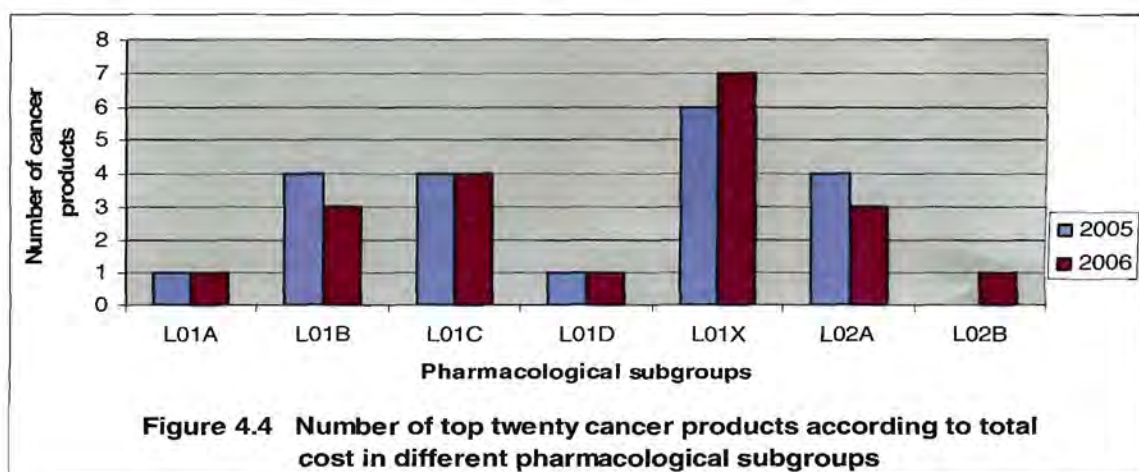
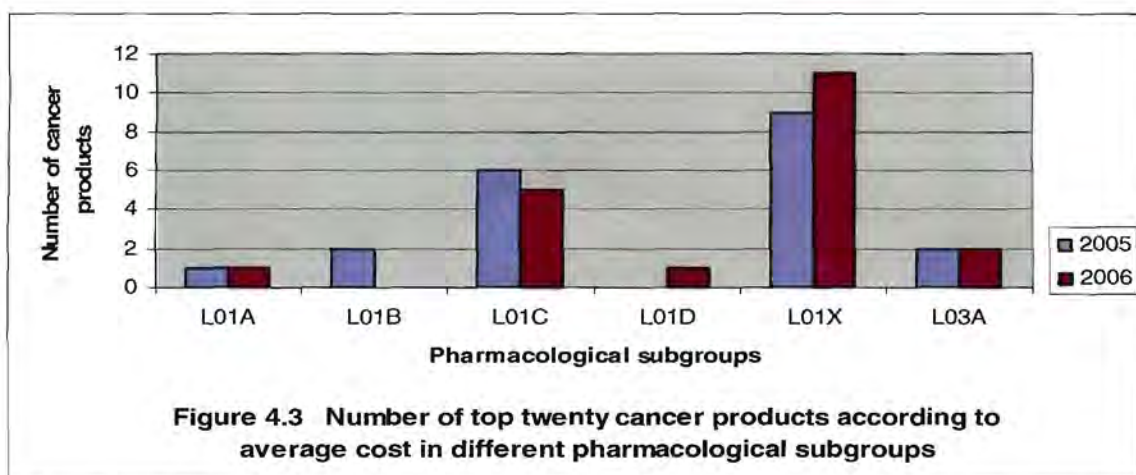
- P&U Cytarabine CSV 25ml® is a *generic cancer medicine item* and had the **highest average cost** in 2005 (refer to table 4.12). These medicine items were only claimed twice in 2005 and were not at all included in the *average cost top 20* in 2006. The total cost of P&U Cytarabine CSV® 25ml for 2005 was only R17 125 (0.02% of total cost of all cancer medicine items). The CPI of P&U Cytarabine CSV 25ml® for 2005 was 8.14, which is relatively high (refer to section 3.8.4.6).
- The active ingredient in P&U Cytarabine CSV 25ml® is cytarabine. Cytarabine, a pyrimidine nucleoside analogue, is an anti-metabolite antineoplastic (L01BC01 – refer to Appendix A).
- Cytarabine (P&U Cytarabine CSV 25ml®) is mainly used in the management of *leukaemias*, especially *acute myeloid leukaemia (AML)*. It may be used alone or in combination with other cancer drugs. These medicine items are

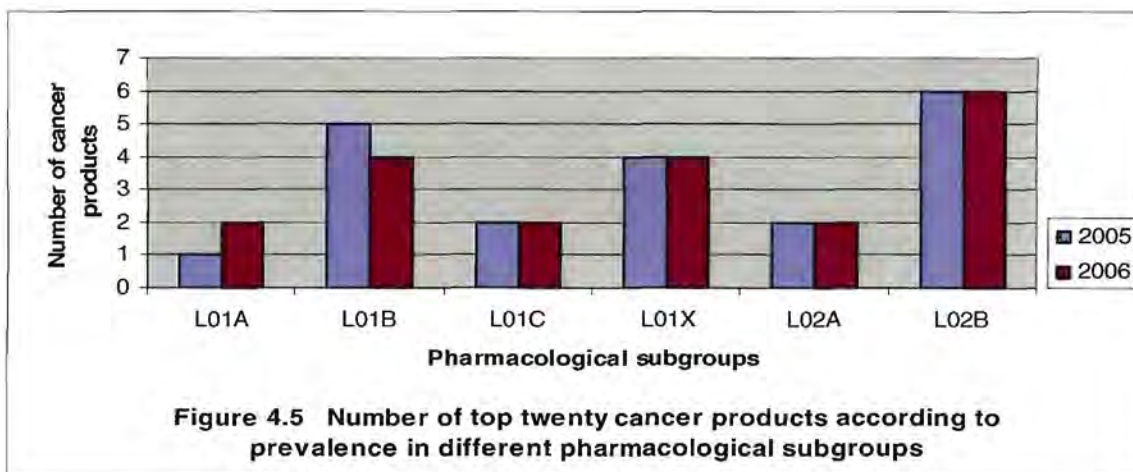
more effective when used in combination with other therapies (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008).

4.3.9 Other insights derived from tables 4.11 – 4.13

4.3.9.1 Pharmacological classification

Figure 4.3 – 4.5 shows the distribution of the different *top twenty cancer products* between the different pharmacological subgroups (refer to Appendix A for ATC classification and to section 4.4 for more information on the classification of the cancer medicine items):

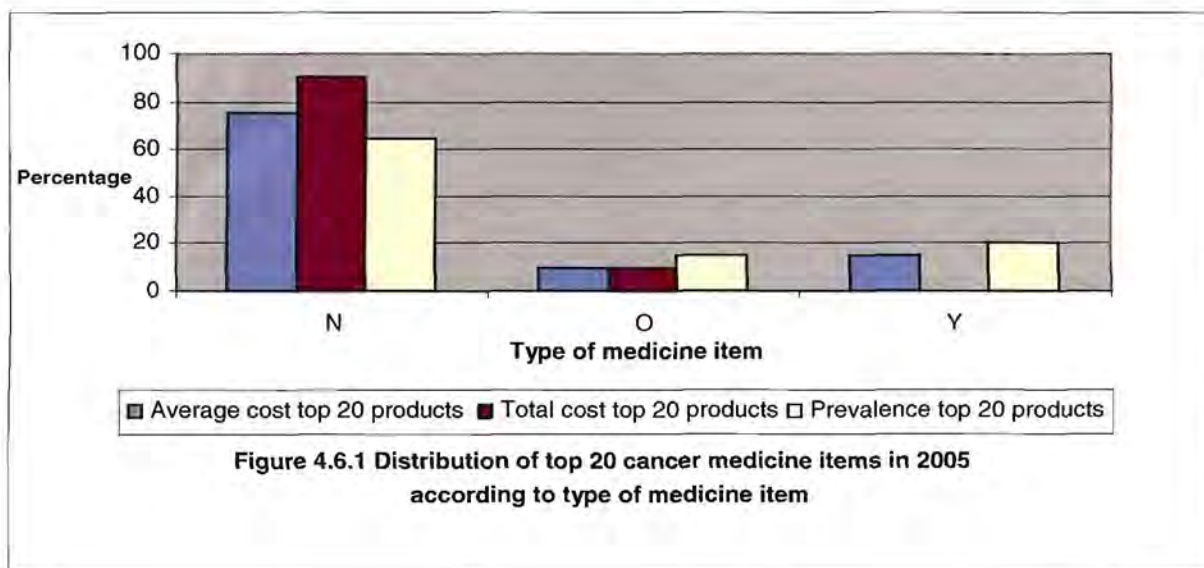


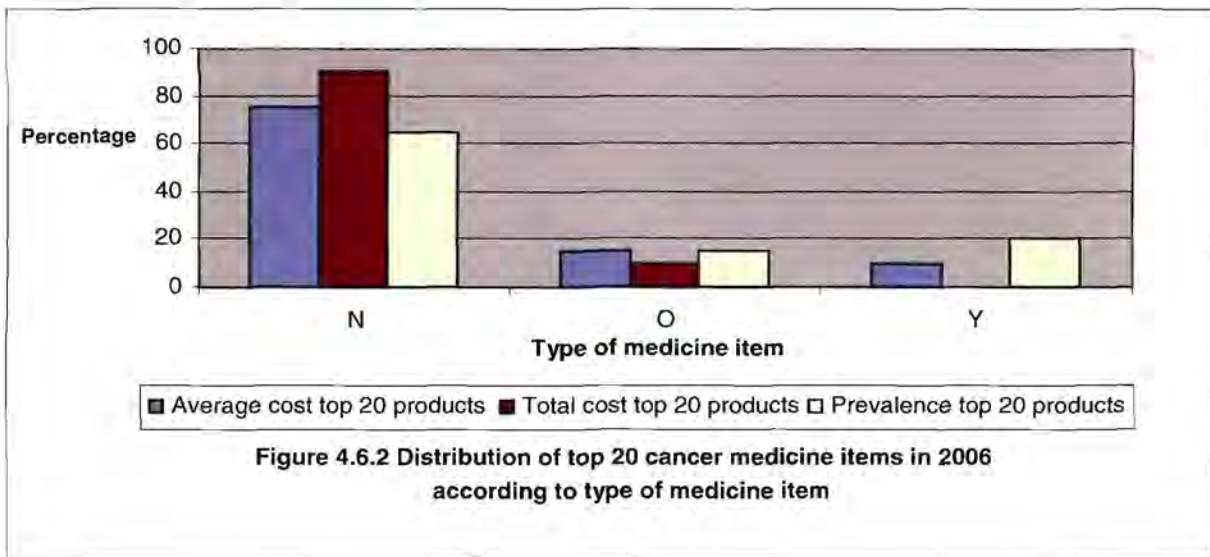


As seen in figure 4.3 and figure 4.4, the pharmacological subgroups L01X (other antineoplastic agents) and L01C (plant alkaloids and other natural products) contained more than half of the *top twenty products* according to average cost and total cost. Refer to section 4.4 for more information and a discussion of the classification of cancer medicine items. From figure 4.5 it can be calculated that cancer medicine items from the pharmacological subgroup L02B (hormone antagonists and related agents) represented 60% of the prevalence of the top twenty cancer medicine items (refer to figure 4.5).

4.3.9.2 Types of cancer medicine items

Figure 4.6.1 and figure 4.6.2 shows the distribution of *no-generic* ("N"), *original* ("O") and *generic* ("Y") cancer products in the top twenty cancer products for both 2005 and 2006. (Refer to section 3.2 for definition of *no-generic*, *original* and *generic* cancer medicine items).





4.3.9.2.1 No-generic cancer medicine items ("N")

For both 2005 and 2006:

- ✓ 75% of the cancer products included in the **top twenty products according to average cost** were *cancer products with no generic medicine item available* (also refer to table 4.12).
- ✓ 90% of the cancer products included in the **top twenty products according to total cost** were *cancer products with no generic medicine items available* (also refer to table 4.11).
- ✓ 65% of the cancer products included in the **top twenty products according to prevalence** were *cancer products with no generic medicine item available* (refer to table 4.13).

4.3.9.2.2 Original cancer medicine items ("O")

For 2005:

- ✓ 10% of the cancer products included in the **top twenty products according to average cost** were *original cancer products*. These cancer products were the Taxol 300mg/50ml injection and Taxol 100mg/vial injection (see table 4.12).
- ✓ 10% of the cancer products included in the **top twenty products according to total cost** were *original cancer products* (refer to table 4.11).

- ✓ 15% of the cancer products included in the **top twenty products according to prevalence** were *original cancer products*. These cancer products were Methotrexate 2.5mg tablets®, the Endoxan 1000mg injection® and Fluroblastin 500mg/10ml® (see table 4.13).

For 2006:

- ✓ 15% of the cancer products included in the **top twenty products according to average cost** were *original cancer products*. These were the Taxol 300mg/50ml injection, the Taxol 100mg/vial injection and Caelyx 20mg/10ml (refer to table 4.12).
- ✓ 10% of the cancer products included in the **top twenty products according to total cost** were *original cancer products* (refer to table TOTAL). These were the Taxol 100mg/vial injection and Caelyx 20mg/10ml (refer to table 4.11).
- ✓ 15% of the cancer products included in the **top twenty products according to prevalence** were *original cancer products*. These cancer products were Methotrexate 2.5mg tablets®, the Endoxan 1000mg injection® and the Endoxan 200mg injection® (see table 4.13).

4.3.9.2.3 Generic cancer medicine items ("Y")

For 2005:

- ✓ 15% of the cancer products included in the **top twenty products according to average cost** were *generic cancer products*. These were P&U Cytarabine CSV 25ml®, Biolyse Paclitaxel for Injection 5ml® and Anzatax 150mg/25ml® (refer to table 4.12).
- ✓ No *generic cancer products* were included in the **top twenty products according to total cost** (refer to table 4.11).
- ✓ 20% of the cancer products included in the **prevalence cost top twenty products** were *generic cancer products*. These were Neophedan 20mg tablets®, Kessar 20mg tablets®, Cipla Cyproterone acetate® and Abic Flurouracil 500mg/10ml® (refer to table 4.13).

For 2006:

- ✓ 10% of the cancer products included in the **top twenty products according to average cost** were *generic cancer products*. These products were Biolyse Paclitaxel for Injection 5ml and Anzatax 150mg/25ml (refer to table 4.12).
- ✓ No *generic cancer products* were included in the **top twenty products according to total cost** (refer to table 4.11).
- ✓ 20% of the cancer products included in the **prevalence cost top twenty products** were *generic cancer products*. These were Neophedan 20mg tablets®, Kessar 20mg tablets®, Cipla Cyproterone acetate® and Abic Flurouracil 500mg/10ml® (refer to table 4.13).

4.3.9.3 Total cost percentage

- The **top twenty cancer products according to total cost** comprised 71% (R53 797 971) and 73% (R79 065 475) of the total cost of all cancer medicine items on the medicine claims database, for 2005 and 2006 respectively (refer to table 4.11).
- The *total cost percentage* of the **top twenty cancer products according to average cost** represented 48% (R36 644 544) and 49% (R53 449 146) of all cancer medicine items, for 2005 and 2006 respectively (refer to table 4.12).
- The *total cost percentage* of the **top twenty cancer products according to prevalence** were 59% (R44 781 827) and 56% (R61 032 342) of all cancer medicine items for 2005 and 2006 respectively (refer to table 4.13).

4.3.9.4 Total prevalence percentage

- The **top twenty cancer products according to total cost** represented 19% (n=13 958) and 23% (n=18 859) of the total number of all cancer medicine items on the medicine claims database for 2005 and 2006 respectively (refer to table 4.11).
- The **top twenty cancer products according to average cost** represented 10% of the total number of cancer medicine items on the medicine claims database, for both 2005 (n=6 891) and 2006 (n=8 133) respectively (refer to table 4.12).

- The **top twenty cancer products according to prevalence** represented 75% (n=53 857) and 72% (n=59 808) of all cancer medicine items for 2005 and 2006 respectively (refer to table 4.13).

4.4 CLASSIFICATION OF CANCER MEDICINE

This section will focus on the ATC classification of cancer medicine and the prevalence and cost of cancer medicine items in the different subgroups.

4.4.1 Classification of cancer medicine items according to therapeutic subgroups

According to the ATC index, antineoplastic and immunomodulating agents (L) can be divided into four main therapeutic subgroups:

- Antineoplastic agents (L01)
- Endocrine therapy (L02)
- Immunostimulants (L03)
- Immunosuppressants (L04)

Immunosuppressants (L04) will not be included in this study, because medicine included in this subgroup is not exclusively indicated for the treatment of cancer. Subgroups L01-L03 are presented in table 4.14.1 and table 4.14.2 and will now be discussed according to the prevalence and cost of these subgroups.

Table 4.14.1. Classification of cancer medicine according to therapeutic subgroups in 2005.

2005							
Therapeutic subgroup	ATC code	Prevalence (N)*	Prevalence % ¹	Average cost (R)	Total cost (R)**	Cost % ²	Cost index
Antineoplastic agents	L01	46534	64.66	1211.71±2225.24	56385765.85	74.45	1.15
Endocrine therapy	L02	24859	34.54	693.90±923.90	17237754.62	22.76	0.66
Immunostimulants	L03	579	0.80	3649.59±2367.98	2113110.30	2.79	3.47
TOTAL		71972	100.00	1052.31±1912.21	75736630.77	100.00	

¹Prevalence % was determined by dividing Prev. (N)* by the total number of cancer medicine items claimed in the specific study year (refer to table 4.2).

²Cost % was determined by dividing Total cost (R)** by the total cost of cancer medicine items claimed in the specific study year (refer to table 4.2).

Table 4.14.2 Classification of cancer medicine according to therapeutic subgroups in 2006.

2006							
Therapeutic subgroup	ATC code	Prevalence (N)*	Prevalence % ¹	Average cost (R)	Total cost (R)**	Cost % ²	Cost index
Antineoplastic agents	L01	56651	68.65	1523.33±2598.96	86298423.63	79.41	1.16
Endocrine therapy	L02	25346	30.71	788.15±967.98	19976462.19	18.38	0.60
Immunostimulants	L03	528	0.64	4547.27±2328.64	2400956.43	2.21	3.45
TOTAL		82525	100.00	1316.88±2267.40	108675842	100.00	

¹Prevalence % was determined by dividing Prev. (N)* by the total number of cancer medicine items claimed in the specific study year (refer to table 4.2).

²Cost % was determined by dividing Total cost (R)** by the total cost of cancer medicine items claimed in the specific study year (refer to table 4.2).

4.4.1.1 Prevalence of cancer medicine items in different therapeutic subgroups

In 2005 and 2006 respectively, the antineoplastic agents (L01) comprised 64.66% (n=46 534) and 68.65% (n=56 651) of all cancer medicine items prescribed. Cancer medicine items included in the endocrine therapy subgroup (L02) comprised 34.54% (n=24 859) and 30.71% (n=25 346) of all cancer medicine items prescribed in 2005 and 2006 respectively. As seen in table 4.14.1 and 4.14.2, less than 1% of all cancer medicine items prescribed in both study years, was immunostimulants (L03). Only 579 medicine items in 2005 and 528 medicine items in 2006 included in this subgroup were claimed through the medicine claims database. This may be because of the high cost of these medicine items, which will be discussed in section 4.4.1.2.

4.4.1.2 Cost of cancer medicine items in different therapeutic subgroups

A parallel can be drawn between the *cost percentage* distribution of the total cost of each therapeutic subgroup for each study year and the *prevalence percentage* distribution of medicine items in each subgroup for each study year.

The total cost of the antineoplastic agents was R56 385 765.85 (74.45%) in 2005 and R86 298 423.63 (79.41%) in 2006. Endocrine therapy accounted for 22.76% (R17 237 754.62) and 18.38% (R19 976 462.19) of the total cost of all cancer medicine items for 2005 and 2006 respectively. The total cost of immunostimulants

for the year 2005 and 2006 was R 2 113 110.30 (2.79%) and R2 400 956.43 (2.21%) respectively (refer to table 4.14.1 and 4.14.2).

In table 4.14.1 and 4.14.2, the average cost of cancer medicine items in each subgroup shows that immunostimulants (L03) were the *most expensive cancer treatment*, with an average cost of R3 649.59 $\pm$ 2 367.98 (2005) and R4 547.27 $\pm$ 2 328.64 (2006). Calculations made from table 4.14.1 and 4.14.2 showed that in some cases, the cost of immunostimulants had been as high as R6 017.57 (2005) and R6 875.91 (2006) per medicine item.

The average cost per medicine item for antineoplastic agents amounted to R1 211.71 $\pm$ 2 225.24 for 2005 and R1 523.33 $\pm$ 2 598.96 for 2006 (refer to table 4.14.1 and 4.14.2). The maximum cost per medicine item for antineoplastic agents in 2005 was R3 436.95, and in 2006 it was R4 122.29 (calculated from table 4.14.1 and 4.14.2).

Endocrine therapy is *the least expensive cancer treatment* with an average cost of R693.90 $\pm$ 923.90 and R788.15 $\pm$ 967.98 for each medicine item in 2005 and 2006 respectively (refer to table 4.14.1 and 4.14.2). In some cases, the cost of endocrine therapy had been as high as R1 617.80 (2005) and R1 756.13 (2006) (calculated from table 4.14.1 and 4.14.2).

The conclusion can be made from the previous paragraphs that the individual cost values of each cancer medicine item were widely spread around the average cost value. Possible reasons for this may be that not only dosages may vary but also treatment periods. However, these aspects are outside of the framework of this study.

Table 4.15 Effect sizes (d-values) of the cost of cancer medicine items according to the different therapeutic subgroups

Therapeutic subgroups	2005		2006	
	Antineoplastic agents	Immunostimulants	Antineoplastic agents	Immunostimulants
Antineoplastic agents		1.03		1.16
Endocrine therapy	0.23	1.25	0.28	1.61
Immunostimulants				

Effect sizes (d-values) calculated from the average costs in table 4.14.1 and 4.14.2

****For the purpose of this study effect sizes (d-values) of 0.8 or higher will be assumed to have practical significance (refer to paragraph 3.8.4.5)**

Table 4.15 represents the effect sizes (d-values) of the average cost of cancer medicine items according to the different therapeutic subgroups. As explained in paragraph 3.8.4.5, effect sizes of 0.8 or higher will be assumed to have practical significance.

Table 4.15 shows that the effect sizes (d-values) between immunostimulants and antineoplastic and between immunostimulants and endocrine therapy were higher than 0.8 in both study years. This implies that there was a practical significant difference between the average cost of immunostimulants and the antineoplastic agents and endocrine therapy respectively. This also confirms the relatively high average cost of immunostimulants as discussed in a previous paragraph.

4.4.2 Classification of cancer medicine items according to pharmacological subgroups

According to the ATC index, the therapeutic subgroups, as discussed in paragraph 4.4.1, can be further divided into eight different pharmacological subgroups. Table 4.16.1 and 4.16.2 present the prevalence and cost of these different pharmacological subgroups.

The therapeutic group, antineoplastic agents (L01), can be divided into five pharmacological subgroups:

- Alkylating agents (L01A)
- Anti-metabolites (L01B)
- Plant alkaloids and other natural products (L01C)
- Cytotoxic antibiotics and related substances (L01D)
- Other antineoplastic agents (L01X)

The therapeutic group, endocrine therapy (L02), can be divided into 2 pharmacological subgroups:

- Hormones and related agents (L02A)
- Hormone antagonists and related agents (L02B)

The therapeutic group, immunostimulants (L03), only has one pharmacological subgroup, which is also classified as immunostimulants (L03A).

4.4.2.1 Prevalence of cancer medicine items in different pharmacological subgroups

Antineoplastic and immunomodulating agents are divided into eight pharmacological subgroups. The group “anti-metabolites (L01B)” comprised 40.90% (n=29 439) and 40.30% (n=33 258) of all cancer medicine items claimed in 2005 and 2006 respectively. Of all cancer medicine items claimed during 2005 and 2006, 24.17% (n=17 395) and 21.49% (n=17 735) respectively, were “hormone antagonists & related agents (L02B)”. In table 4.18 and table 4.25 these subgroups will be further divided into chemical subgroups and individual active ingredients and discussed thereafter. In 2005, “hormones and related agents (L02A)” were claimed 3rd most frequently, comprising 10.37% (n=7 462) of all cancer medicine items. In 2006, the number of cancer medicine items in this subgroup (L02A) increased with 149 items but the total prevalence percentage in 2006 decreased with 1.15% to 9.22% (n= 7 611) of all cancer medicine items claimed in 2006. “Other antineoplastic agents (L01X)” comprised 9.69% (n=6 973) of all cancer medicine items claimed in 2005 and increased to 13.01% (n=10 740) in 2006.

These four groups, (L01B; L01X; L02A; L02B) made up 85.13% and 84.02% of all cancer medicine items claimed during 2005 and 2006 respectively. The subgroup comprising the smallest proportion of all cancer medicine items claimed were immunostimulants (L03A), with 579 (0.80%) medicine items claimed in 2005 and 528 (0.64%) medicine items claimed in 2006.

4.4.2.2 Cost of cancer medicine items in different pharmacological subgroups.

The cancer medicine items included in the pharmacological subgroups “Other antineoplastic agents – L01X” and “Plant alkaloids and other natural products – L01C” comprised more than 50% of the total cost of all cancer medicine items in both study years (refer to table 4.16.1 and 4.16.2).

Table 4.16.1 Classification of cancer medicine according to pharmacological subgroups in 2005

Pharmacological subgroup	ATC code	2005					
		Prev. (N)	Prev. % ¹	Average cost (R)	Total cost (R) ²	Cost % ²	Cost index
Alkylating agents	L01A	3489	4.85	749.27±1637.09	2614212	3.45	0.71
Anti-metabolites	L01B	29439	40.90	1195.26±31.66	11261438	14.87	0.36
Plant alkaloids and other natural products	L01C	4036	5.61	3708.69±2481.18	14968264	19.76	3.52
Cytotoxic antibiotics and related substances	L01D	2597	3.61	1394.36±1426.14	3621162	4.78	1.33
Other antineoplastic agents	L01X	6973	9.69	3430.47±3130.52	23920690	31.58	3.26
Hormones and related agents	L02A	7462	10.37	937.59±1167.66	6998196.3	9.24	0.89
Hormone antagonists and related agents	L02B	17395	24.17	588.65±773.51	10239558	13.52	0.56
Immunostimulants	L03A	579	0.80	3649.59±2367.98	2113110.30	2.79	3.47

¹Prev. % was determined by dividing Prev. (N)* by the total number of cancer medicine items claimed in the specific study year (refer to table 4.2).

²Cost % was determined by dividing Total cost (R)** by the total cost of cancer medicine items claimed in the specific study year (refer to table 4.2).

Table 4.16.2 Classification of cancer medicine according to pharmacological subgroups in 2005

Pharmacological subgroup	ATC code	2005					
		Prev. (N)	Prev. % ¹	Average cost (R)	Total cost (R) ²	Cost % ²	Cost index
Alkylating agents	L01A	4781	5.79	1093.37±2210.98	5227423.5	4.81	0.83
Anti-metabolites	L01B	33258	40.30	399.75±1229.86	13294852	12.23	0.30
Plant alkaloids and other natural products	L01C	4858	5.89	3749.44±2715.98	18214783	16.76	2.85
Cytotoxic antibiotics and related substances	L01D	3014	3.65	1495.14±2013.34	4506346.4	4.15	1.14
Other antineoplastic agents	L01X	10740	13.01	4195.07±3305.35	45055019	41.46	3.19
Hormones and related agents	L02A	7611	9.22	1008.29±1200.36	7674073.3	7.06	0.77
Hormone antagonists and related agents	L02B	17735	21.49	693.68±831.32	12302389	11.32	0.53
Immunostimulants	L03A	528	0.64	4547.27±2328.64	2400956.4	2.21	3.45

¹Prev. % was determined by dividing Prev. (N)* by the total number of cancer medicine items claimed in the specific study year (refer to table 4.2).

²Cost % was determined by dividing Total cost (R)** by the total cost of cancer medicine items claimed in the specific study year (refer to table 4.2).

The total cost of anti-metabolites (L01B) made up 14.87% and 12.23% of the total cost of cancer medicine items for 2005 and 2006 respectively. Cancer medicine item in the pharmacological subgroups L02B (Hormone antagonists and related agents) comprised 13.52% (2005) and 11.32% (2006) of the total cost of cancer medicine items. The total cost of cancer medicine items in the remaining three

pharmacological subgroups (L01A, L02A, L03A) combined, comprised 20.06% and 18.23% of the total cost of all cancer medicine items. See figure 4.6.1 and 4.6.2 for the percentage distribution of the total cost of cancer medicine items for the different pharmacological subgroups.

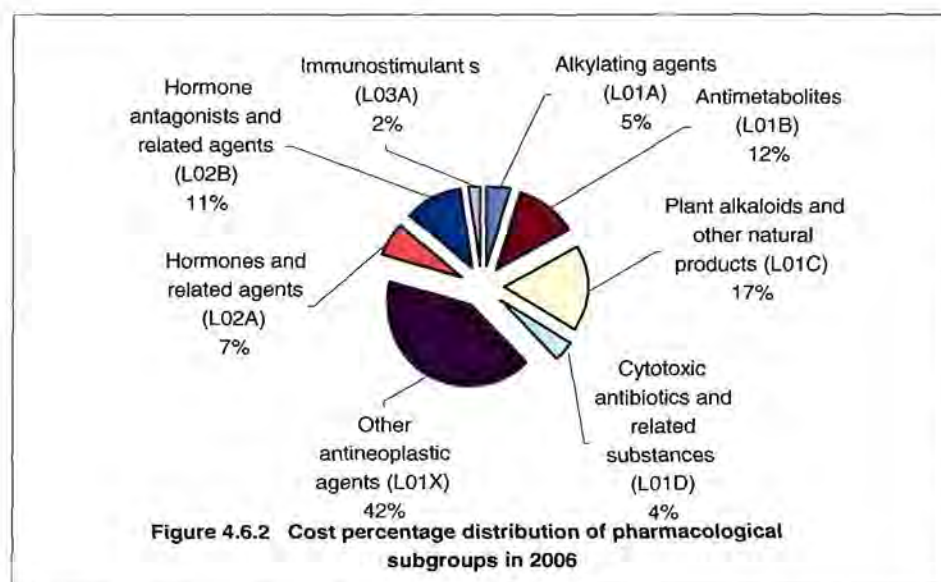
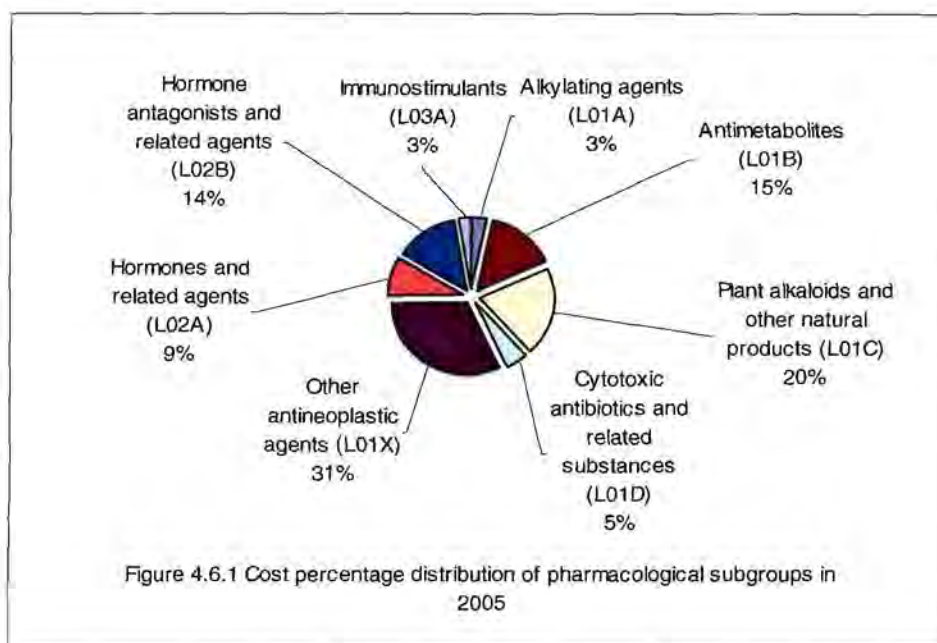


Figure 4.6.1-4.6.2 Percentage distribution of the total cost of cancer medicine items according to pharmacological subgroups

* Refer to Table 4.16.1 and 4.16.2 for percentages of different pharmacological subgroups.

In Table 4.17, the effect sizes between the different pharmacological subgroups are presented. For the purpose of this study, an effect size (d-values) of 0.8 or more will be assumed to have practical significance (refer to section 3.8.4.5).

Table 4.17 Effect sizes of the cost of cancer medicine items according to the different pharmacological subgroups

	L01A	L01B	L01C	L01D	L01X	L02A	L02B	L03A
L01A			1.2	0.5	0.9	0.2		1.2
L01B	0.2		1.3	0.7	1.0	0.5	0.2	1.4
L01C								
L01D			0.9		0.7			0.9
L01X			0.1					0.07
L02A			1.1	0.3	0.8	0.3		1.1
L02B			1.3	0.6	0.9			1.3
L03A	0.1		0.02					

**Effect sizes (d-values) calculated from the average costs in table 4.16.1 and 4.16.2*

***For the purpose of this study effect sizes (d-values) of 0.8 or higher will be assumed to have practical significance (refer to paragraph 3.8.4.5)*

It can be concluded from table 4.17, that the pharmacological subgroups L01C “Plant alkaloids and other natural products”, L01X “Other antineoplastic agents” and L03A “Immunostimulants” is of practical cost importance and relatively more expensive than other cancer medicine items.

4.4.3 Classification of cancer medicine items according to chemical subgroups

According to the ATC index, antineoplastic and immunomodulating agents can be divided even further into different chemical subgroups (refer to Appendix A). Table 4.18 presents the prevalence and cost of cancer medicine items in these chemical subgroups.

4.4.3.1 Prevalence of cancer medicine items in different chemical subgroups

There are 36 chemical subgroups of antineoplastic and immunomodulating agents according to the ATC classification. Five of these chemical subgroups comprised more than 60% of the prevalence of all cancer medicine items in both study years. In

2005, these subgroups were (in descending order): Folic acid analogues (L01BA); anti-estrogens (L02BA); estrogens (L02AA); pyrimidine analogues (L01BC) and enzyme inhibitors (L02BG). In 2006 the top five chemical subgroups were: Folic acid analogues (L01BA); anti-estrogens (L02BA); pyrimidine analogues (L01BC); estrogens (L02AA) and enzyme inhibitors (L02BG) (refer to table 4.18).

In eleven of the chemical subgroups, no cancer medicine items were claimed through the medicine claims database, in both 2005 and 2006. These groups were:

- Ethylene imines (L01AC)
- Epoxides (L01AG)
- Colchicine derivates (L01CC)
- Other plant alkaloids and natural products (L01CX)
- Methylhydrazines (L01XB)
- Agents used in photodynamic therapy (L01XD)
- Combinations of antineoplastic agents (L01XY)
- Other hormones (L02AX)
- Other hormone antagonists and related agents (L02BX)
- Colony stimulating factors (L03AA)
- Other cytokines and immunomodulators (L03AX)

Therefore, only 25 chemical subgroups contained cancer medicine items that were claimed through the medicine claims database during 2005 and 2006.

The prevalence of monoclonal antibodies (L01XC) increased from 2.58% (n=1 858) in 2005 to 4.80% (n=3 963) in 2006 of all cancer medicine items. The prevalence of estrogens (L02AA) decreased from 7.32% (n=5 267) in 2005 to 6.20% (n=5 120) in 2006, as well as anti-estrogens (L02BA) for which the prevalence decreased from 16.51% (n=11 879) in 2005 to 13.03% (n=10 749) in 2006 (refer to table 4.18).

4.4.3.2 Cost of cancer medicine items in different chemical subgroups

The total cost of cancer medicine items in only 5 of the 36 chemical subgroups comprised 59.4% and 62.72% of the total cost of all cancer medicine items for 2005

and 2006 respectively. These subgroups differ from those that were relatively high in prevalence. In 2005 the chemical subgroups with the highest total cost (in descending order) were: taxanes (L01CD), monoclonal antibodies (L01XC), pyrimidine analogues (L01BC), protein kinase inhibitors (L01XE) and gonatropin releasing hormone analogues (L02AE). In 2006, the monoclonal antibodies (L01XC) had the highest total cost, followed by the taxanes (L01CD), pyrimidine analogues (L01BC), protein kinase inhibitors (L01XE) and gonatropin releasing hormone analogues (L02AE) (refer to table 4.18).

In 2005, taxanes (L01CD) comprised 15.54% (R11 768 884.89) of the total cost of all cancer medicine items (refer to table 4.18). The group taxanes contains the cancer medicine items, paclitaxel and docetaxel (active ingredients).

In 2006, monoclonal antibodies (L01XC) such as rituximab, trastuzumab and bevacizumab comprised 24% (R26 082 373.86) of the total cost of all cancer medicine items. This is almost a 10% increase of the cost of monoclonal antibodies in 2005, which amounted to R11 038 116.92 (14.57% of the total cost of all cancer medicine items in 2005). Although the total cost of monoclonal antibodies increased, the CPI of monoclonal antibodies decreased from 5.65 to 5.00 (refer to table 4.18). This can be because of the increase in prevalence of monoclonal antibodies on the cancer database (see section 4.4.3.1).

As seen in table 4.18, the CPIs of 15 chemical subgroups (42%) are above 1.00. It can therefore be deducted that the cancer medicine items included in these chemical subgroups (refer to Appendix A) were relatively expensive (refer to section 3.8.4.6). Only 10 chemical subgroups (28%) had CPIs below 1.00, and these cancer medicine items can be described as relatively inexpensive. As discussed before, 11 of the chemical subgroups (30%) were not included on the database.

Table 4.18 Classification of cancer medicine items according to chemical subgroups

Chemical Subgroup	ATC code	2005						2006					
		Prevalence (N)*	Prevalence %	Average cost (R)	Total cost (R)**	Cost %	Cost index	Prevalence (N)*	Prevalence %	Average cost (R)	Total cost (R)**	Cost %	Cost index
	L01AA	2915	4.05	252.30±570.13	735448.21	0.97	0.24	3772	4.57	247.05±606.78	931857.71	0.86	0.19
Alkyl sulfonates	L01AB	14	0.02	214.80±246.78	3007.20	0.00	0.20	5	0.01	116.94±71.46	584.69	0.00	0.09
Ethylene imines	L01AC												
Nitrosoureas	L01AD	15	0.02	1042.29±632.79	15634.36	0.02	0.99	12	0.01	1831.29±1106.74	21975.54	0.02	1.39
Epoxides	L01AG												
Other alkylating agents	L01AX	545	0.76	3413.07±2643.68	1860122.26	2.46	3.24	992	1.20	4307.47±3014.27	4273005.59	3.93	3.27
Folic acid analogues	L01BA	24453	33.98	35.32±106.46	863734.07	1.14	0.03	27573	33.41	35.04±52.40	966313.33	0.89	0.03
Purine analogues	L01BB	282	0.39	2440.44±2181.29	688203.61	0.91	2.32	354	0.43	2716.83±2449.90	961758.25	0.88	2.06
Pyrimidine analogues	L01BC	4704	6.54	2064.09±2211.40	9709500.08	12.82	1.96	5331	6.46	2132.20±2227.79	11366779.96	10.46	1.62
Vinca alkaloids and analogues	L01CA	1289	1.79	2136.01±2094.09	2753310.59	3.64	2.03	1673	2.03	1738.41±2009.99	2908363.22	2.68	1.32
Podophyllotoxin derivatives	L01CB	387	0.54	1152.63±770.71	446068.3	0.59	1.10	408	0.49	1330.74±815.84	542940.63	0.50	1.01
Colchicine derivatives	L01CC												
Taxanes	L01CD	2360	3.28	4986.82±1995.24	11768884.89	15.54	4.74	2777	3.37	5316.34±2149.91	14763479.47	13.58	4.04
Other plant alkaloids and natural products	L01CX												
Actinomycines	L01DA	18	0.03	200.32±111.09	3605.72	0.00	0.19	11	0.01	267.99±109.04	2947.93	0.00	0.20
Anthracyclines and related substances	L01DB	2365	3.29	1470.59±1454.02	3477953.44	4.59	1.40	2680	3.25	1587.98±2102.93	4255796.93	3.92	1.21
Other cytotoxic antibiotics	L01DC	214	0.30	652.35±764.72	139602.80	0.18	0.62	323	0.39	766.57±693.10	247601.53	0.23	0.58
Platinum compounds	L01XA	2332	3.24	981.37±1521.04	2288563.16	3.02	0.93	3503	4.24	1565.65±2253.38	5484465.87	5.05	1.19
Methylhydrazines	L01XB												
Monoclonal antibodies	L01XC	1858	2.58	5940.86±2208.86	11038116.92	14.57	5.65	3963	4.80	6581.47±2215.16	26082373.86	24.00	5.00
Agents used in photodynamic therapy	L01XD												
Protein kinase inhibitors	L01XE	1051	1.46	6676.04±1495.82	7016518.26	9.26	6.34	1471	1.78	6609.28±1505.13	9722258.09	8.95	5.02
Other antineoplastic agents	L01XX	1732	2.41	2065.63±2580.81	3577491.98	4.72	1.96	1803	2.18	2088.70±2728.18	3765921.03	3.47	1.59
Combinations of antineoplastic agents	L01XY												

¹Prevalence % was determined by dividing Prev. (N)* by the total number of cancer medicine items claimed in the specific study year (refer to table 4.2).

³Cost % was determined by dividing Total cost (R)** by the total cost of cancer medicine items claimed in the specific study year (refer to table 4.2).

Table 4.18 Classification of cancer medicine items according to chemical subgroups (continued)

Chemical subgroup	ATC code	2005						2006					
		Prevalence (N)	Prevalence % ¹	Average cost (R)	Total cost (R)**	Cost %	Cost index	Prevalence (N)	Prevalence % ¹	Average cost (R)	Total cost (R)**	Cost %	Cost index
Estrogens	L02AA	5267	7.32	279.91±292.51	1474311.43	1.95	0.27	5120	6.20	266.31±240.65	1363531.48	1.25	0.20
Progestogens	L02AB	129	0.18	483.84±264.87	62414.73	0.08	0.46	156	0.19	522.29±299.63	86157.62	0.08	0.42
Gonadotropin releasing hormone analogues	L02AE	2068	2.87	2640.94±826.16	5461470.11	7.21	2.51	2335	2.83	2665.69±771.39	6224384.24	5.73	2.02
Other hormones	L02AX												
Anti-estrogens	L02BA	11879	16.51	140.32±44.73	1666822.95	2.20	0.13	10749	13.03	138.97±43.74	1493858.81	1.37	0.11
Anti-androgens	L02BB	2368	3.29	1949.60±940.60	4616652.65	6.10	1.85	2494	3.02	2092.86±1012.65	5219604.19	4.80	1.59
Enzyme inhibitors	L02BG	3148	4.37	1256.70±187.53	3956082.75	5.22	1.19	4492	5.44	1244.20±168.44	5588925.85	5.14	0.94
Other hormone antagonists and related agents	L02BX												
Colony stimulating factors	L03AA												
Interferons	L03AB	466	0.65	3218.70±2338.35	1499916.38	1.98	3.06	341	0.41	3703.79±2469.24	1262992.76	1.16	2.81
Interleukins	L03AC	113	0.16	5426.49±1509.36	613193.92	0.81	5.16	187	0.23	6085.37±732.01	1137963.67	1.05	4.62
Other cytokines and immunomodulators	L03AX												

¹Prevalence % was determined by dividing Prev. (N)* by the total number of cancer medicine items claimed in the specific study year (refer to table 4.2).

³Cost % was determined by dividing Total cost (R)** by the total cost of cancer medicine items claimed in the specific study year (refer to table 4.2).

4.4.4 Classification of cancer medicine items according to active ingredient

Table 4.25 presents the individual active ingredients and ATC codes of the cancer medicine items included on the database. The prevalence and cost of the different active ingredients are also presented. The data in table 4.19 – table 4.24 was extracted from table 4.25.

Table 4.19 Summary of cancer medicine items with CPI <1 and CPI >1

2005				2006			
CPI < 1		CPI > 1		CPI < 1		CPI > 1	
Active ingredient	CPI	Active ingredient	CPI	Active ingredient	CPI	Active ingredient	CPI
Cyproterone	0.27	Ifosfamide	1.78	Cyproterone	0.20	Ifosfamide	1.42
Cyclophosphamide	0.10	Temozolomide	4.28	Cyclophosphamide	0.08	Carmustine	1.39
Chlorambucil	0.48	Tioguanine	2.48	Chlorambucil	0.32	Temozolomide	3.83
Melphalan	0.53	Fludarabine	4.04	Melphalan	0.36	Fludarabine	3.87
Busulphan	0.20	Cytarabine	1.46	Busulphan	0.09	Cytarabine	1.34
Carmustine	0.99	Gemcitabine	4.03	Dacarbazine	0.71	Gemcitabine	3.35
Dacarbazine	0.66	Capecitabine	2.49	Methotrexate	0.03	Capecitabine	1.98
Methotrexate	0.03	Vindesine	2.08	Mercaptopurine	0.81	Vinorelbine	2.67
Mercaptopurine	0.98	Vinorelbine	3.31	Tioguanine	0.91	Etoposide	1.01
Fluorouracil	0.08	Etoposide	1.10	Fluorouracil	0.11	Paclitaxel	3.97
Vinblastine	0.38	Paclitaxel	4.07	Vinblastine	0.31	Docetaxel	4.08
Vincristine	0.17	Docetaxel	5.16	Vincristine	0.13	Doxorubicin	1.50
Dactinomycin	0.19	Doxorubicin	1.81	Dactinomycin	0.20	Daunorubicin	2.53
Bleomycin	0.71	Daunorubicin	1.01	Epirubicin	0.82	Mitoxantrone	1.60
Mitomycin	0.53	Epirubicin	1.05	Bleomycin	0.68	Oxaliplatin	3.92
Cisplatin	0.30	Mitoxantrone	1.86	Mitomycin	0.45	Rituximab	4.75
Carboplatin	0.70	Oxaliplatin	4.42	Cisplatin	0.24	Trastuzumab	5.36
Hydroxycarbamide	0.13	Rituximab	5.12	Carboplatin	0.55	Bevacizumab	4.74
Estramustine	0.74	Trastuzumab	6.45	Hydroxycarbamide	0.10	Imatinib	5.02
Medroxyprogesterone	0.46	Bevacizumab	5.94	Estramustine	1.11	L-Asparaginase	3.28
Tamoxifen	0.13	Imatinib	6.34	Medroxyprogesterone	0.42	Tretinoin	2.20
Flutamide	0.77	Asparaginase	3.26	Tamoxifen	0.11	Topotecan	3.51
		Tretinoin	2.48	Flutamide	0.56	Irinotecan	3.40
		Topotecan	4.95	Anastrozole	0.93	Buserelin	2.21
		Irinotecan	4.04			Leuprorelin	1.92
		Buserelin	2.76			Goserelin	2.02
		Leuprorelin	2.42			Bicalutamide	1.73
		Goserelin	2.51			Exemestane	1.09
		Bicalutamide	2.03			Interferon alfa2A	2.88
		Anastrozole	1.17			Interferon alfa2B	2.75
		Exemestane	1.34			Aldesleukin	4.62
		Interferon alfa2A	3.02				
		Interferon alfa2B	3.08				
		Aldesleukin	5.16				

**CPI values taken from table 4.25*

***For the purpose of this study CPI values higher than one (1) will indicate relatively expensive treatment (refer to paragraph 3.8.4.6)*

In table 4.19, the cancer medicine items with a CPI lower than one ($CPI < 1$) and the cancer medicine items with a CPI higher than one ($CPI > 1$) are listed. Cancer medicine items with a CPI higher than one is considered to be expensive treatment while cancer medicine items lower than one is considered to be inexpensive (refer to section 3.8.4.6).

In 2005, the CPIs of 61% of the cancer medicine items (active ingredients) were higher than one and therefore relatively expensive treatment whilst the remaining 39% of the cancer medicine items (active ingredients) were relatively inexpensive ($CPI < 1$). In 2006, the CPI of 56% of the cancer medicine items (active ingredients) was higher than one and therefore considered to be relatively expensive treatment whilst the remaining 44% of the cancer medicine items (active ingredients) were relatively inexpensive ($CPI < 1$). The cancer medicine items with the highest CPI in both study years were trastuzumab and imatinib (refer to table 4.19). These two cancer medicine items will now be discussed.

- **Trastuzumab (L01XC03)**

Some aspects of Trastuzumab have already been discussed in section 4.3.2. Trastuzumab (L01XC03) is the active ingredient in Herceptin®. Herceptin® is an cancer medicine item with no generic substitution and thus the only trade name containing trastuzumab that is available on the medicine claims database. Herceptin® (trastuzumab) had a CPI of 6.45 in 2005 (highest CPI of all cancer medicine items for both study years) and 5.36 in 2006 (refer to table 4.19).

From table 4.25 it can be seen that Trastuzumab also comprised 5.64% of the total cost of all cancer medicine items in 2005. In 2006, the total cost of trastuzumab increased with 4.82% to 10.46% of the total cost of all cancer medicine items (refer to table 4.25).

- **Imatinib (L01XE01)**

Some aspects of imatinib have already been discussed in section 4.3.1. Imatinib (L01XE01) is the active ingredient in Gleevec 100mg capsules®, Gleevec 100mg tablets® and Gleevec 400mg tablets®. There are no generic substitution for these trade names. The CPI for imatinib for 2005 was 6.34 (second highest of all cancer medicine items for both study years) and for 2006 it was 5.02 (refer to table 4.19). Also refer to table 4.24 for a listing of cancer medicine items with a relatively high

cost percentage, including imatinib. According to the available data, no Gleevec 100mg tablets® and Gleevec 400mg tablets® were claimed through the medicine claims database during 2005 (refer to appendix B). In 2006, the prevalence of Gleevec 100mg tablets® amounted to n=163 and for Gleevec 400mg tablets® it was n=988 (refer to Appendix B). Refer to section 4.3.1 for the discussion of Gleevec 100mg capsules®.

Table 4.20 Summary of cancer medicine items with a relatively high prevalence percentage

	Prevalence %*	
	2005	2006
Cyproterone	7.32	6.20
Methotrexate	33.98	33.41
Tamoxifen	16.51	13.03

*Prevalence % shown in table 4.20 was taken from table 4.25.

Cyproterone (G03HA01), Methotrexate (L01BA01) and Tamoxifen (L02BA01) comprised 57.81% (2005) and 52.64% (2006) of the total prevalence of all cancer medicine items. These cancer medicine items are presented in table 4.20 and discussed below.

- **Cyproterone (G03HA01)**

According to the 8th South African Medicines Formulary (SAMF) cyproterone is classified in two anatomical main groups i.e. "Genitourinary system and sex hormones (G)" and "Antineoplastic and immunomodulating agents (L)". The complete classification of cyproterone is presented below:

G	Genitourinary system and sex hormones
G03	Sex hormones, modulators of the genital system and contraception
G03H	Anti-androgens
G03HA	Anti-androgens
G03HA01	Cyproterone

and

L	Antineoplastic and Immunomodulating agents
L02	Endocrine therapy
L02B	Hormone antagonists and related agents
L02BB	Anti-androgens
GO3HA01	Cyproterone

Cyproterone is used in cancer treatment for the palliative treatment of *inoperable prostatic carcinoma*. Cyproterone is also used in other diseases such as *male sexual deviation*, and in lower dosages for *severe acne* and *hirsutism in woman*. The medicine claims database used for this study did not distinguish between different diagnoses and/or dosages. This could be part of the explanation of the relatively high prevalence of cyproterone on the database. This is seen as a limitation to this study (see Chapter 5).

In 2005, 7.32% (n=5 267) of all cancer medicine items contained the active ingredient cyproterone. In 2006, 6.20% (n=5 120) of all cancer medicine items contained the active ingredient cyproterone. The total cost of cancer medicine items containing cyproterone amounted to 1.95% (2005) and 1.25% (2006) of the total prevalence of cancer medicine items and the CPI of cyproterone in both study years indicates that it is a relatively inexpensive cancer treatment (see table 4.19).

The different trade names available on the medicine claims database containing cyproterone are Androcur 100mg tablets, Androcur 10mg tablets and the Androcur 100mg/ml injection (refer to Appendix B).

- **Methotrexate (L01BA01)**

There were 10 different trade names containing the active ingredient, Methotrexate (refer to Appendix B) on the medicine claims database. These trade names comprised 33.98% (n=24 453) and 33.41% (n=27 572) of the total prevalence of cancer medicine items in 2005 and 2006 respectively. Methotrexate 2.5mg tablets were already discussed in section 4.3.6, and were claimed the most of all the trade names available containing methotrexate (refer to section 4.3.6, table 4.13, Appendix B). Other trade names include Abitrexate 1000mg/10ml, Emthexate RTU 50-2 2ml

Inj. and P&U Methotrexate 50mg/2ml (refer to Appendix B). See the indications of Methotrexate in section 4.3.6.

- **Tamoxifen (L02BA01)**

Tamoxifen is an estrogen antagonist (refer to Appendix B), and more specifically a selective estrogen receptor modulator (SERM). Tamoxifen is used in early and advanced hormone receptor-positive breast cancer and in the treatment of metastatic disease and for prophylaxis in woman at an increased risk of breast cancer. Duminy (2008) is of the opinion that there is not adequate usage data to justify the use of Tamoxifen as prophylaxis in woman at an increased risk of breast cancer.

Cancer medicine items containing Tamoxifen comprised 16.51% (n=11 879) and 13.03% (n=10 749) of all cancer medicine items claimed in 2005 and 2006 respectively (see table 4.25). On the medicine claims database, there were 6 different trade names containing tamoxifen (refer to Appendix B). The two trade names with the highest prevalence in both 2005 and 2006 were Kessar 20mg tablets and Neophedan 20mg tablets. These are both generic substitutions for Nolvadex D 20mg tablets. Neophedan 20mg tablets were claimed more than Kessar 20mg tablets even though Kessar 20mg tablets are less expensive than Neophedan 20mg tablets.

In table 4.21 the effect sizes (d-values) between these three trade names are presented. Effect sizes of 0.8 or higher will be assumed to have practical significance (see section 3.8.4.5). From table 4.21, it can be seen that the original trade name, Nolvadex D 20mg is more expensive than the generic substitutions, Neophedan 20mg tablets and Kessar 20mg tablets. Table 4.21 also shows that there is a significant difference in cost between Neophedan 20mg tablets and Kessar 20mg tablets.

Table 4.21 Effect sizes between the Nolvadex D 20 mg, Neophedan 20mg tablets and Kessar 20mg tablets

	Nolvadex D 20mg tablets (original)	Neophedan 20mg tablets (generic)
Kessar 20mg tablets (generic)	4.3	1.6
Neophedan 20mg tablets (generic)	3.8	

**Effect sizes (d-values) calculated from the average costs of the specific cancer medicine items shown in Appendix B.*

***For the purpose of this study effect sizes (d-values) of 0.8 or higher will be assumed to have practical significance (refer to paragraph 3.8.4.5)*

A potential cost saving calculation was made (refer to section 3.8.4.6) to determine what the potential cost saving could be if Nolvadex D 20 mg tablets were substituted by either Neophedan 20mg tablets or Kessar 20mg tablets. This cost-minimization analysis (refer to section 2.9.3.3) is performed assuming that the treatment periods are the same. The results are presented in table 4.22.

From table 4.22 it can be seen that if Nolvadex D 20mg tablets were fully substituted (100%) by the least expensive generic substitution, Kessar 20mg tablets, the cost savings could be R83 727.06 (2005) and R68 513.71 (2006). If Nolvadex D 20mg tablets were fully substituted (100%) by the most expensive generic substitution, Neophedan 20mg tablets, the costs saved could amount to R72 996.54 (2005) and R59 531.75 (2006).

Table 4.22 Potential cost saving by substituting Nolvadex D 20mg tablets with either Kessar 20mg tablets or Neophedan 20mg tablets

Product		2005			
		Prev.(N) ¹	Avg. cost (R) ²	Total cost (R) ³	Cost saving (R)*
Original product	Nolvadex D 20 mg Tab.	369	345.91±52.44	127 641.75	
Generic –least expensive	Kessar 20mg Tab.	5 148	119.01±12.90	612 677.12	83 727.06
Generic – most expensive	Neophedan 20mg Tab.	5 535	148.09±18.53	819 660.39	72 996.54
Product		2006			
		Prev.(N) ¹	Avg. cost (R) ²	Total cost (R) ³	Cost saving (R)*
Original product	Nolvadex D 20 mg Tab.	299	346.78±54.91	103 688.07	
Generic –least expensive	Kessar 20mg Tab.	4 634	117.64±13.96	545 158.74	68 513.71
Generic - most expensive	Neophedan 20mg Tab.	5 080	147.68±19.33	750 227.29	59 531.75

* 100% substitution of Nolvadex D 20mg tablets

^{1 2 3} The prevalence (Prev.), average cost (avg. cost) and the total cost of these specific cancer medicine items were taken from Appendix B

Table 4.23 presents the cost savings by substituting 75 percent, 50 percent or 25 percent of the original product (Nolvadex D 20mg tablets) with either Kessar 20mg tablets or Neophedan 20mg tablets.

Table 4.23 Potential percentage cost saving by substituting Nolvadex D 20mg tablets with the generic substitution

Product	Cost saving (R)					
	2005			2006		
	75%	50%	25%	75%	50%	25%
Kessar 20mg Tab.	62795.30	41863.53	20931.77	51385.28	34256.86	17128.43
Neophedan 20mg Tab.	54747.41	36498.27	18249.14	44648.81	29765.88	14882.94

From table 4.23 it can be seen that even when only 25 percent of the Nolvadex 20mg tablets were substituted with Kessar 20mg tablets, there could still have been a cost saving of R20 931.77 in 2005 and R17 128.43 in 2006. If 25 percent of Nolvadex 20mg tablets were substituted with Neophedan 20mg tablets, the cost saving would be R14 882.94.

Table 4.24 presents a summary of the cancer medicine items with a cost percentage of 4 percent or more. The following cancer medicine items had cost percentages higher than 10%: Docetaxel (2005), Rituximab (2006) and Trastuzumab (2006). Trastuzumab have already been discussed earlier in this section and therefore only docetaxel and rituximab will now be discussed.

Table 4.24 Summary of cancer medicine items with a relatively high cost percentage

2005			
4-6%	6-8%	8-10%	>10%
Capecitabine Irinotecan Goserelin Anastrozole Paclitaxel Trastuzumab Bicalutamide	Gemcitabine Rituximab	Imatinib	Docetaxel
2006			
4-6%	6-8%	8-10%	>10%
Paclitaxel Bicalutamide Anastrozole	Gemcitabine	Docetaxel Imatinib	Rituximab Trastuzumab

* Cost percentages used in table 4.24 were obtained from table 2.25

- **Docetaxel (L01CD02)**

In 2005, docetaxel comprised 10.42% of the total cost of all cancer medicine items and in 2006 docetaxel comprised 8.54% of the total cost of cancer medicine items (refer to table 4.25). The prevalence of docetaxel comprised 2.02% of all cancer medicine items in 2005 and 2.10% in 2006. The CPI for docetaxel was 5.16 for 2005 and 4.08 for 2006 (also refer to table 4.19). This is higher than 1.00 and it can therefore be said that cancer medicine items containing docetaxel are relatively expensive cancer medicine items (refer to section 3.8.4.6).

Docetaxel is the active ingredient in the Taxotere 20mg/1.5ml injection and the Taxotere 80mg injection (refer to Appendix B). These cancer medicine items are classified as taxanes (L01CD), which are used in the management of advanced or metastatic breast, ovarian and non-small cell lung cancer. Duminy (2008) added that docetaxel may also be used in prostate cancer. Docetaxel is a more potent analogue of paclitaxel, which is the active ingredient in Taxol 100mg/vials and Taxol 300mg/5ml injections (refer to section 4.3.7).

- **Rituximab (L01XC02)**

In 2005, Rituximab comprised 7.51% of the total cost of all cancer medicine items. The total cost of Rituximab increased with 3.17% in 2006 and comprised 10.68% of the total cost of all cancer medicine items during 2006. Rituximab encompassed 1.47% and 2.25% of the total number of cancer medicine items claimed in 2005 and 2006 respectively. The prevalence of rituximab also increased with 0.78% between 2005 and 2006.

The trade names on the database containing rituximab are the Mabthera 100mg vial and the Mabthera 500mg vial. Refer to section 4.3.3 for a further discussion of the Matbthera 500mg vial®. The indications for the two trade names containing rituximab, the Mabthera 100mg vial® and the Mabthera 500mg vial®, are the same (refer to section 4.3.3).

Table 4.25 Classification of cancer medicine items according to active ingredient

ATC code	Active ingredient	2005						2006					
		Prev. (N)	Prev. % ¹	Average cost (R)	Total cost (R)**	Cost % ²	Cost index	Prev. (N)	Prev. % ¹	Average cost (R)	Total cost (R)**	Cost % ²	Cost index
G03HA01	Cyproterone	5267	7.32	279.91±292.51	1474311.43	1.95	0.27	5120	6.20	266.31±240.86	1363531.48	1.25	0.20
L01AA01	Cyclophosphamide	2299	3.19	101.00±56.22	232203.70	0.31	0.10	3074	3.72	102.25±61.76	314327.78	0.29	0.08
L01AA02	Chlorambucil	296	0.41	501.48±366.15	148437.53	0.20	0.48	301	0.36	414.83±266.40	124864.02	0.11	0.32
L01AA03	Melphalan	186	0.26	556.15±732.92	103444.66	0.14	0.53	178	0.22	467.87±584.90	83281.59	0.08	0.36
L01AA06	Ifosfamide	134	0.19	1875.84±1644.31	251362.32	0.33	1.78	219	0.27	1869.33±1709.24	409384.32	0.38	1.42
L01AB01	Busulfan	14	0.02	214.80±246.78	3007.20	0.00	0.20	5	0.01	116.94±71.46	584.69	0.00	0.09
L01AD01	Carmustine	15	0.02	1042.29±632.79	15634.36	0.02	0.99	12	0.01	1831.29±1106.74	21975.54	0.02	1.39
L01AX03	Temozolomide	389	0.54	4502.70±2366.75	1751551.22	2.31	4.28	814	0.99	5044.89±2829.72	4106538.78	3.78	3.83
L01AX04	Dacarbazine	156	0.22	695.97±312.18	108571.04	0.14	0.66	178	0.22	935.21±391.95	166466.81	0.15	0.71
L01BA01	Methotrexate	24453	33.98	35.32±106.46	863734.07	1.14	0.03	27573	33.41	35.05±52.40	966313.33	0.89	0.03
L01BB02	Mercaptopurine	153	0.21	1029.31±429.04	157484.38	0.21	0.98	186	0.23	1068.91±556.93	198817.69	0.18	0.81
L01BB03	Tioguanine	11	0.02	2605.26±1839.29	28657.87	0.04	2.48	24	0.03	1196.91±585.44	28725.81	0.03	0.91
L01BB05	Fludarabine	118	0.16	4254.76±2229.96	502061.36	0.66	4.04	144	0.17	5098.71±2310.35	734214.75	0.68	3.87
L01BC01	Cytarabine	101	0.14	1531.56±2110.79	154687.43	0.20	1.46	101	0.12	1768.89±2238.33	178657.79	0.16	1.34
L01BC02	Fluorouracil	1894	2.63	128.46±112.59	154687.43	0.20	0.08	2196	2.66	142.79±119.92	313557.34	0.29	0.11
L01BC05	Gemcitabine	1370	1.90	4237.86±2015.12	5805869.89	7.67	4.03	1645	1.99	4409.57±1883.18	7253737.99	6.67	3.35
L01BC06	Capecitabine	1339	1.86	2618.10±1487.62	3505640.45	4.63	2.49	1389	1.68	2606.79±1353.07	3620826.84	3.33	1.98
L01CA01	Vinblastine	122	0.17	403.71±254.22	49252.64	0.07	0.38	162	0.20	408.29±190.44	66143.56	0.06	0.31
L01CA02	Vincristine	401	0.56	175.99±84.70	70573.34	0.09	0.17	739	0.90	173.96±70.75	128554.38	0.12	0.13
L01CA03	Vindesine	24	0.03	2190.71±112.77	52577.14	0.07	2.08						
L01CA04	Vinorelbine	742	1.03	3478.31±1797.28	2580907.47	3.41	3.31	772	0.94	3515.11±1694.27	2713665.28	2.50	2.67
L01CB01	Etoposide	387	0.54	1152.63±770.71	446068.30	0.59	1.10	408	0.49	1330.74±815.84	542940.63	0.50	1.01
L01CD01	Paclitaxel	905	1.26	4280.09±2322.77	3873479.32	5.11	4.07	1048	1.27	5233.44±2874.44	5484640.48	5.05	3.97

¹Prev. % was determined by dividing Prev. (N)* by the total number of cancer medicine items claimed in the specific study year (refer to table 4.2).

²Cost % was determined by dividing Total cost (R)** by the total cost of cancer medicine items claimed in the specific study year (refer to table 4.2).

Table 4.25 Classification of cancer medicine items according to active ingredient (continued)

ATC code	Active ingredient	2005						2006					
		Prev. (N)*	Prev. % ¹	Average cost (R)	Total cost (R)**	Cost % ²	Cost Index	Prev. (N)*	Prev. % ¹	Average cost (R)	Total cost (R)**	Cost % ²	Cost Index
L01CD02	Docetaxel	1455	2.02	5426.40±1612.51	7895405.57	10.42	5.16	1729	2.10	5366.59±1553.21	9278838.99	8.54	4.08
L01DA01	Dactinomycin	18	0.03	200.32±111.09	3605.72	0.00	0.19	11	0.01	267.99±109.04	2947.93	0.00	0.20
L01DB01	Doxorubicin	955	1.33	1909.10±2057.49	1823186.81	2.41	1.81	1366	1.66	1969.15±2813.20	2689853.06	2.48	1.50
L01DB02	Daunorubicin	1	0.00	1059.08±0	1059.08	0.00	1.01	7	0.01	3338.00±1102.94	23366.02	0.02	2.53
L01DB03	Epirubicin	1300	1.81	1107.88±654.72	1440244.05	1.90	1.05	1185	1.44	1084.70±623.29	1285371.45	1.18	0.82
L01DB07	Mitoxantrone	109	0.15	1958.38±449.24	213463.50	0.28	1.86	122	0.15	2108.25±447.99	257206.40	0.24	1.60
L01DC01	Bleomycin	107	0.15	746.55±562.54	79880.37	0.11	0.71	188	0.23	894.65±654.55	168195.26	0.15	0.68
L01DC03	Mitomycin	107	0.15	558.15±916.93	59722.43	0.08	0.53	135	0.16	588.19±708.10	79406.27	0.07	0.45
L01XA01	Cisplatin	951	1.32	312.15±213.39	296852.46	0.39	0.30	1193	1.45	317.77±214.82	379095.87	0.35	0.24
L01XA02	Carboplatin	1132	1.57	737.25±370.59	834569.92	1.10	0.70	1537	1.86	722.55±366.82	1110552.44	1.02	0.55
L01XA03	Oxaliplatin	249	0.35	4647.15±2337.39	1157140.78	1.53	4.42	773	0.94	5167.94±2424.87	3994817.56	3.68	3.92
L01XC02	Rituximab	1056	1.47	5386.13±2354.04	5687754.46	7.51	5.12	1856	2.25	6253.26±2043.08	11606045.00	10.68	4.75
L01XC03	Trastuzumab	629	0.87	6787.62±1686.08	4269416.08	5.64	6.45	1609	1.95	7063.74±2313.89	11365564.90	10.46	5.36
L01XC07	Bevacizumab	173	0.24	6248.24±1923.63	1080946.38	1.43	5.94	498	0.60	6246.51±2224.23	3110763.62	2.86	4.74
L01XE01	Imatinib	1051	1.46	6676.04±1495.82	7016518.26	9.26	6.34	1471	1.78	6609.28±1505.13	9722258.09	8.95	5.02
L01XX02	L-Asparaginase	4	0.01	3427.39±1788.28	13709.55	0.02	3.26	3	0.00	4321.54±2477.93	12964.61	0.01	3.28
L01XX05	Hydroxycarbamide	862	1.20	132.11±55.16	113876.91	0.15	0.13	960	1.16	135.64±57.45	130217.24	0.12	0.10
L01XX11	Estramustine	75	0.10	775.93±635.22	58194.57	0.08	0.74	47	0.06	1459.59±1254.16	68600.73	0.06	1.11
L01XX14	Tretinoin	3	0.00	2608.21±66.04	7824.64	0.01	2.48	4	0.00	2891.47±3137.61	11565.89	0.01	2.20
L01XX17	Topotecan	33	0.05	5205.80±2169.88	171791.25	0.23	4.95	40	0.05	4620.53±2156.78	184821.38	0.17	3.51
L01XX19	Irinotecan	755	1.05	4254.43±2314.34	3212095.06	4.24	4.04	749	0.91	4482.98±2550.39	3357751.18	3.09	3.40

¹Prev. % was determined by dividing Prev. (N)* by the total number of cancer medicine items claimed in the specific study year (refer to table 4.2).

²Cost % was determined by dividing Total cost (R)** by the total cost of cancer medicine items claimed in the specific study year (refer to table 4.2).

Table 4.25 Classification of cancer medicine items according to active ingredient (continued)

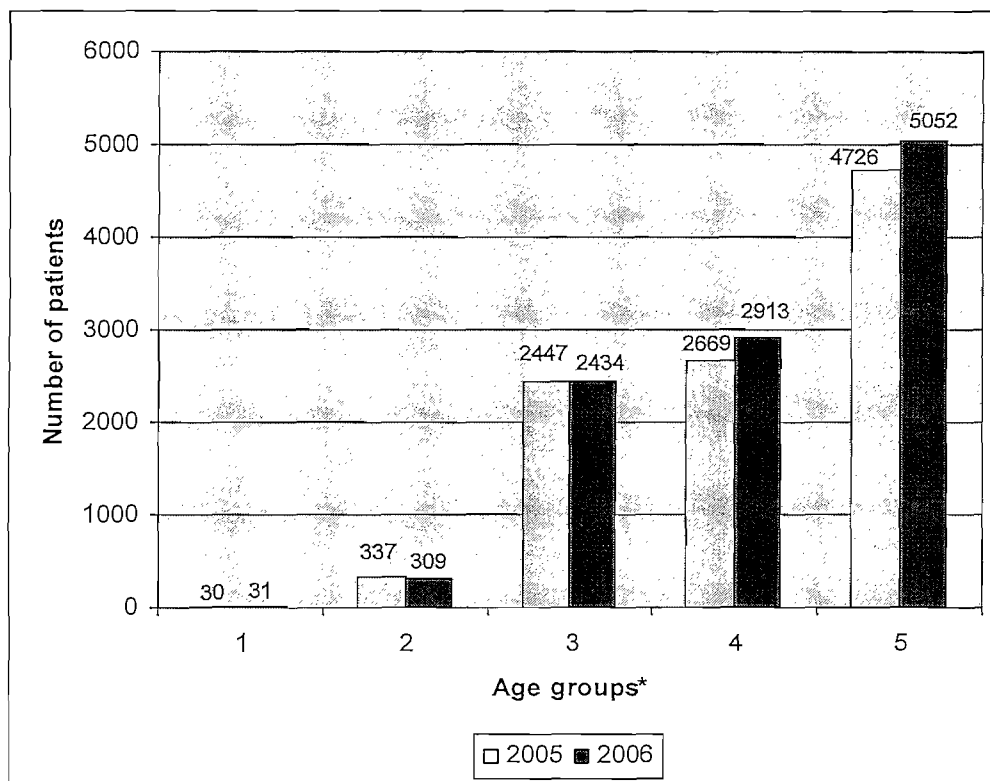
ATC code	Active ingredient	2005						2006					
		Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	Cost index	Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	Cost index
L02AB02	Medroxyprogesterone	129	0.18	483.84±264.87	62414.73	0.08	0.46	156	0.19	552.29±299.63	86157.62	0.08	0.42
L02AE01	Buserelin	222	0.31	2908.43±387.10	645671.98	0.85	2.76	396	0.48	2907.29±413.90	1151285.11	1.06	2.21
L02AE02	Leuprorelin	640	0.89	2543.86±973.99	1628068.39	2.15	2.42	647	0.78	2528.76±952.98	1636108.21	1.51	1.92
L02AE03	Goserelin	1206	1.68	2643.23±788.70	3187729.74	4.21	2.51	1292	1.57	2660.21±735.94	3436990.92	3.16	2.02
L02BA01	Tamoxifen	11879	16.51	140.32±44.73	1666822.95	2.20	0.13	10749	13.03	138.98±43.74	1493858.81	1.37	0.11
L02BB01	Flutamide	324	0.45	805.68±324.11	261040.69	0.34	0.77	295	0.36	733.38±308.17	216347.21	0.20	0.56
L02BB03	Bicalutamide	2044	2.84	2130.93±876.37	4355611.96	5.75	2.03	2199	2.66	2275.24±932.23	5003256.98	4.60	1.73
L02BG03	Anastrozole	2724	3.78	1232.03±178.45	3356062.09	4.43	1.17	4015	4.87	1221.41±146.69	4903970.70	4.51	0.93
L02BG06	Exemestane	424	0.59	1415.14±166.06	600020.66	0.79	1.34	477	0.58	1435.96±212.10	684955.15	0.63	1.09
L03AB04	Interferon alfa-2A	161	0.22	3180.51±1671.14	512062.39	0.68	3.02	162	0.20	3795.81±1832.61	614920.87	0.57	2.88
L03AB05	Interferon alfa-2B	305	0.42	3238.87±2625.39	987853.99	1.30	3.08	179	0.22	3620.51±2931.52	648071.89	0.60	2.75
L03AC01	Aldesleukin	113	0.16	5426.49±1509.36	613193.92	0.81	5.16	187	0.23	6085.37±732.01	1137963.67	1.05	4.62

¹Prev. % was determined by dividing Prev. (N)* by the total number of cancer medicine items claimed in the specific study year (refer to table 4.2).

²Cost % was determined by dividing Total cost (R)** by the total cost of cancer medicine items claimed in the specific study year (refer to table 4.2).

4.5 PREVALENCE AND COST OF CANCER MEDICINE ITEMS ACCORDING TO AGE GROUPS

The cancer medicine items claimed through the medicine claims database by the different age groups (refer to section 4.2.2) in both 2005 and 2006 is presented in table 4.26 – 4.29. The number of patients receiving cancer medicine items in the different age groups is presented below in figure 4.8 (also see table 4.5).



*Refer to section 4.2.2. for the age group classifications

Figure 4.8 Number of cancer patients in different age groups

As can be seen in figure 4.8, the number of patients increased significantly from age group 1 to age group 5. In 2005, there were 30 cancer patients in age group 1 while there were 4 726 cancer patients in age group 5. In 2006, there were 31 cancer patients in age group 1 while in age group 5 there were 5 052 cancer patients. Cancer patients 59 years of age or over comprised almost 50% of all cancer patients on the medicine claims database in both study years.

4.5.1 Prevalence of cancer medicine items in the different age groups

There was, in accordance with the number of patients, a dramatic increase in the number of items (prevalence) claimed through the medicine claims database, from age group 1 to age group 5. In the first study year the prevalence for the age groups 1-5 respectively were 162; 1 280; 12 496; 20 123 and 37 911 and for the second year 270; 1 322; 13 652; 23 323 and 43 958 (refer to table 4.5).

As seen in table 4.5, the most cancer medicine items (52.67%; 53.27%) in the respective study years, were claimed by persons in age group 5 (59 years and over). This is because cancer is a disease of the elderly (refer to section 2.5.2.5, section 2.5.2.5, section 2.5.3.5, section 2.5.4.5 and section 2.5.5.5.2) and the risk of getting cancer increases with age. Cancer medicine items claimed for the treatment of childhood cancers (age group 1 and 2 combined) comprised only 2% of all cancer medicine items claimed in both study years. Cancer medicine items claimed by patients in age group 3 comprised 17.36% and 16.54% of the total number of cancer medicine items in 2005 and 2006 respectively. Cancer medicine items claimed by patients in age group 4 encompassed 27.96% and 28.26% of the total number of cancer medicine items. It is noticeable that the prevalence of cancer medicine items increases with age with a percentage difference of more than 50% between age group 1 (≥ 0 to ≤ 9 years of age) and age group 5 (≥ 59 years of age).

4.5.2 Cost of cancer medicine items in the different age groups

Consequently, partly because of the relatively large prevalence difference between the age groups, there is also a relatively large difference in total cost of cancer medicine items in the different age groups. In figure 4.9 and figure 4.10 the total cost of cancer medicine items for the different age groups is presented. From figure 4.9 and figure 4.10 it can be seen that there is a steep increase in total cost from age group 1 to age group 5. Patients in age groups 1 and 2 (≥ 0 to ≤ 19 years of age) attributed less than 1% of the total cost of cancer medicine items in both study years. Cancer medicine items claimed by patients in age group 3 (≥ 19 to ≤ 45 years of age) comprised 13.31% of the total cost of cancer medicine items in 2005 and 11.21% of the total cost of cancer medicine items in 2006. Patients between 45 and 59 years of age (age group 4) contributed 27.50% and 29.62% of the total cost of all cancer medicine items in both study years respectively. As seen in figure 4.9 and 4.10, cancer medicine items claimed by patients over the age of 59 contributed the biggest percentage of the total cost of cancer medicine items. In 2005, the total cost of

cancer medicine items claimed by patients over the age of 59 comprised 58.39% of the total cost of all cancer medicine items while in 2006 it amounted to 58.30%.

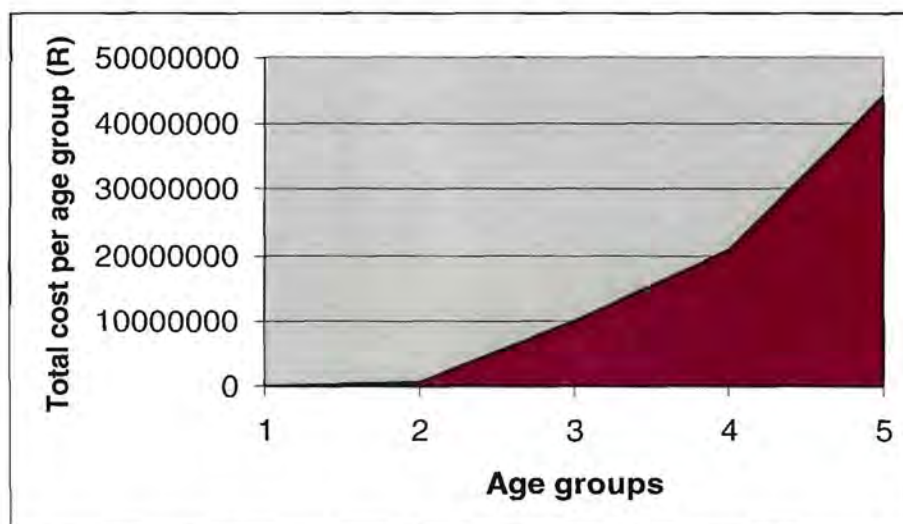


Figure 4.9 Total cost of cancer medicine items in different age groups in 2005

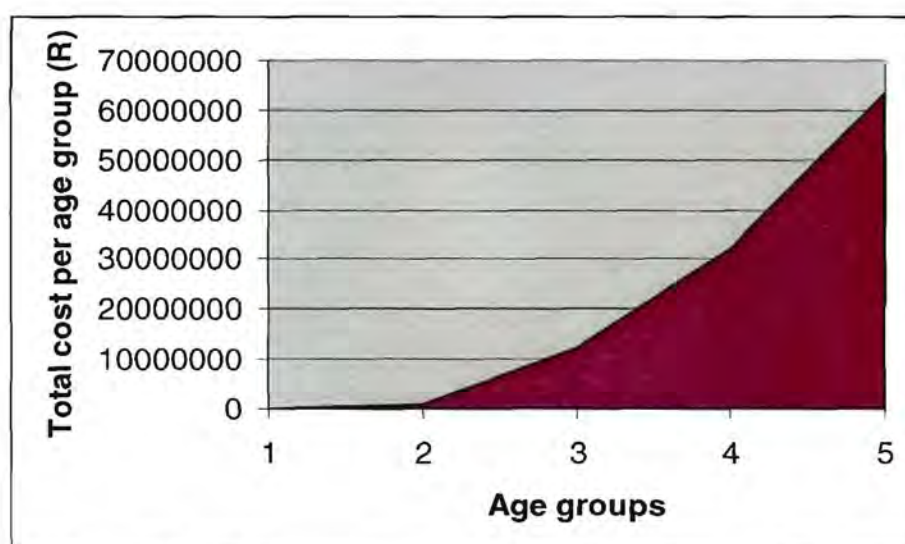


Figure 4.10 Total cost of cancer medicine items in different age group in 2006

The cancer medicine items claimed by each age group are presented in table 4.26 – table 4.29. Table 4.26 and table 4.27 present the prevalence and cost of cancer medicine items claimed by patients in age group 1 and 2. Table 4.28 and table 4.29 give a summary of the prevalence and cost of cancer medicine items claimed by patients in age groups 3-5.

Table 4.26. Prevalence and cost of age group 1 & 2 during 2005

ATC codes	Active ingredient	Age group 1 (0 to ≤9 years)						Age group 2 (>9 to ≤19 years)					
		Prev. (N) (a)	Prev. % (b)	Average cost (R)	Total cost (R) (c)	Cost % (d)	CPI	Prev. (N) (a)	Prev. % (b)	Average cost (R)	Total cost (R) (c)	Cost % (d)	CPI
L01XA02	Carboplatin	5	3.09	90.57±103.06	452.86	1.20	0.39						
L01XA01	Cisplatin							44	3.44	420.15±291.33	13864.89	2.49	0.72
L01AA01	Cyclophosphamide	2	1.23	143.54±0	287.08	0.76	0.62	29	2.27	96.67±51.38	2803.47	0.50	0.22
G03HA01	Cyproterone	4	2.47	197.63±155.14	790.5	2.10	0.85	808	63.13	222.58±93.37	179841.28	32.27	0.51
L01DA01	Dactinomycin							10	0.78	288.24±63.11	2882.44	0.52	0.66
L01DB01	Doxorubicin							2	0.16	908.13±809.50	1816.26	0.33	2.09
L01DB03	Epirubicin							6	0.47	1663.08±72.45	9978.46	1.79	3.82
L01CB01	Etoposide	4	2.47	61.90±69.96	247.59	0.66	0.27	33	2.58	1396.28±834.87	46077.23	8.27	3.21
L02BG06	Exemestane	1	0.62	85.83±0	85.83	0.23	0.37						
L01BC05	Gemcitabine							10	0.78	3788.77±1665.23	37887.74	6.80	8.70
L02AE02	Goserelin	5	3.09	1207.00±5.10	6035	16.04	5.20	1	0.08	1209.28±0	1209.28	0.22	2.78
L01XX05	Hydroxyurea	4	2.47	42.23±16.9	168.92	0.45	0.18	4	0.31	211.84±19.13	847.34	0.15	0.49
L0XX06	Ifosfamide							7	0.55	7092.13±1794.88	49644.94	8.91	16.29
L01XE01	Imatinib							22	1.72	6274.09±1789.00	138029.98	24.77	14.40
L01XX02	L-asparaginase	1	0.62	744.9 ±0	744.96	1.98	3.21						
L02AE02	Leuprolide	1	0.62	2563.13±0	2563.13	6.81	11.04	2	0.16	1300.83±0	2601.66	0.47	2.99
L02AB02	Medroxyprogesterone							2	0.16	223.76±64.29	447.52	0.08	0.51
L01BB02	Mercaptopurine	33	20.37	644.89±217.64	21281.3	56.56	2.78	11	0.86	1466.60±151.30	16132.58	2.90	3.37
L01BA01	Methotrexate	89	54.94	27.00±12.15	2403.39	6.39	0.12	276	21.56	38.38±58.25	10592.9	1.90	0.09
L01CD01	Paclitaxil							2	0.16	6271.60±0	12543.2	2.25	14.41
L02BA01	Tamoxifen							5	0.39	91.23±49.90	456.17	0.08	0.21
L01AX03	Temozolomide							5	0.39	5614.22±2772.85	28071.08	5.04	12.90
L01CA02	Vincristine	13	8.02	197.27±45.41	2564.51	6.82	0.85	12	0.94	124.23±2.68	1490.81	0.27	0.29
	TOTAL	162	100	232.25±368.96	37625	100		1280	100	435.33±1149.69	557219	100	

Table 4.27. Prevalence and cost of age groups 1&2 during 2006

ATC codes	Active ingredient	Age group 1 (0 to ≤9 years)						Age group 2 (>9 to ≤19 years)					
		Prev. (N) (a)	Prev. % (b)	Average cost (R)	Total cost (R) (c)	Cost % (d)	CPI	Prev. (N) (a)	Prev. % (b)	Average cost (R)	Total cost (R) (c)	Cost % (d)	CPI
L01DC01	Bleomycin	4	1.48	356.47±0	1425.88	0.99	0.67	23	1.74	1056.35±394.95	24296.04	3.08	1.77
L01XA02	Carboplatin	6	2.22	752.58±84.74	4515.48	3.13	1.41	6	0.45	1340.64±0	8043.84	1.02	2.25
L01XA01	Cisplatin							42	3.18	369.12±256.95	15503.57	1.97	0.62
L01AA02	Chorambucil	3	1.11	350.01±116.82	1050.02	0.73	0.66						
L01AA01	Cyclophosphamide	2	0.74	85.05±21.69	170.09	0.12	0.16	16	1.21	98.33±46.46	1573.31	0.20	0.17
G03HA01	Cyproterone	7	2.59	133.71±0	935.97	0.65	0.25	694	52.50	217.88±96.92	151209.73	19.20	0.37
L01BC01	Cytarabine	10	3.70	115.34±34.84	1153.37	0.80	0.22	1	0.08	1289.96±0	1289.96	0.16	2.16
L01AX04	Dacarbazine							19	1.44	957.16±211.31	18185.95	2.31	1.61
L01DA01	Dactinomycin	4	1.48	368.68±135.62	1474.71	1.02	0.69						
L01DB02	Daunorubicin							1	0.08	5339.76±0	5339.76	0.68	8.96
L01CD02	Doxetaxel							2	0.15	5552.85±0	11105.7	1.41	9.32
L01DB01	Doxorubicin	1	0.37	788.16±0	788.16	0.55	1.48	18	1.36	1031.01±487.40	18558.13	2.36	1.73
L01DB03	Epirubicin	4	1.48	631.71±641.61	2526.83	1.75	1.18	12	0.91	1748.67±460.85	20984.00	2.66	2.93
L01CB01	Etoposide	13	4.81	240.14±232.65	3121.85	2.17	0.45	20	1.51	2051.63±759.78	41032.63	5.21	3.44
L01BC02	Fluorouracil							40	3.03	47.33±31.75	1893.36	0.24	0.08
L02BB01	Flutamide							9	0.68	145.63±27.20	1310.69	0.17	0.24
L01BC05	Gemcitabine							6	0.45	4939.79±2474.82	29638.72	3.76	8.29
L02AE03	Goserelin	5	1.85	3009.01±0	15045.05	10.44	5.64	5	0.38	3009.01±0	15045.05	1.91	5.05
L01XX05	Hydroxyurea	2	0.74	50.68±23.90	101.36	0.07	0.09	7	0.53	96.01±63.33	672.09	0.09	0.16
L01AA06	Ifosfamide	2	0.74	2664.98±2003.81	5329.95	3.70	4.99	8	0.61	1849.39±653.83	14795.12	1.88	3.10
L01XE01	Imatinib							27	2.04	7336.66±0	198089.82	25.15	12.31
L01XX02	L-asparaginase							3	0.23	4321.54±2477.93	12964.61	1.65	7.25
L02AE02	Leuprolide							8	0.61	1534.05±672.19	12272.36	1.56	2.57
L02AB02	Medroxyprogesterone							2	0.15	170.36±0	340.72	0.04	0.29
L01BB02	Mercaptopurine	50	18.52	1043.88±861.41	52194.21	36.21	1.96	13	0.98	1299.43±392.84	16892.59	2.14	2.18
L01BA01	Methotrexate	102	37.78	36.57±30.51	3730.55	2.59	0.07	285	21.56	47.35±78.29	13493.91	1.71	0.08
L02BA01	Tamoxifen	4	1.48	117.09±0	468.36	0.32	0.22	9	0.68	149.87±107.56	1348.83	0.17	0.25
L01AX03	Temozolomide	9	3.33	3844.85±1631.44	34603.66	24.00	7.2	19	1.44	5782.38±3917.46	109865.27	13.95	9.70
L01BB03	Thioguanine	7	2.59	935.45±791.09	6548.12	4.54	1.75	1	0.08	1956.21±0	1956.21	0.25	3.28
L01CA01	Vinblastine							13	0.98	565.96±205.21	7357.48	0.93	0.95
L01CA02	Vincristine	35	12.96	256.37±206.51	8973.00	6.22	0.48	6	0.45	237.03±196.82	1422.2	0.18	0.40
L01CA04	Vinorelbine							7	0.53	4457.62±0	31203.34	3.96	7.48
	TOTAL	270	100	533.91 ± 974.96	144156.62	100		1322	100	595.83 ± 1447.78	787684.99	100	

Table 4.28 Prevalence and cost of cancer medicine items for age groups 3-5 in 2005

ATC codes	Active ingredient	Age group 3 (>19 to ≤45 years of age)						Age group 4 (>45 to ≤59 years of age)						Age group 5 (≥59 years of age)					
		Prev. (N) (a)	Prev. % (b)	Average cost (R)	Total cost (R) (c)	Cost % (d)	CPI	Prev. (N) (a)	Prev. % (b)	Average cost (R)	Total cost (R) (c)	Cost % (d)	CPI	Prev. (N) (a)	Prev. % (b)	Average cost (R)	Total cost (R) (c)	Cost % (d)	CPI
L03AC01	Alidestleukin	30	0.24	4909.26±1418.96	147277	1.46	6.08	15	0.07	5679.01±1456.82	85185.18	0.41	5.49	68	0.18	5598.9±1526.13	380731.03	0.86	4.80
L01XX14	All-Trans Retinoic	1	0.01	2682.51±0	2682.51	0.03	3.32	1	0.00	2585.94±0	2585.94	0.01	2.50	1	0.00	2556.19±0	2556.19	0.01	2.19
L02BG03	Anastrozole	109	0.87	1208.90±111.80	131770.27	1.31	1.50	701	3.48	1239.32±222.72	868761.18	4.17	1.20	1914	5.05	1230.68±162.54	2355530.64	5.33	1.06
L01XC07	Bevacizumab	0						16	0.08	7013.94±2110.20	112223.11	0.54	6.77	157	0.41	6170.21±1893.53	968723.27	2.19	5.29
L02BB03	Bicalutamide	2	0.02	1751.15±2156.10	3502.29	0.03	2.17	256	1.27	2441.32±957.86	624978.87	3.00	2.36	1786	4.71	2086.86±854.07	3727130.8	8.43	1.79
L01DC01	Bleomycin	93	0.74	729.46±593.95	67840.23	0.67	0.90	12	0.06	821.12±211.19	9853.46	0.05	0.79	2	0.01	1093.34±512.19	2186.68	0.00	0.94
L02AE01	Buserelin	1	0.01	2852.17±0	2852.17	0.03	3.53	8	0.04	2852.17±0	22817.36	0.11	2.75	213	0.56	2910.81±395.05	620002.45	1.40	2.50
L01AB01	Busulphan	0						1	0.00	1033.96±0	1033.96	0.00	1.00	13	0.03	151.79±75.88	1973.24	0.00	0.13
L01BC06	Capecitabine	157	1.26	2014.70±1376.64	316307.45	3.14	2.50	296	1.47	2861.86±1554.40	847110.21	4.07	2.76	886	2.34	2643.59±1456.43	2342222.79	5.30	2.27
L01XA02	Carboplatin	81	0.65	763.14±448.56	61814.74	0.61	0.95	304	1.51	775.15±399.17	235647.09	1.13	0.75	742	1.96	723.55±344.98	536655.23	1.21	0.62
L01AD01	Carbustine	3	0.02	2054.29±739.61	6162.86	0.06	2.54	0						12	0.03	789.29±247.05	9471.5	0.02	0.68
L01AA02	Chlorambucil	2	0.02	333.14 ±0	666.28	0.01	0.41	47	0.23	508.60±227.29	23904.32	0.11	0.49	247	0.65	501.49±388.42	123866.93	0.28	0.43
L01XA01	Cisplatin	97	0.78	346.58±276.77	33617.87	0.33	0.43	172	0.85	269.67±167.83	46382.68	0.22	0.26	243	0.64	242.27±146.15	58872.29	0.13	0.21
L01AA01	Cyclophosphamide	404	3.23	111.28±85.70	44958.29	0.45	0.14	797	3.96	96.42±50.89	76843.48	0.37	0.09	1067	2.81	100.57±44.44	107311.38	0.24	0.09
G03HA01	Cyproterone	3455	27.65	221.77±110.74	766221.47	7.60	0.27	470	2.34	273.71±253.84	128641.76	0.62	0.26	530	1.40	752.48±670.95	398816.42	0.90	0.65
L01BC01	Cytarabine	54	0.43	1614.40±2107.93	87177.46	0.86	2.00	16	0.08	1577.36±1675.01	25237.78	0.12	1.52	31	0.08	1363.62±2357.12	42272.19	0.10	1.17
L01AX04	Dacarbazine	62	0.50	537.82±242.29	33344.7	0.33	0.67	33	0.16	758.85±318.66	25042.15	0.12	0.73	61	0.16	822.69±305.90	50184.19	0.11	0.71
L01DA01	Dactinomycin	8	0.06	90.41±0	723.28	0.01	0.11	0							0.00				
L01DB02	Daunorubicin	0						0						1	0.00	1059.08±0	1059.08	0.00	0.91
L01CD02	Docetaxel	172	1.38	5378.34±1568.95	925074.38	9.17	6.66	526	2.61	5170.10±1696.31	2719472.07	13.05	4.99	757	2.00	5615.40±1537.47	4250859.12	9.61	4.81
L01DB01	Doxorubicin	284	2.27	1853.44±2085.16	526376.67	5.22	2.30	317	1.58	2543.27±1866.95	489218.17	2.35	1.49	352	0.93	2289.14±2141.62	805775.71	1.82	1.96
L01DB03	Epirubicin	261	2.09	1031.73±735.33	269280.52	2.67	1.28	604	3.00	1112.58±664.53	672000.63	3.23	1.07	429	1.13	1138.82±584.28	488984.44	1.11	0.98
L01XX11	Estramustine	0						3	0.01	682.97±83.10	2048.92	0.01	0.66	72	0.19	779.80±648.06	56145.65	0.13	0.67
L01CB01	Etoposide	97	0.78	1246.26±793.57	120887.32	1.20	1.54	120	0.60	1178.19±859.63	141382.94	0.68	1.14	133	0.35	1033.63±609.51	137473.22	0.31	0.89
L02BG06	Exemestane	10	0.08	1421.44±12.55	14214.42	0.14	1.76	79	0.39	1486.00±97.81	117393.92	0.56	1.44	334	0.88	1402.18±161.60	468326.49	1.06	1.20
L01BB05	Fludarabine	0						17	0.08	6044.65±2295.33	102759.1	0.49	5.84	101	0.27	3953.49±2082.98	399302.26	0.90	3.39
L01BC02	Fluorouracil	167	1.34	121.98±90.14	20371.09	0.20	0.15	626	3.11	108.53±103.66	67938.52	0.33	0.10	1101	2.90	140.77±118.74	154992.7	0.35	0.12

Table 4.28 Prevalence and cost of cancer medicine items for age groups 3-5 in 2005 (continued)

ATC codes	Active ingredient	Age group 3 (>19 to ≤45 years of age)						Age group 4 (>45 to ≤59 years of age)						Age group 5 (≥59 years of age)					
		Prev. (N) (a)	Prev. % (b)	Average cost (R)	Total cost (R) (c)	Cost % (d)	CPI	Prev. (N) (a)	Prev. % (b)	Average cost (R)	Total cost (R) (c)	Cost % (d)	CPI	Prev. (N) (a)	Prev. % (b)	Average cost (R)	Total cost (R) (c)	Cost % (d)	CPI
L02BB01	Flutamide	4	0.03	780.80±434.29	3123.2	0.03	0.97	6	0.03	239.40±0	1436.4	0.01	0.23	314	0.83	816.82±316.73	256481.09	0.58	0.70
L01BC05	Gemcitabine	145	1.16	3948.52±1850.48	572535.38	5.68	4.89	539	2.68	4435.86±2133.10	2390926.45	11.48	4.28	676	1.78	4148.70±1944.58	2804520.32	6.34	3.56
L02AE03	Goserelin	193	1.54	1778.68±828.31	343284.77	3.40	2.20	76	0.38	2613.13±761.46	198598.13	0.95	2.52	931	2.46	2834.16±642.33	2638602.56	5.97	2.43
L01XX05	Hydroxyurea	54	0.43	142.64±64.25	7702.33	0.08	0.18	149	0.74	159.84±60.60	23815.5	0.11	0.15	651	1.72	124.95±50.29	81342.82	0.18	0.11
L01XX06	Ifosfamide	48	0.38	1513.70±1206.02	72657.56	0.72	1.88	22	0.11	1631.82±828.68	35900.13	0.17	1.58	57	0.15	1634.38±1000.81	93159.69	0.21	1.40
L01XE01	Imatinib	186	1.49	5983.58±1584.80	1112946.56	11.03	7.41	392	1.95	6721.22±1595.79	2634719.75	12.65	6.49	451	1.19	6941.96±1243.96	3130821.97	7.08	5.95
L03AB04	Interferon Alfa 2A	47	0.38	3117.37±2273.39	146516.19	1.45	3.86	50	0.25	3253.78±908.76	162688.91	0.78	3.14	64	0.17	3169.65±1633.78	202857.29	0.46	2.72
L03AB05	Interferon Alfa 2B	60	0.48	3349.55±2273.39	200973.04	1.99	4.15	120	0.60	4077.28±2791.44	489273.19	2.35	3.94	125	0.33	2380.86±2294.78	297607.76	0.67	2.04
L01XX19	Irinotecan	70	0.56	4145.34±2737.26	290174.04	2.88	5.14	190	0.94	4060.56±2201.69	771506.48	3.70	3.92	495	1.31	4344.27±2291.26	2150414.54	4.86	3.72
L01XX02	L-asparaginase	3	0.02	4321.53±0	12964.59	0.13	5.35	0						0					
L02AE02	Leuprolide	59	0.47	1272.45±825.85	75074.41	0.74	1.58	28	0.14	2935.53±681.59	82194.88	0.39	2.84	550	1.45	2664.79±898.59	1465634.31	3.31	2.28
L02AB02	Medroxyprogesterone	15	0.12	391.10±295.48	5866.5	0.06	0.48	17	0.08	491.65±259.04	8358.01	0.04	0.47	95	0.25	502.55±260.56	47742.7	0.11	0.43
L01AA03	Melphalan	7	0.06	2741.86±1047.03	19193.01	0.19	3.40	25	0.12	1059.55±1379.22	26488.77	0.13	1.02	154	0.41	375.08±123.16	57762.88	0.13	0.32
L01BB02	Mercaptopurine	47	0.38	1338.08±289.01	5866.5	0.06	0.15	8	0.04	931.88±409.45	7455.02	0.04	0.90	54	0.14	920.84±413.15	49725.56	0.11	0.79
L01BA01	Methotrexate	4310	34.49	40.21±167.14	173287.09	1.72	0.05	8387	41.68	34.92±73.02	292850.2	1.41	0.03	11391	30.05	33.76±98.71	384600.49	0.87	0.03
L01DC03	Mitomycin	18	0.14	301.88±271.44	5433.75	0.05	0.37	38	0.19	495.49±236.82	18828.75	0.09	0.48	51	0.13	695.29±1292.30	35459.93	0.08	0.60
L01DB07	Mitoxantrone	9	0.07	2104.53±0	18940.77	0.19	2.61	19	0.09	1756.87±507.31	33380.54	0.16	1.70	81	0.21	1989.41±448.91	161142.19	0.36	1.71
L01XA03	Oxaliplatin	5	0.04	7672.13±0	38360.65	0.38	9.50	49	0.24	4314.04±2485.88	211388.04	1.01	4.17	195	0.51	4653.29±2278.44	907392.09	2.05	3.99
L01CD01	Paclitaxel	106	0.85	4132.57±2003.64	438052.85	4.34	5.12	303	1.51	4548.59±2457.51	1378223.11	6.62	4.39	494	1.30	4138.99±2292.06	2044660.16	4.62	3.55
L01XC02	Rituximab	210	1.68	5368.82±2317.69	1127452.69	11.18	6.65	195	0.97	5254.28±2411.01	1024584.85	4.92	5.07	651	1.72	5431.21±2350.49	3535716.92	8.00	4.66
L02BA01	Tamoxifen	887	7.10	141.12±53.53	125169.52	1.24	0.17	3119	15.50	138.12±38.58	430788.53	2.07	0.13	7868	20.75	141.13±45.85	1110408.73	2.51	0.12
L01AX03	Temozolomide	15	0.12	5456.78±1539.80	81851.63	0.81	6.76	180	0.89	3918.77±2578.82	705378.87	3.39	3.79	189	0.50	4953.70±2062.03	936249.64	2.12	4.25
L01BB03	Thioguanine	1	0.01	1715.38±0	1715.38	0.02	2.13	4	0.02	4316.24±2099.85	17264.97	0.08	4.17	6	0.02	1612.92±662.03	9677.52	0.02	1.38
L01XX17	Topotecan	0						10	0.05	6326.77±2122.84	63267.7	0.30	6.11	23	0.06	4718.42±2045.85	108523.55	0.25	4.05
L01XC03	Trastuzumab	183	1.46	7074.17±1345.88	1294573.81	12.83	8.76	249	1.24	6805.39±1744.04	1694542.19	8.13	6.57	197	0.52	6498.99±1848.61	1280300.08	2.90	5.57
L01CA01	Vinblastine	60	0.48	291.13±158.62	17467.53	0.17	0.36	32	0.16	362.43±211.03	11597.75	0.06	0.35	30	0.08	672.91±260.37	20187.36	0.05	0.58
L01CA02	Vincristine	114	0.91	189.23±104.77	21572.31	0.21	0.23	105	0.52	179.28±92.63	18824.72	0.09	0.17	157	0.41	166.38±63.99	26120.99	0.06	0.14
L01CA03	Vindesine	0						15	0.07	2187.85±115.55	32817.77	0.16	2.11	9	0.02	2195.49±114.71	19759.37	0.04	1.88
L01CA04	Vinorelbine	50	0.40	4245.31±2040.21	212265.64	2.10	5.26	166	0.82	3310.89±1582.20	549608.47	2.64	3.20	526	1.39	3458.24±1821.72	1819033.36	4.11	2.96
	TOTAL	12496	100	807.24±1752.52	10087228	100		20123	100	1035.34±2010.35	20834076	100		37911	100	1166.43±1921.08	44220482	100	

Table 4.29 Prevalence and cost of cancer medicine items for age groups 3-5 during 2006

ATC codes	Active ingredient	Age group 3 (>19 to ≤45 years of age)						Age group 4 (>45 to ≤59 years of age)						Age group 5 (≥60 years of age)					
		Prev. (N) (a)	Prev. % (b)	Average cost (R)	Total cost (R) (c)	Cost % (d)	CPI	Prev. (N) (a)	Prev. % (b)	Average cost (R)	Total cost (R) (c)	Cost % (d)	CPI	Prev. (N) (a)	Prev. % (b)	Average cost (R)	Total cost (R) (c)	Cost % (d)	CPI
L03AC01	Aldesleukin							162	0.69	6103.73±712.24	988804.07	3.07	4.42	25	0.06	5966.38±856.00	149159.60	0.24	0.08
L01XX14	All-Trans Retinoic Acid							4	0.02	2891.47±3137.61	11565.89	0.04	2.09						
L02BG03	Anastrozole	143	1.05	1198.02±56.98	171316.58	1.41	1.34	1141	4.89	1229.89±183.77	1403309.4	4.36	0.89	2731	6.21	1219.09±131.56	3329344.7	5.25	1.75
L01XC07	Bevacizumab	5	0.04	8621.41±913.58	43107.04	0.35	9.66	208	0.89	6478.05±2266.95	1347433.6	4.19	4.69	285	0.65	6035.87±2171.87	1720222.9	2.71	0.90
L02BB03	Bicalutamide	3	0.02	1536.57±0	4609.71	0.04	1.72	203	0.87	2630.47±896.16	533985.43	1.66	1.91	1993	4.53	2240.17±928.75	4464661.8	7.05	2.35
L01DC01	Bleomycin	100	0.73	1023±810.06	102321.88	0.84	1.15	21	0.09	793.17±386.48	16656.61	0.05	0.57	40	0.09	587.37±184.66	23494.85	0.04	0.01
L02AE01	Buserelin	3	0.02	2852.17±0	8556.51	0.07	3.19	19	0.08	2849.74±5.63	54145.13	0.17	2.06	374	0.85	2910.65±425.69	1088583.5	1.72	0.57
L01AB01	Busulphan							3	0.01	111.40±38.78	334.19	0.00	0.08	2	0.00	125.25±131.10	250.50	0.00	0.00
L01BC06	Capecitabine	109	0.80	2579.35±1580.30	281149.68	2.31	2.89	397	1.70	2797.62±1359.61	1110655.80	3.45	2.03	883	2.01	2524.37±1312.27	2229021.4	3.52	1.17
L01XA02	Carboplatin	108	0.79	726.09±410.47	78418.00	0.64	0.81	408	1.75	741.33±344.41	302460.68	0.94	0.54	1009	2.30	710.72±369.67	717114.44	1.13	0.38
L01AD01	Carmustine	1	0.01	2938.08±0	2938.08	0.02	3.29	4	0.02	2428.54±959.56	9714.16	0.03	1.76	7	0.02	1331.90±1025.81	9323.30	0.01	0.00
L01AA02	Chlorambucil							54	0.23	475.29±216.25	25665.82	0.08	0.34	244	0.56	402.25±276.19	98148.18	0.15	0.05
L01XA01	Cisplatin	113	0.83	228.24±160.42	25791.13	0.21	0.26	140	0.60	290.32±238.84	40644.35	0.13	0.21	360	0.82	260.78±155.79	93880.04	0.15	0.05
L01AA01	Cyclophosphamide	600	4.39	107.08±68.31	64246.09	0.53	0.12	918	3.94	107.46±80.00	98644.31	0.31	0.08	1538	3.50	97.33±43.81	149693.98	0.24	0.08
GO3HA01	Cyproterone	3410	24.98	223.42±106.70	761861.75	6.25	0.25	480	2.06	248.98±124.29	119509.02	0.37	0.18	529	1.20	623.85±564.87	330015.01	0.52	0.17
L01BC01	Cytarabine	33	0.24	1479.91±2682.60	48837.08	0.40	1.66	19	0.08	3456.24±2349.67	65668.58	0.20	2.50	38	0.09	1623.93±1525.62	61708.80	0.10	0.03
L01AX04	Dacarbazine	48	0.35	793.04±326.09	38065.87	0.31	0.89	53	0.23	1180.66±511.82	62574.79	0.19	0.86	58	0.13	821.38±223.38	47640.20	0.08	0.03
L01DA01	Dactinomycin	7	0.05	210.46±0	1473.22	0.01	0.24												
L01DB02	Daunorubicin	2	0.01	2153.69±0	4307.38	0.04	2.41	3	0.01	3235.55±17.18	9706.65	0.03	2.34	1	0.00	4012.23±0	4012.23	0.01	0.00
L01CD02	Docetaxel	186	1.36	5387.21±1650.16	1002021.20	8.22	6.03	638	2.74	5310.32±1545.66	3387982.9	10.52	3.85	903	2.05	5401.69±1540.24	4877729.2	7.70	2.57
L01DB01	Doxorubicin	396	2.90	2475.87±3343.56	980444.52	8.04	2.77	466	2.00	1593.34±2521.01	742498.50	2.31	1.15	485	1.10	1953.74±2588.40	947563.75	1.50	0.50
L01DB03	Epirubicin	241	1.77	1094.55±648.33	263796.30	2.16	1.23	426	1.83	1145.50±673.73	487983.17	1.52	0.83	502	1.14	1016.12±551.81	510091.15	0.81	0.27
L01XX11	Estramustine Phosphate													47	0.11	1459.59±1254.16	68600.73	0.11	0.04
L01CB01	Etoposide	137	1.00	1373.50±755.63	188169.48	1.54	1.54	74	0.32	1221.59±680.86	90397.78	0.28	0.88	164	0.37	1342.80±789.32	220218.89	0.35	0.12
L02BG06	Exemestane	22	0.16	1415.49±0	31140.78	0.26	1.59	108	0.46	1484.08±439.42	160280.58	0.50	1.08	347	0.79	1422.29±35.24	493533.79	0.78	0.26
L01BB05	Fludarabine							37	0.16	6947.29±1260.31	257049.80	0.80	5.03	107	0.24	4459.49±2248.59	477164.95	0.75	0.25
L01BC02	Fluorouracil	278	2.04	140.02±120.62	38925.34	0.32	0.16	632	2.71	124.94±113.18	78961.02	0.25	0.09	1246	2.83	155.52±122.38	193777.62	0.31	0.10
L02BB01	Flutamide	16	0.12	285.46±159.15	4567.35	0.04	0.32	3	0.01	570.08±153.87	1710.25	0.01	0.41	267	0.61	781.87±277.35	208758.92	0.33	0.11

Table 4.29 Prevalence and cost of cancer medicine items for age groups 3-5 during 2006 (continued)

ATC codes	Active Ingredient	Age group 3 (>19 to ≤45 years of age)						Age group 4 (>45 to ≤59 years of age)						Age group 5 (≥60 years of age)					
		Prev. (N) (a)	Prev. % (b)	Average cost (R)	Total cost (R) (c)	Cost % (d)	CPI	Prev. (N) (a)	Prev. % (b)	Average cost (R)	Total cost (R) (c)	Cost % (d)	CPI	Prev. (N) (a)	Prev. % (b)	Average cost (R)	Total cost (R) (c)	Cost % (d)	CPI
L01BC05	Gemcitabine	128	0.94	3679.23±2039.77	470940.82	3.86	4.12	478	2.05	4410.78±1833.57	2108352	6.55	3.20	1033	2.35	4496.42±1865.07	4644806.50	7.33	2.44
L02AE03	Goserelin	207	1.52	1623.22±756.78	336005.99	2.76	1.82	76	0.33	2579.98±768.46	196078.19	0.61	1.87	999	2.27	2877.69±515.68	2874816.6	4.54	1.51
L01XX05	Hydroxyurea	73	0.53	103.20±54.60	7533.61	0.06	0.12	200	0.86	187.37±55.69	37474.02	0.12	0.14	678	1.54	124.54±48.43	84436.16	0.13	0.04
L01XX06	Ifosfamide	117	0.86	1727.75±1896.02	202146.96	1.66	1.94	28	0.12	2420.19±1953.00	67765.24	0.21	1.75	64	0.15	1864.80±1245.80	119347.05	0.19	0.06
L01XE01	Imatinib	154	1.13	5918.07±1807.45	911383.07	7.48	6.63	517	2.22	6798.03±1319.50	3514582.1	10.92	4.92	773	1.76	6595.35±1537.73	5098203.1	8.05	4.57
L03AB04	Interferon Alfa 2A	35	0.26	4862.89±1949.40	170201.18	1.40	5.45	29	0.12	2585.62±1360.04	74982.87	0.23	1.87	98	0.22	3772.82±1690.91	369736.82	0.58	0.19
L03AB05	Interferon Alfa 2B	60	0.44	5395.27±2678.50	323716.48	2.66	6.04	59	0.25	2296.06±2670.11	135467.38	0.42	1.66	60	0.14	3148.13±2561.21	188888.03	0.30	0.10
L01XX19	Irinotecan	88	0.64	4366.18±2841.66	384223.65	3.15	4.89	189	0.81	4385.25±2672.44	828812.60	2.57	3.18	472	1.07	4543.89±2444.88	2144714.9	3.38	1.13
L01XX02	L-asparaginase																		
L02AE02	Leuprolide	46	0.34	1019.60±461.96	46901.43	0.38	1.14	50	0.21	2450.99±977.31	122549.34	0.38	1.78	543	1.24	2678.43±861.18	1454385.1	2.30	0.77
L02AB02	Medroxyprogesterone	21	0.15	340.56±158.09	7151.87	0.06	0.38	26	0.11	675.34±432.73	17558.73	0.05	0.49	107	0.24	571.09±258.26	61106.30	0.10	0.03
L01AA03	Melphalan	6	0.04	810.01±1171.92	4860.06	0.04	0.91	7	0.03	284.41±142.01	1990.90	0.01	0.21	165	0.38	463.22±566.46	76430.63	0.12	0.04
L01BB02	Mercaptopurine	55	0.40	1276.99±293.97	70234.30	0.58	1.43	10	0.04	725.89±63.53	7258.89	0.02	0.53	58	0.13	900.65±387.20	52237.70	0.08	0.03
L01BA01	Methotrexate	4813	35.25	44.30±114.52	213219.13	1.75	0.05	9573	41.05	33.93±21.06	324855.49	1.01	0.02	12800	29.12	32.11±21.56	411014.25	0.65	0.22
L01DC03	Mitomycin	18	0.13	210.98±93.13	3797.56	0.03	0.24	48	0.21	729.99±1104.49	35039.33	0.11	0.53	69	0.16	587.96±301.44	40569.38	0.06	0.02
L01DB07	Mitoxantrone	4	0.03	1891.30±406.94	7565.20	0.06	2.12	21	0.09	2056.21±584.69	43180.36	0.13	1.49	97	0.22	2128.46±416.66	206460.84	0.33	0.11
L01XA03	Oxaliplatin	69	0.51	4860.11±2321.19	335347.39	2.75	5.44	209	0.90	5372.09±2461.95	1122766.4	3.49	3.89	495	1.13	5124.65±2421.26	2536703.8	4.00	1.33
L01CD01	Paclitaxil	102	0.75	5039.04±2942.08	513982.56	4.22	5.64	408	1.75	4957.88±2832.97	2022813.4	6.28	3.59	538	1.22	5479.26±2876.30	2947844.6	4.65	1.55
L01XC02	Rituximab	131	0.96	6322.34±1747.18	828227.10	6.80	7.08	526	2.26	6169.12±2119.32	3244955.4	10.08	4.47	1199	2.73	6282.62±2039.44	7532862.8	11.89	3.96
L02BA01	Tamoxifen	754	5.52	138.11±51.03	104132.94	0.85	0.15	2776	11.90	138.02±42.63	383133.70	1.19	0.10	7206	16.39	139.44±43.23	1004775	1.59	0.53
L01AX03	Temozolomide	79	0.58	4772.19±3354.01	377003.24	3.09	5.35	286	1.23	5577.49±2549.13	1595161.2	4.95	4.04	421	0.96	4726.62±2815.81	1989905.4	3.14	1.05
L01BB03	Thioguanine	16	0.12	1263.84±447.30	20221.48	0.17	1.42							7	0.02	5908.00±1637.12	41355.97	0.07	0.02
L01XX17	Topotecan							33	0.14	4347.44±2174.22	143465.41	0.45	3.15						
L01XC03	Trastuzumab	316	2.31	7116.38±2057.16	2248775.1	18.45	7.97	583	2.50	6764.55±2354.00	3943731.3	12.25	4.90	710	1.62	7286.00±2364.27	5173058.6	8.16	2.72
L01CA01	Vinblastine	41	0.30	511.51±217.59	20971.83	0.17	0.57	20	0.09	391.17±199.09	7823.35	0.02	0.28	88	0.20	340.81±132.20	29990.90	0.05	0.02
L01CA02	Vincristine	149	1.09	168.95±38.38	25173.44	0.21	0.19	197	0.84	172.39±55.64	33960.78	0.11	0.12	352	0.80	167.68±51.91	59024.96	0.09	0.03
L01CA03	Vindesine																		
L01CA04	Vinorelbine	85	0.62	4182.75±1394.89	355533.91	2.92	4.69	226	0.97	3192.92±1638.49	721600.84	2.24	2.31	454	1.03	3535.96±1744.08	1605327.2	2.53	0.84
	TOTAL	13652	100		12187676	100		23323	100		32143702	100		43669	99		63261120	100	33

Take note of the following points in the interpretation of table 4.26 – table 4.29

Percentage (b) was determined by dividing (a) by the total number of cancer medicine items in the specific age group.

Percentage (d) was determined by dividing (c) by the total cost of cancer medicine items in the specific age group.

4.5.3 Comparison between prevalence and cost of cancer medicine items in different age groups

In this section the prevalence and cost of cancer medicine items in the different age groups will be discussed and compared (refer to table 4.26 – table 4.29). Some of the cancer medicine items were identified from table 4.26 – table 4.29 based on their high prevalence, high cost, high CPI and/or increase/decrease in prevalence or cost of these cancer medicine items between 2005 and 2006. These cancer medicine items will now be discussed. All data presented in table 4.30 – table 4.62 were extracted from table 4.26 – table 4.29.

4.5.3.1 Goserelin (L02AE03)

Goserelin is part of the endocrine therapy (L02) and more specifically a gonadotropin-releasing hormone (GnRH) analogue (L02AE – refer to Appendix A) and is indicated in prostate cancer, hormone receptor-positive breast cancer in pre- and peri-menopausal woman and in the management of endometriosis and uterine fibroids (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). The trade names containing goserelin are Zoladex depot injection 3.6mg® and the Zoladex depot injection 10.8mg® (refer to Appendix B).

In age group 1 (≥ 0 to ≤ 9 years of age) goserelin comprised 3.09% (2005) and 1.85% (2006) of all cancer medicine items claimed (refer to table 4.26 & table 4.27). Goserelin encompassed 0.08% (2005) and 0.38% (2006) of all cancer medicine items claimed by age group 2 (refer to table 4.26 & table 4.27). Because goserelin is mainly a cancer drug used in prostate cancer and breast cancer, it is unusual to see goserelin claimed by patients younger than 19 years of age. According to the New England Journal of Medicine (Brunner & Otten, 1999:1763) GnRH analogues such as goserelin have been used in precocious puberty. The efficacy of goserelin in the treatment of girls with central precocious or early puberty was also assessed in a study done by Paterson *et al.* (1998:323-327). This may be part of the explanation

why goserelin was claimed by patients younger than 19 years of age (age group 1 and 2).

Goserelin comprised 1.54% (n=193) of all cancer medicine items claimed by age group 3 in 2005 and 1.52% (n=207) in 2006. In 2005, goserelin encompassed 0.38% (n=76) of all cancer medicine items claimed by patients in age group 4, and in 2006 goserelin comprised 0.33% (n=76). In age group 5, goserelin comprised 2.46% (n=931) of all cancer medicine items claimed by patients older than 59 in 2005. Goserelin comprised 2.27% (n=999) of all cancer medicine items claimed by patients older than 59 in 2006.

From table 4.25 it can be seen that the total number of items of goserelin amounted to 1 206 (2005) and 1 292 (2006). In table 4.30 the prevalence percentage distribution between the different age groups is presented.

Table 4.30 Prevalence percentage distribution of goserelin between the different age groups

	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
	% ¹	%	%	%	%
2005	0.41	0.08	16.00	6.30	77.20
2006	0.41	0.41	16.02	5.88	77.32

¹Prevalence percentage distribution of goserelin was calculated by dividing the prevalence (Prev. (N)*) of goserelin in each age group (shown in table 4.26 – table 4.29) by the total prevalence of goserelin in 2005 (n=1 206) and 2006 (n=1 292) (refer to table 4.25) and multiplying it by 100

From the results in Table 4.30 it can be concluded that goserelin is mostly used by patients older than 59 years of age. Patients in age group 3 (≥ 19 to ≤ 45 years of age) claimed 16.00% and 16.02% in the two study years respectively, which is also relatively high compared to the other age groups. These two age groups (3 and 5) combined comprised 93.20% and 93.34% of the total prevalence of goserelin in 2005 and 2006 respectively. This may be because this cancer drug is mainly used for prostate cancer and peri- and post-menopausal breast cancer, which are largely diseases of the elderly (refer to section 2.5.1.5 and section 2.5.2.5).

Table 4.31 Average costs of goserelin in different age groups

Average cost of goserelin in different age groups (R)					
	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
2005	1 207.00 ±5.10	1 209.28±0	1 778.68±828.31	2 613.13±762.46	2 834.16±642.33
2006	3 009.01±0	3 009.01±0	1 623.22±756.78	2 579.98±768.46	2 877.69±515.68

*Average costs shown in table 4.31 were taken from table 4.26 – table 4.29.

In table 4.31 the average costs of goserelin in the different age groups is compared. The *highest average cost* (R3 009.01 ± 0) for goserelin is found in age group 1 as well as in age group 2 in 2006. In 2005, the average cost for goserelin increased from age group 1 (R1 207.00 ± 0) to age group 5 (R2 834.16 ± 642.33).

The CPI of goserelin is higher than 1.00 in all the age groups in 2005 and 2006 (refer to table 4.19 - table 4.21) and this indicates that goserelin is a relatively expensive cancer drug (refer to section 3.8.4.6 and table 4.19).

4.5.3.2 L-asparaginase (L01XX02)

L-asparaginase (*syn.* Asparaginase) is an antineoplastic agent (L01) and is classified as “other antineoplastic agents” (L01XX – refer to Appendix A). It is mainly indicated for the induction of remissions in acute lymphoblastic leukaemia. It is usually used in combination with other antineoplastic agents (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). The trade name for asparaginase is the Laspar Injection® (refer to Appendix B).

L-asparaginase was only claimed 7 times throughout the two study years (refer to table 4.25). In 2005, L-asparaginase comprised 0.62% of all cancer medicine items claimed by patients in age group 1 and 0.02% of all cancer medicine items claimed by age group 3. In 2006, L-asparaginase comprised 0.23% of all cancer medicine items claimed by patients between the ages of 19 and 45 years.

Table 4.32 The CPI of L-asparaginase in some age groups in 2005 and 2006

CPI of L-asparaginase		
	2005	2006
Age group 1	3.21	
Age group 2		7.25
Age group 3	5.53	

**CPI values shown in table 4.32 was taken from table 4.26 – table 2.29*

***For the purpose of this study CPI values higher than one (1) will indicate relatively expensive treatment (refer to paragraph 3.8.4.6)*

From table 4.32 it can be seen that the CPI of L-asparaginase is higher than 1.00 (refer to section 3.8.4.6) and therefore it was a relatively expensive cancer medicine item (refer to table 4.19).

4.5.3.3 Leuprolide (L02AE02)

Leuprolide (*syn.* Leuprorelin) is part of endocrine therapy (L02) and a gonadotropin-releasing hormone (GnRH) analogue (L02AE). It is mainly indicated in palliative treatment of advanced prostate cancer. It has also been used in central precocious puberty, in the management of endometriosis and uterine fibroids and in the treatment of breast cancer in pre-menopausal woman (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). The trade names on the database containing Leuprolide is Lucrin 2.8ml 5mg/ml®, Lucrin depot injection 3.75mg®, Lucrin depot injection 11.25mg/vial.

Table 4.33 Comparison of prevalence and cost of leuprolide between the different age groups

Age group	2005					2006				
	Prev. (N)	Prev. (%)	Average cost (R)	Total cost (R)	CPI	Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	CPI
1	1	0.62	2563.13±0	2563.13	11.04					
2	2	0.16	1300.83±0	2601.66	2.99	8	0.61	1534.05±672.19	12272.36	2.57
3	59	0.47	1272.45±825.85	75074.41	1.58	46	0.34	1019.60±461.96	46901.43	1.14
4	28	0.14	2935.53±681.59	82194.88	2.84	50	0.21	2450.99±977.31	122549.34	1.78
5	550	1.45	2664.79±898.59	1465634.3	2.28	543	1.24	2678.43±861.18	1454385.1	1.86

* All data in table 4.33 was taken from table 4.26 – 4.29

The number of items increased from age group 1 to age group 5 in both 2005 and 2006. In 2005, the highest average cost per medicine item was in age group 4 (R2 935 ± 681.59). In 2006, it was in age group 5 (R2 678.43 ± 861.18).

The CPI of leuprolide was relatively high in all the different age groups in both study years. This indicates that leuprolide is a relatively expensive cancer drug (refer to table 4.19 and section 3.8.4.6).

4.5.3.4 Mercaptopurine (L01BB02)

Mercaptopurine acts as an anti-metabolite (L01B) and more specifically it is a purine analogue (L01BB – refer to Appendix A). It is used as maintenance therapy for *acute leukaemias*, usually in combination with methotrexate. It may also be used in *chronic myeloid leukemia* (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). The trade name containing mercaptopurine is Puri-Nethol 50mg tablets®.

Mercaptopurine comprised 20.37% (2005) and 18.52% (2006) of all cancer medicine items claimed by age group 1 (≥0 to ≤9 years of age) (refer to table 4.26 and table 4.27). In age group 2, mercaptopurine comprised only 0.86% and 0.98% of all cancer medicine items claimed in 2005 and 2006 respectively (refer to table 4.26 and 4.27).

In 2005, mercaptopurine comprised 0.38% of all cancer medicine items claimed by age group 3 and in 2006 mercaptopurine encompassed 0.40% of all cancer medicine items claimed by this specific age group. Mercaptopurine comprised only 0.04% of all cancer medicine items claimed by patients in age group 4 in both 2005 and 2006. In age group 5, mercaptopurine comprised 0.14% (2005) and 0.13% (2006) of all cancer medicine items claimed by patients older than 59 years (refer to table 4.28 and table 4.29).

From table 4.25 it can be seen that the total prevalence of mercaptopurine amounted to 153 (0.21% of all cancer medicine items) in 2005 and 186 (0.23% of all cancer medicine items) in 2006. In table 4.34 the total prevalence percentage distribution of mercaptopurine between the different age groups is presented

Table 4.34 Prevalence percentage distribution of mercaptopurine between the different age groups

	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
	% ¹	%	%	%	%
2005	21.57	7.19	30.72	5.23	35.30
2006	26.88	6.99	29.57	5.38	31.18

¹Prevalence percentage distribution of mercaptopurine was calculated by dividing the prevalence (Prev. (N)*) of mercaptopurine in each age group (shown in table 4.26 – 4.29) by the total prevalence of mercaptopurine in 2005 (n=153) and 2006 (n=186) (refer to table 4.25) and multiplying it by 100.

From the results in table 4.34 it can be seen that mercaptopurine was largely claimed by patients in age group 1, age group 3 and age group 5. Calculated from table 4.34, only 12.42% (2005) and 12.37% (2006) was claimed by patients in age group 2 and age group 4 combined.

The average costs of mercaptopurine in the different age groups are presented in table 4.35.

Table 4.35 Average costs of mercaptopurine in different age groups

Average cost of mercaptopurine in different age groups (R)					
	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
2005	644.89±217.64	1466.60±1551.30	1338.08±289.01	931.88±409.45	920.84±413.15
2006	1043.88±861.41	1299.43±392.84	1276.99±293.97	725.89±63.53	900.65±387.20

*Average costs shown in table 4.35 were taken from table 4.26 – 4.29.

The average cost of mercaptopurine in all the age groups decreased from 2005 to 2006, except in age group 1 the average cost increased from 2005 to 2006. The

effect size (d-value) between the average cost of mercaptopurine in age group 1 (2005) and age group 1 (2006) was 0.46, and was therefore of no practical significance.

The effect sizes (d-values) that were of practical significance are shown in table 4.36. An effect size (d-value) equal to or higher than 0.8 is considered to have practical significance (refer to section 3.8.4.5).

Table 4.36 Effect sizes (d-values) for mercaptopurine between the different age groups

	Age group 2 (2006)	Age group 3 (2005)	Age group 3 (2006)
Age group 1(2005)	1.67	0.88	2.15
Age group 1(2006)	0.30	0.34	0.27
Age group 2 (2005)			
Age group 2 (2006)		0.10	
Age group 3 (2005)			
Age group 3 (2006)	0.08	0.21	
Age group 4 (2005)	0.90	1.00	0.84
Age group 4 (2006)	1.46	2.12	1.87
Age group 5 (2005)	0.92	1.01	0.86
Age group 5 (2006)	1.02	1.13	0.97

**Effect sizes (d-values) calculated from the average costs in table 4.35 (taken from table 4.26 – 4.29)*

***For the purpose of this study effect sizes (d-values) of 0.8 or higher will be assumed to have practical significance (refer to paragraph 3.8.4.5)*

It can be concluded from the results of table 4.36 that mercaptopurine was relatively more expensive for patients in age group 2 in 2006 and age group 3 in both study years.

4.5.3.5 Methotrexate (L01BA01)

Aspects of methotrexate were already discussed in section 4.3.6 and section 4.4.4. Methotrexate acts as an anti-metabolite (L01B – refer to Appendix A) and is a folic acid analogue (L01BA) used in various cancers and other diseases (refer to section 4.3.6). The trade names containing methotrexate are presented in Appendix B.

In age group 1, methotrexate comprised 54.94% (n=89) of all cancer medicine items claimed in 2005 and 37.78% (n=102) in 2006, for the specific age group. Methotrexate encompassed 21.56% (n=276) and 21.56% (n=285) of cancer medicine items claimed by patients in age group 2 in 2005 and 2006 respectively. In 2005, 34.49% (n=4 310) of all cancer medicine items claimed by patients in age group 3 were methotrexate. In 2006, methotrexate comprised 35.25% (n=4 813) of all

cancer medicine items claimed by patients in age group 3. In age group 4, methotrexate comprised 41.05% (n=9 573) of all cancer medicine items claimed by patients in age group 4 and 41.68% (n=8 387) in 2006. Methotrexate comprised 29.12% (n=12 800) and 30.05% (n=11 391) of cancer medicine items claimed by patients older than 59 (age group 5), in 2005 and 2006 respectively.

From table 4.25 it can be seen that the total prevalence of methotrexate amounted to 24 453 items (33.98% of all cancer medicine items) in 2005 and 27 573 items (33.41% of all cancer medicine items) in 2006. In table 4.37 the prevalence percentage distribution of methotrexate between the different age groups is presented.

Table 4.37 Prevalence percentage distribution of methotrexate between the different age groups.

	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
	%	%	%	%	%
2005	0.36	1.13	17.62	34.30	46.58
2006	0.37	1.03	17.46	34.72	46.42

¹Prevalence percentage distribution of methotrexate was calculated by dividing the prevalence (Prev. (N)*) of methotrexate in each age group (shown in table 4.26 – 4.29) by the total prevalence of methotrexate in 2005 (n=24 453) and 2006 (n=27 573) (refer to table 4.25) and multiplying it by 100.

In both study years, more than 80% of methotrexate claimed through the database, were claimed by patients older than 45 years of age (age group 4 and 5 combined). Only 0.36% (2005) and 0.37% (2006) were claimed by patients in age group 1, while methotrexate claimed by patients in age group 2 comprised 1.13% (2005) and 1.03% (2006) of the total prevalence of methotrexate. Methotrexate claimed by patients between the ages of 35 and 45 years of age (age group 3) comprised 17.62% and 17.46% of the total prevalence of methotrexate on the database, in 2005 and 2006 respectively.

The CPI of methotrexate was less than 1.00 in all the age groups (refer to table 4.38). It can therefore be concluded that methotrexate is a relatively inexpensive cancer drug (refer to section 3.8.4.6 and table 4.19).

Table 4.38 CPI values of methotrexate in the different age groups

CPI of methotrexate		
Age groups	2005	2006
Age group 1	0.12	0.07
Age group 2	0.09	0.08
Age group 3	0.05	0.05
Age group 4	0.03	0.02
Age group 5	0.03	0.22

*CPI values shown in table 4.38 was taken from table 4.26 –2.29

**For the purpose of this study CPI values higher than one (1) will indicate relatively expensive treatment (refer to paragraph 3.8.4.6)

The average costs of methotrexate are presented in table 4.39. The average cost of methotrexate increased from 2005 to 2006 in all the age groups, except in age group 3. The average cost of methotrexate for patients in age group 3 decreased from 44.30 ± 114.52 in 2005 to 40.21 ± 167.14 in 2006.

Table 4.39 Average costs of mercaptopurine for different age groups

Average cost of methotrexate for different age groups (R)					
	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
2005	27.00 ± 12.15	38.38 ± 58.85	44.30 ± 114.52	33.93 ± 21.06	32.11 ± 21.56
2006	36.57 ± 30.51	47.35 ± 78.29	40.21 ± 167.14	34.92 ± 73.02	33.76 ± 98.71

*Average costs shown in Table 4.39 were taken from Table 4.26 – 4.29.

4.5.3.6 Cyproterone (G03HA01)

Aspects of cyproterone had already been discussed in section 4.4.4. Cyproterone is part of the endocrine therapy (L02) and more specifically cyproterone is an anti-androgen (L02BB). Cyproterone is used in palliative treatment of inoperable prostate carcinoma and some other diseases (refer to section 4.4.4). The trade names containing cyproterone is presented in Appendix B.

Cyproterone comprised 2.37% (n=4) and 2.59% (n=7) of all cancer medicine items claimed by patients in age group 1. In age group 2, cyproterone encompassed 63.13% (n=808) of all cancer medicine items claimed in 2005 and 52.50% (n=694) in 2006. Cyproterone comprised 27.65% (n=3 455) and 24.98% (n=3 410) of all cancer medicine items claimed by patients in age group 3, in 2005 and 2006 respectively. In 2005, cyproterone encompassed 2.34% (n=470) of all cancer medicine items claimed by patients in age group 4, while in 2006 it comprised 2.06% (n=480). In age group 5,

cyproterone comprised 1.40% (n=530) and 1.20% (n=529) of all cancer medicine items claimed, in 2005 and 2006 respectively.

Cyproterone has been used in precocious puberty in children and is still used in short courses with gonadorelin analogue therapy (Sweetman, 2008) and this may be part of the explanation why there were cyproterone claimed by patients in age group 1. The high prevalence of cyproterone in age group 2 may be because cyproterone is also used in *severe acne* (refer to section 4.4.4). Acne is predominantly a disorder of adolescents and teenagers and nearly 85% of adolescents will be affected by acne to some extent (Brieva *et al.*, 1997:161).

As seen in table 4.40, the CPI of cyproterone in all the age groups is below 1.00 and it can therefore be seen as a relatively inexpensive cancer drug (refer to section 3.8.4.6 and table 4.19).

Table 4.40 CPI values of cyproterone in the different age groups

CPI of cyproterone		
Age groups	2005	2006
Age group 1	0.85	0.25
Age group 2	0.51	0.37
Age group 3	0.27	0.25
Age group 4	0.26	0.18
Age group 5	0.65	0.17

*CPI values shown in table 4.40 was taken from table 4.26 – 4.29

**For the purpose of this study CPI values higher than one (1) will indicate relatively expensive treatment (refer to paragraph 3.8.4.6)

The average cost of cyproterone in different age groups is presented in table 4.41. The average cost of cyproterone decreased from 2005 to 2006 in age group 1, 2, 4 and 5 and increased slightly in age group 3. There is a relatively large difference between the average cost of cyproterone in age group 1 and age group 5. The average cost of cyproterone increased with a relatively large margin from age group 1 to age group 5, in both study years.

Table 4.41 Average costs of cyproterone in different age groups

Average cost of cyproterone in different age groups (R)					
	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
2005	197.63 ± 155.14	222.58 ± 93.37	221.77 ± 110.74	273.71 ± 253.84	752.48 ± 670.95
2006	133.71 ± 0	217.00 ± 96.92	223.42 ± 106.70	248.98 ± 124.29	623.85 ± 564.87

*Average costs shown in table 4.41 were taken from table 4.26 – 4.29.

In table 4.42 the relevant effect sizes (d-values) of cyproterone in the different age groups are presented. An effect size of higher than 0.8 is of practical significance (refer to section 3.8.4.5). The effect size of cyproterone between all the age groups in both study years (except age group 1 in 2005) and age group 1 in 2006 was higher than 0.8 (see highlighted digits in table 4.42). This shows that cyproterone was the most inexpensive when claimed by patients in age group 1 in 2006 and cyproterone in age group 2 to 5 in both study years was relatively expensive. In 2005, the effect size (d-value) between cyproterone claimed by patients older than 59 years (age group 5) and cyproterone claimed by patients in age group 1 and 2 (both study years) and age group 3 (2005) was higher than 0.8 (see highlighted digits in table 4.42). This shows that cyproterone claimed by patients older than 59 years of age is relatively more expensive than cyproterone claimed by patients in the specified age groups. This aspect is not in the scope of this study, however further research is needed as Duminy (2008) stated that age should not necessarily play a role in the cost of cancer medicine items of different age groups.

Table 4.42 Relevant effect sizes (d-values) for cyproterone between the different age groups

Age groups	2 (2005)	2 (2006)	3 (2005)	3 (2006)	4 (2006)	5 (2005)	5 (2006)
1(2005)	0.16	0.12	0.16	0.17	0.33	0.82	0.75
1(2006)	0.95	0.86	0.80	0.84	0.93	0.92	0.87
2 (2005)				0.00	0.21	0.80	0.71
2 (2006)	0.05		0.04	0.06	0.26	0.80	0.72
3 (2005)	0.00			0.01	0.22	0.80	0.71
3 (2006)					0.21	0.80	0.71
4 (2005)						0.71	0.62
4 (2006)						0.75	0.66

*Effect sizes (d-values) calculated from the average costs in table 4.41 (taken from table 4.26 – 4.29)

**For the purpose of this study effect sizes (d-values) of 0.8 or higher will be assumed to have practical significance (refer to paragraph 3.8.4.5)

4.5.3.7 Tamoxifen (L02BA01)

Aspects of tamoxifen had already been discussed in section 4.4.4. Tamoxifen is a part of the endocrine therapy (L02) and more specifically a selective estrogen receptor modulator (L02BA). Tamoxifen is used in early and advanced hormone receptor-positive breast cancer and in the treatment of metastatic disease (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008).

In age group 1 (≥ 0 to ≤ 9 years of age) tamoxifen was only claimed in 2006, which amounted to 1.48% (n=4) of cancer medicine items claimed by age group 1 (refer to

table 4.26 & table 4.27). Tamoxifen encompassed 0.39% (n= 5) and 0.68% (n=9) of all cancer medicine items claimed by age group 2 (refer to table 4.26 and table 4.27) in 2005 and 2006 respectively. A phase I study was done in 1997 to determine the efficacy and safety of high-dose Tamoxifen in malignant gliomas in children between the age of 3 and 18 years of age (Pollack *et al.*, 1997:1109). Tamoxifen may also be used to improve height potential in short pubertal boys (Kreher *et al.*, 2005:1513). This may be part of the reason why Tamoxifen was claimed by patients in age groups 1 and 2 (≥ 0 to ≤ 19 years of age).

Tamoxifen comprised 7.10% (n=887) of all cancer medicine items claimed by age group 3 in 2005 and 5.52% (n=754) in 2006. In 2005, tamoxifen encompassed 15.50% (n=3 119) of all cancer medicine items claimed by patients in age group 4, and in 2006 tamoxifen comprised 11.90% (n=2 776). In age group 5, tamoxifen comprised 20.75% (n=7 868) of all cancer medicine items claimed by patients older than 59 in 2005. Tamoxifen comprised 16.39% (n=7 206) of all cancer medicine items claimed by patients older than 59 in 2006.

From table 4.25 it can be seen that the total prevalence of tamoxifen amounted to 11 879 (2005) and 10 749 (2006). In table 4.43 the prevalence percentage distribution between the different age groups is presented.

Table 4.43 Prevalence percentage distribution of Tamoxifen between the different age groups

	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
	% ¹	%	%	%	%
2005		0.04	7.47	26.26	66.23
2006	0.04	0.08	7.01	25.82	67.04

¹Prevalence percentage distribution of tamoxifen was calculated by dividing the prevalence (Prev. (N)*) of tamoxifen in each age group (shown in table 4.26 – 4.29) by the total prevalence of tamoxifen in 2005 (n=11 879) and 2006 (n=10 749) (refer to table 4.25) and multiplying it by 100.

Tamoxifen was mainly claimed by patients in age groups 4 and 5 (≥ 45 years of age), with 89.60% (2005) and 92.86% (2006) claimed by patients in these two age groups. Tamoxifen claimed by age groups 1-3 comprised the remaining 7.51% and 7.13% in 2005 and 2006 respectively.

Table 4.44 Average costs of tamoxifen in different age groups

Average cost of tamoxifen in different age groups (R)					
	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
2005		91.23 ± 49.90	141.12 ± 53.53	138.12 ± 38.58	141.13 ± 45.85
2006	117.09 ± 0	149.87 ± 107.56	138.11 ± 51.03	138.02 ± 42.43	139.44 ± 43.23

*Average costs shown in table 4.44 were taken from table 4.26 – 4.29.

The average cost of tamoxifen in the different age groups is presented in table 4.44. The average cost of tamoxifen was the lowest for patients in age group 2 (R91.23 ± 49.90) in 2005, while in 2006 the lowest average cost of tamoxifen was in age group 1 (117.09 ± 0). The average cost of tamoxifen increased from 2005 to 2006 in age group 2, while in age group 3,4 and 5 the average cost of tamoxifen decreased from 2005 to 2006.

In table 4.45, the relevant effect sizes in the different age groups are presented. From the results in table 4.46, it is evident that there was a practical significant difference between the cost of tamoxifen claimed by patients in age group 2 in 2005 and age groups 3,4 and 5 (2005 and 2006). The effect size of tamoxifen between age group 3 and age group 2 (2005) was 0.93 (2005) and 0.92 (2006), while the effect size between age group 4 and age group 2 (2005) is 0.94 in both study years. The effect size between age group 5 and age group 2 (2005) is 1.00 and 0.97 in 2005 and 2006 respectively. All these effect sizes are higher than 0.8 and therefore of practical significance (refer to section 3.8.4.6). Tamoxifen claimed by patients older than 19 years of age was relatively more expensive than tamoxifen claimed by patients in age group 2 in 2005. As mentioned in section 4.5.3.6, this aspect does not fall in the scope of this study, however further research is needed as Duminy (2008) stated that age should not necessarily play a role in the cost of cancer medicine items for different age groups.

Table 4.45 Relevant effect sizes (d-values) for tamoxifen between the different age groups.

AGE GROUP 2 (2005)		
	2005	2006
Age group 3	0.93	0.11
Age group 4	0.94	0.94
Age group 5	1.00	0.97

*Effect sizes (d-values) calculated from the average costs in table 4.44 (taken from table 4.26 – 4.29)

**For the purpose of this study effect sizes (d-values) of 0.8 or higher will be assumed to have practical significance (refer to paragraph 3.8.4.5)

4.5.3.8 Imatinib (L01XE01)

Aspects of imatinib had already been discussed in section 4.3.1 and section 4.4.4. Imatinib is an antineoplastic agent (L01) and is further classified as a protein kinase inhibitor (L01XE – refer to Appendix A). This cancer drug is indicated for the *treatment of chronic myeloid leukaemia* in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). Imatinib is the active ingredient in Gleevec 100mg capsules®, Gleevec 100mg tablets® and Gleevec 400mg tablets® (refer to appendix B).

There were no imatinib claimed in either 2005 or 2006 by age group 1. Imatinib comprised 1.72% (n=22) and 2.04% (n=27) of all cancer medicine items claimed by age group 2 in 2005 and 2006 respectively. In age group 3, imatinib encompassed 1.49% (n=186) in 2005 and 1.13% (n=154) in 2006 of all cancer medicine items claimed. In 2005, imatinib comprised 1.95% (n=392) of all cancer medicine items claimed by age group 4 and in 2006 imatinib comprised 2.22% (n=517). Imatinib encompassed 1.19% (n=451) and 1.76% (n=773) of all cancer medicine items claimed by age group 5 in 2005 and 2006 respectively.

In table 4.25, the total prevalence of imatinib is presented and it amounted to 1 051 in 2005 and 1 471 in 2006. The prevalence percentage distribution of imatinib between the different age groups is presented in table 4.46.

Table 4.46 Prevalence percentage distribution of imatinib between the different age groups

	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
	%	%	%	%	%
2005		2.10	17.70	37.30	42.91
2006		1.84	10.47	35.15	52.55

¹Prevalence percentage distribution of imatinib was calculated by dividing the prevalence (Prev. (N)*) of imatinib in each age group (shown in table 4.26 – 4.29) by the total prevalence of imatinib in 2005 (n=1 051) and 2006 (n=1 471) (refer to table 4.25) and multiplying it by 100.

From the results in table 4.46, it is evident that imatinib is mostly claimed by patients in age group 4 and 5, with 80.21% (2005) and 87.70% (2006) claimed by patients in these age groups. The prevalence percentage decreased between 2005 and 2006 for every age group except age group 5, for which it increased with 9.64% between 2005 and 2006 (refer to table 4.46).

Table 4.47 Average costs of imatinib in different age groups

Average cost of imatinib in different age groups (R)					
	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
2005		6274.09±1789.00	5983.59±1584.80	6721.22±1595.79	6941.96±1243.96
2006		7336.66±0	5918.07±1807.45	6798.03±1360.04	6595.35±1537.73

*Average costs shown in table 4.47 were taken from table 4.26 – 4.29.

The average cost of imatinib in every age group is relatively high when compared to most other cancer medicine items (refer to table 4.12 as well as table 4.31, 4.33, 4.35, 4.39, 4.41, 4.45). The highest average cost of imatinib was in age group 5 in 2005 (R6 941.96 ± 1 243.96) and in age group 2 in 2006 (R7 336.66 ± 0). The average cost of imatinib was the lowest for patients in age group 3 for both 2005 (R5 983.59 ± 1 584.80) and 2006 (R5 918.07 ± 1 807.45). The average cost of imatinib increased from 2005 to 2006 in age groups 2 and age group 4, while it decreased in age groups 3 and age group 5. As mentioned in section 4.5.3.6 and section 4.5.3.7, this aspect is not in the scope of this study, however further research is needed as Duminy (2008) stated that age should not necessarily play a role in the cost of cancer medicine items in different age groups.

Imatinib contributed a relatively large percentage of the total cost of cancer medicine items in each age group. The total cost of imatinib comprised 24.77% (2005) and 12.31% (2006) of all cancer medicine items in age group 2. In age group 3, the total cost of imatinib comprised 11.03% and 7.48% of cancer medicine items in 2005 and 2006 respectively. The total cost of imatinib encompassed 12.65% of all cancer medicine items claimed by patients in age group 4 in 2005, and 10.92% in 2006. In age group 5, the total cost of imatinib comprised 7.08% (2005) and 8.05% (2006) of cancer medicine items claimed.

According to table 4.25, the total cost percentage of imatinib was 9.26% (R 7 016 518.26) in 2005 and 8.95% (R 9 722 258.09) in 2006 of all cancer medicine items claimed. Table 4.48 summarised the cost percentage distribution of imatinib between the different age groups.

Table 4.48 Cost percentage distribution of imatinib between the different age groups

	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
	%	%*	%*	%*	%*
2005		1.97	15.86	37.55	44.62
2006		2.04	9.37	36.15	52.44

¹Cost percentage distribution of imatinib was calculated by dividing the total cost** of imatinib in each age group (shown in table 4.26 – 4.29) by the total cost** of imatinib in 2005 (R7 016 518.26) and 2006 (R9 722 258.09) (refer to table 4.25) and multiplying it by 100.

The CPI of imatinib was relatively high when compared to the other medicine items. The CPI values are presented in table 4.49.

Table 4.49 CPI values of imatinib in the different age groups

CPI of imatinib		
Age groups	2005	2006
Age group 1		
Age group 2	14.40	12.31
Age group 3	7.41	6.63
Age group 4	6.49	4.92
Age group 5	5.95	4.57

*CPI values shown in table 4.49 was taken from table 4.26 –2.29

**For the purpose of this study CPI values higher than one (1) will indicate relatively expensive treatment (refer to paragraph 3.8.4.6)

The CPI value for imatinib claimed by patients in age group 2 is the highest in both 2005 (14.40) and 2006 (12.31). In both study years, the CPI values decreases from age group 2 to age group 5 but it remains above 1.00 in each age group and imatinib can therefore be seen as a relatively expensive cancer drug (refer to section 3.8.4.6 and section 4.3.1).

From table 4.47, the effect sizes (d-values) of imatinib can be calculated. The only effect size that was of practical significance, is the effect size between the average cost of imatinib in age group 2 (2006) and age group 3 (2005). The calculated effect size was 0.85, and this indicates that imatinib was more expensive in 2006 for patients in age group 2 than in 2005 for patients in age group 3.

4.5.3.9 Trastuzumab (L01XC03)

Some aspects of Trastuzumab had already been discussed in section 4.3.2 as well as section 4.4.4. Trastuzumab is an antineoplastic agent (L01) and more specifically a monoclonal antibody (L01XC). Trastuzumab is indicated for *metastatic breast cancer* in patients with tumours over expressing the human epidermal growth factor receptor 2 (HER2). It is also given in *early breast cancer* after surgery, chemotherapy and radiotherapy (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). The trade name containing trastuzumab is Herceptin®, which is discussed in section 4.3.2 as well as in some sections of chapter 2.

No trastuzumab was claimed by patients younger than 19 years of age (≥ 0 years to ≤ 19 years) (refer to table 4.26 and 4.27). This may be because trastuzumab is mainly used in breast cancer and therefore mostly claimed by older patients. Another reason may be the high cost of trastuzumab (refer to section 1.2 and section 2.11.1).

In age group 3, the prevalence of trastuzumab comprised 1.46% (n=183) in 2005 and 2.31% (n=316) in 2006 of all cancer medicine items claimed by the specific age group (refer to table 4.28 and 4.29). Trastuzumab encompassed 1.24%(n=249) and 2.50% (n=583) in 2005 and 2006 respectively, of cancer medicine items claimed by patients in age group 4 (refer to table 4.28 and table 4.29). In 2005, trastuzumab comprised 0.52% (n=197) and 1.62% (n=710) of all cancer medicine items claimed by patients ≥ 59 years of age (age group 5) (refer to table 4.28 and 4.29).

There is a steep increase in the prevalence of trastuzumab in all age groups between 2005 and 2006. The prevalence of trastuzumab increased with 0.85% (age group 3), 1.26% (age group 4) and 1.10% (age group 5) from 2005 to 2006.

In table 4.25, the total prevalence of trastuzumab is presented which amounted to 629 in 2005 and 1 609 in 2006. The prevalence percentage distribution of trastuzumab between the different age groups is presented in table 4.50. In 2005, the biggest percentage of trastuzumab was claimed by patients in age group 4 (39.59%) and in 2006, by patients in age group 5 (44.13%).

Table 4.50 Prevalence percentage distribution of trastuzumab between the different age groups

	Age group 3	Age group 4	Age group 5
	%	%	%
2005	29.09	39.59	31.32
2006	19.64	36.23	44.13

¹Prevalence percentage distribution of trastuzumab was calculated by dividing the prevalence (Prev. (N)*) of trastuzumab in each age group (shown in table 4.26 – 4.29) by the total prevalence of trastuzumab in 2005 (n=629) and 2006 (n=1 609) (refer to table 4.25) and multiplying it by 100.

The average cost of trastuzumab in the different age groups is presented in table 4.51. The average cost of trastuzumab was relatively high in all age groups when compared to most other cancer medicine items (refer to table 4.12 and table 4.31, 4.33, 4.35, 4.39, 4.41 and 4.45). In 2005, the average cost of trastuzumab was the highest for patients in age group 3 (R7 074.17 $\pm$ 1 345.88) while in 2006 the average cost of trastuzumab in age group 5 was the highest (R7 286.00 $\pm$ 2 364.27).

Table 4.51 Average costs of trastuzumab in different age groups

Average cost of trastuzumab in different age groups (R)			
	Age group 3	Age group 4	Age group 5
2005	7074.17 ± 1345.88	6805.39 ± 1744.04	6498.99 ± 1848.61
2006	7116.38 ± 2364.27	6764.55 ± 2354.00	7286.00 ± 2364.27

*Average costs shown in table 4.51 were taken from table 4.26 – 4.29.

The total cost of trastuzumab in each age group represents a relatively large percentage of the total cost of cancer medicine items in the specific age group. In age group 3, the total cost of trastuzumab represented 12.83% (2005) and 18.45% (2006) of cancer medicine items claimed. Trastuzumab comprised 8.13% and 12.25% of cancer medicine items claimed by patients in age group 4, in 2005 and 2006 respectively. In age group 5, the total cost of trastuzumab encompassed 2.90% in 2005 and 2.72% in 2006.

According to table 2.25, trastuzumab represented 5.64% and 5.36% of the total cost of all cancer medicine items in 2005 and 2006 respectively. The cost percentage distribution of trastuzumab between the different age groups is presented in table 4.52.

Table 4.52 Cost percentage distribution of trastuzumab between the different age groups

	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
	%	%	%	%	%
2005			30.32	39.69	29.99
2006			19.79	34.70	45.52

¹Cost percentage distribution of trastuzumab was calculated by dividing the total cost** of trastuzumab in each age group (shown in table 4.26 – 4.29) by the total cost of trastuzumab in 2005 (R4 269 416.08) and 2006 (R11 365 564.90) respectively (refer to table 4.25) and multiplying it by 100.

From the results in table 4.52, it can be seen that the cost percentage of trastuzumab represented by age group 3 decreased with 10.53% between 2005 and 2006. This correlates with the decrease in prevalence percentage of trastuzumab in age group 3 (refer to table 4.51). The cost percentage of trastuzumab also decreased with 5% in age group 4 from 2005 to 2006, this also correlates with the drop in prevalence percentage of trastuzumab in age group 4 (refer to table 4.51). The cost percentage of trastuzumab represented by age group 5 increased with 15.53% from 2005 to 2006. As seen in table 4.51, the prevalence percentage of trastuzumab in age group 5 also increased with 12.81% between 2005 and 2006. The average cost of trastuzumab for patients in age group 5 also increased between 2005 and 2006 and

may have contributed to the rise in the total cost of trastuzumab in age group 5 (refer to table 4.52).

The CPI values of trastuzumab in each different age group are presented in table 4.53. All these values were higher than 1.00, and therefore trastuzumab can be classified as an relatively expensive cancer drug (refer to section 3.8.4.6 and table 4.19).

Table 4.53 CPI values of trastuzumab in the different age groups

CPI of trastuzumab		
Age groups	2005	2006
Age group 3	8.76	7.97
Age group 4	6.57	4.90
Age group 5	5.57	2.72

*CPI values shown in table 4.53 was taken from table 4.26 –2.29

**For the purpose of this study CPI values higher than one (1) will indicate relatively expensive treatment (refer to paragraph 3.8.4.6)

4.5.3.10 Rituximab (L01XC02)

Some aspects of rituximab had already been discussed in section 4.3.3 and section 4.4.4. Rituximab is an antineoplastic agent (L01) and also, like trastuzumab (refer to section 4.5.3.16) a monoclonal antibody (L01XC). Rituximab is used in the treatment of *Non-Hodgkins lymphomas*. It can be used as monotherapy in *relapsed or refractory low-grade or follicular lymphoma*, or as first-line treatment with combination therapy, such as CVP (cyclophosphamide, vincristine, and prednisolone) (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008).

No patients younger than 19 years of age (≥ 0 years to ≤ 19 years) claimed rituximab. From table 4.26 and table 4.27 it is evident that no monoclonal antibodies (L01XC) were claimed by patients in age group 1 and 2. This may be because of the high cost of these cancer drugs (refer to section 1.2 and section 2.11.1).

In 2005, rituximab comprised 1.68% (n=210) of cancer medicine items claimed by patients in age group 3, while in 2006 rituximab comprised 0.96% (n=131). In age group 4, rituximab encompassed 0.97% (n=195) in 2005 and 2.26% (n=526) in 2006 of cancer medicine items claimed. Rituximab comprised 1.72% (n=651) and 2.73% (n=1199) of cancer medicine items claimed by patients in age group 5, in 2005 and 2006 respectively.

According to table 4.25, rituximab comprised 1.47% (n=1 056) and 2.25% (n=1 856) of all cancer medicine items claimed in 2005 and 2006 respectively. The prevalence

percentage distribution of rituximab between the different age groups is presented in table 4.54.

Table 4.54 Prevalence percentage distribution of rituximab between the different age groups

	Age group 3	Age group 4	Age group 5
	%	%	%
2005	19.89	18.47	61.65
2006	7.06	28.34	64.60

¹Prevalence percentage distribution of rituximab was calculated by dividing the prevalence (Prev. (N)*) of rituximab in each age group (shown in table 4.26 – 4.29) by the total prevalence of rituximab in 2005

From table 4.54, it can be seen that 61.65% (2005) and 64.60% (2006) of rituximab claimed was by patients in age group 5 (≥ 59 years of age). In 2006, patients in age group 3 only claimed 7.06% of all rituximab claimed, while in 2005 it was 19.89%.

Table 4.55 Average costs of rituximab in different age groups

Average cost of rituximab in different age groups (R)			
	Age group 3	Age group 4	Age group 5
2005	5368.82 $\pm$ 2317.69	5254.28 $\pm$ 2411.01	5431.21 $\pm$ 2350.49
2006	6322.34 $\pm$ 1747.18	6169.12 $\pm$ 2119.32	6282.62 $\pm$ 2039.44

*Average costs shown in table 4.55 were taken from table 4.26 – 4.29.

The average cost of rituximab was the lowest for age group 4 in both 2005 (R5 254.28 $\pm$ 2 411.01) and 2006 (R6 169.12 $\pm$ 2 119.32). The highest average cost in 2005 was R5 431.21 $\pm$ 2 350.49 (age group 5) and in 2006 it amounted to R6 322.34 $\pm$ 1 747.18 (age group 3). The average cost of rituximab in all age groups was relatively high compared to other cancer medicine items (refer to table 4.12 and table 4.31, 4.33, 4.35, 4.39, 4.41, 4.44).

The total cost of rituximab in each age group represents a relatively large percentage of the total cost of cancer medicine items in the specific age group. In age group 3, the total cost of rituximab represented 11.18% (2005) and 6.80% (2006) of cancer medicine items claimed. Rituximab comprised 4.92% and 10.08% of cancer medicine items claimed by patients in age group 4, in 2005 and 2006 respectively. In age group 5, the total cost of rituximab encompassed 8.00% in 2005 and 11.89% in 2006.

According to table 2.25, rituximab represented 7.51% (R5 687 754.46) and 10.68% (R11 606 045.00) of the total cost of all cancer medicine items in 2005 and 2006 respectively. The cost percentage distribution of rituximab between the different age groups is presented in table 4.56.

Table 4.56 Cost percentage distribution of rituximab between the different age groups

	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
	% ¹	%	%	%	%
2005			19.82	18.01	62.16
2006			7.14	27.96	64.90

¹Cost percentage distribution of rituximab was calculated by dividing the total cost** of rituximab in each age group (shown in table 4.26 – 4.29) by the total cost of rituximab in 2005 (R5 687 754.46) and 2006 (R11 606 045.00) (refer to table 4.25) and multiplying it by 100.

Table 4.56 shows that 62.16% (2005) and 64.90% (2006) of the cost of rituximab were spent by age group 5. The remaining 37.83% and 35.10% of the total cost of rituximab were claimed by patients in age groups 2 and 3.

The CPI values of rituximab for each age group were relatively high (≥ 1.00). Table 4.57 presents the CPI values of each age group in 2005 and 2006 respectively.

Table 4.57 CPI values of rituximab in the different age groups

CPI of rituximab		
Age groups	2005	2006
Age group 3	6.65	7.08
Age group 4	5.07	4.47
Age group 5	4.66	3.96

*CPI values shown in table 4.53 was taken from table 4.26 – 4.29

**For the purpose of this study CPI values higher than one (1) will indicate relatively expensive treatment (refer to paragraph 3.8.4.6)

When the results in table 4.57 is considered, it is evident that rituximab is a relatively expensive cancer drug (refer to section 3.8.4.6 and table 4.19).

4.5.3.11 Docetaxel

Some aspects of docetaxel had been discussed in section 4.4.4. Docetaxel is an antineoplastic agent (L01) and more specifically classified as a taxane (L01CD). Docetaxel is indicated in the management of *advanced or metastatic breast, ovarian*

and non-small cell lung cancer (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). Docetaxel is a more potent analogue of paclitaxel, which is the active ingredient in the Taxol 100mg/vial and Taxol 300mg/5ml injections (refer to section 4.3.7). Docetaxel is the active ingredient in the Taxotere 20mg/1.5ml injection and the Taxotere 80mg injection (refer to Appendix B).

Docetaxel was not claimed by patients in age group 1 in both study years, while docetaxel comprised 0.15% (n=2) of all cancer medicine items claimed by age group 2 in 2006.

In age group 3, docetaxel comprised 1.38% (n=172) and 1.36% (n=186) of all cancer medicine items claimed, in 2005 and 2006 respectively. Docetaxel encompassed 2.61% (n=2.61) of cancer medicine items claimed by patients in age group 4 in 2005, and 2.74% (n=638) in 2006. Of all cancer medicine items claimed by patients in age group 5, docetaxel comprised 2.00% (n=757) in 2005 and 2.05% (n=903) in 2006.

According to table 4.25, the total prevalence of docetaxel comprised 2.02% (n=1 455) in 2005 and 2.10% (n=1 729) in 2006 of all cancer medicine items claimed. The prevalence percentage distribution of docetaxel between the different age groups is presented in table 4.58.

Table 4.58 Prevalence percentage distribution of docetaxel between the different age groups

	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
	% ¹	%	%	%	%
2005			11.82	36.15	52.03
2006		0.12	10.76	36.90	52.23

¹Prevalence percentage distribution of docetaxel was calculated by dividing the prevalence (Prev. (N)*) of docetaxel in each age group (shown in table 4.26 – 4.29) by the total prevalence of docetaxel in 2005 (n=1 455) and 2006 (n=1 729) (refer to table 4.25) and multiplying it by 100.

Docetaxel claimed by patients in age group 5 comprised more than half of the total prevalence of docetaxel in both 2005 and 2006. Only 0.12% of all docetaxel claimed in 2006 was claimed by patients in age group 2. Age group 3 and 4 combined comprised 47.97% (2005) and 47.66% of all docetaxel claimed in 2005 and 2006 respectively.

Table 4.59 Average costs of docetaxel in different age groups

Average cost of docetaxel in different age groups (R)				
	Age group 2	Age group 3	Age group 4	Age group 5
2005		5378.34±1568.95	5170.10±1696.31	5615.40±1537.47
2006	5552.85±0	5387.21±1650.16	5310.32±1545.66	5401.69±1540.24

*Average costs shown in table 4.59 were taken from table 4.26 – 4.29.

The average cost of docetaxel in each age group did not vary much between the different age groups and study years. In age group 5, the average cost of docetaxel decreased from 2005 to 2006 while in age group 3 and 4 the average cost increased from 2005 to 2006 (refer to table 4.59).

In 2006, the total cost of docetaxel comprised 1.41% (R11 105.70) of the total cost of all cancer medicine items claimed by patients in age group 2 (refer to table 4.27). In age group 3, the total cost of docetaxel represented 9.17% (R925 074.38) in 2005 and 8.22% (R1 002 021.20) in 2006 of cancer medicine items claimed. Docetaxel comprised 13.05% (R2 719 472.07) and 10.52% (R3 387 982.90) of cancer medicine items claimed by patients in age group 4, in 2005 and 2006 respectively. In age group 5, the total cost of docetaxel encompassed 9.61% (R4 250 859.12) in 2005 and 7.70% (R4 877 729.20) in 2006 (refer to table 4.28 and 4.29).

According to table 4.25, docetaxel represented 10.42% (R7 895 405.57) and 8.54% (R9 278 838.99) of the total cost of all cancer medicine items in 2005 and 2006 respectively. The cost percentage distribution of docetaxel between the different age groups is presented in table 4.60.

Table 4.60 Cost percentage distribution of docetaxel between the different age groups

	Age group 1	Age group 2	Age group 3	Age group 4	Age group 5
	%	%	%	%	%
2005			11.72	34.44	53.84
2006		0.12	10.80	36.51	52.57

¹Cost percentage distribution of docetaxel was calculated by dividing the total cost** of docetaxel in each age group (shown in table 4.26 – 4.29) by the total cost** of docetaxel in 2005 (R7 895 405.57) and 2006 (R9 278 838.99) (refer to table 4.25) and multiplying it by 100.

From the results in table 4.60 it is evident that the total cost of docetaxel in age group 5 comprised more than half of the total cost of docetaxel on the database. The total cost of docetaxel for patients in age group 4 comprised 34.44% (2005) and 36.51% (2006) of the total cost of docetaxel on the database. The total cost of docetaxel in

age groups 2 and 3 combined comprised 11.72% of the total cost of docetaxel in 2005 and 10.92% in 2006 (refer to table 4.26 - 4.29).

The CPI of docetaxel was higher than 1.00 in all age groups, and can therefore be classified as a relatively expensive cancer drug (refer to section 3.8.4.6 and table 4.19). The CPI values of docetaxel are presented in table 4.61.

Table 4.61 CPI values of docetaxel in the different age groups

CPI of docetaxel		
Age groups	2005	2006
Age group 2		9.32
Age group 3	6.66	6.03
Age group 4	4.99	3.85
Age group 5	4.81	2.57

**CPI values shown in table 4.61 was taken from table 4.26 –2.29*

***For the purpose of this study CPI values higher than one (1) will indicate relatively expensive treatment (refer to paragraph 3.8.4.6)*

4.6 PREVALENCE AND COST OF CANCER MEDICINE ITEMS ACCORDING TO GENDER

The cancer medicine items claimed through the medicine claims database classified by gender (refer to section 4.2.3) in both 2005 and 2006 is presented in table 4.62 and table 4.63. The percentage distribution of female and male patients who received cancer medicine items during the study period is presented in figure 4.11 (also see table 4.7).

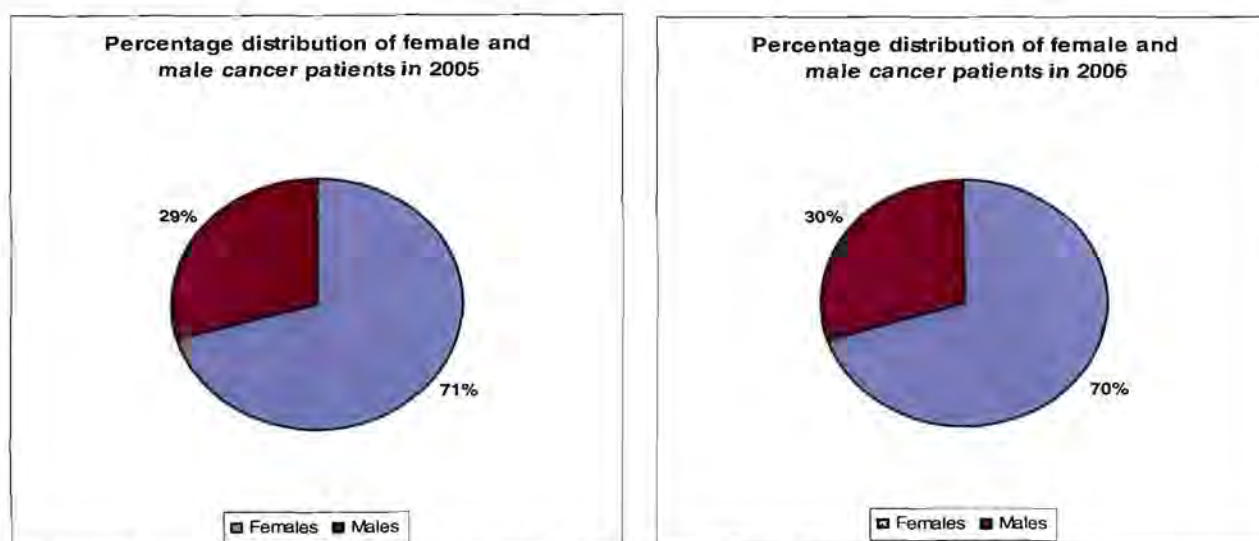


Figure 4.11 Percentage distribution of female and male cancer patients

From figure 4.11 it can be seen that the number of female patients was much higher than male cancer patients in both study years. In 2005, there were 7 065 (71%) female cancer patients and 2 950 (29%) male cancer patients on the medicine claims database. In 2006, the female patients increased to 7 370 (70%) and there were 3 164 (30%) male cancer patients, an increase of 214 male cancer patients from 2005.

From the results of table 4.7 and figure 4.11 the conclusion can be made that because of the higher number of female patients in both study years, the number of cancer medicine items and cost of cancer medicine items claimed by female cancer patients could also be higher than those claimed by male cancer patients. These aspects will also be discussed in forthcoming sections.

4.6.1 Prevalence of cancer medicine items according to gender

As mentioned in section 4.6 there was a correlation between the number of patients and the number of cancer medicine items claimed by a specific gender. In 2005, the number of cancer medicine items claimed by female cancer patients comprised 72% (n=51 491) of all cancer medicine items claimed while cancer medicine items claimed by male cancer patients comprised the remaining 28% (n=20 445). The female cancer patients claimed 70% (n=58 007) of all cancer medicine items in 2006 and cancer medicine items claimed by male patients encompassed 29% (n=24495). In 1% of the cases, the cancer medicine items were not allocated to a specific gender.

4.6.2 Cost of cancer medicine items according to gender

As seen in section 4.6 and section 4.6.1, the number of female cancer patients as well as the number of cancer medicine items claimed by female cancer patients comprised 70% or more of all cancer patients and cancer medicine items claimed. The cost percentage of cancer medicine items claimed by female patients, however, was lower than could be expected. In both 2005 and 2006, the cost of cancer medicine items claimed by female patients comprised 55% of the total cost of all cancer medicine. The cost of cancer medicine items claimed by male cancer patients encompassed the remaining 45% (2005) and 44% (2006) of the total cost of cancer medicine items. Figure 4.12 shows the comparison between the number of cancer medicine items and the total cost of cancer medicine items according to gender.

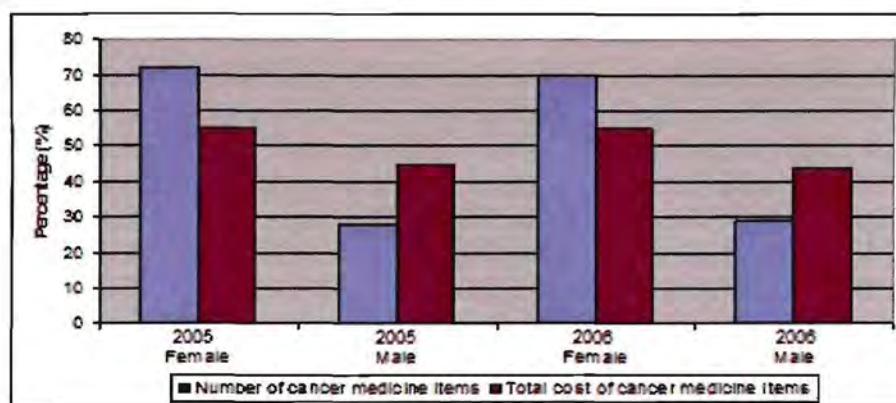


Figure 4.12 Comparison between the number of cancer medicine items and the cost of cancer medicine items according to gender

**Table 4.62 Prevalence and cost of cancer medicine items according to gender
in 2005**

ATC code	Active ingredient	Female						Male					
		Prev. (N)*	Prev. % ¹	Average cost (R)	Total cost (R)**	Cost % ²	CPI	Prev. (N)*	Prev. % ¹	Average cost (R)	Total cost (R)**	Cost % ²	CPI
L03AC01	Aldesleukin	65	0.09	5863.09±1131.28	381100.55	0.50	5.57	48	0.07	4835.28±1750.88	232093.37	0.31	4.59
L01XX14	All-Trans Retinoic Acid	1	0.00	2682.51±0	2682.51	0.00	2.55	2	0.00	2571.07±21.04	5142.13	0.01	2.44
L02BG03	Anastrozole	2692	3.74	1232.25±178.98	3317211.65	4.38	1.17	32	0.04	1214.08±126.34	38850.44	0.05	1.15
L01XC07	Bevacizumab	69	0.10	6722.92±2042.06	463881.32	0.61	6.39	104	0.14	5933.32±1781.89	617065.06	0.81	5.64
L02BB03	Bicalutamide	7	0.01	2588.07±1231.58	18116.51	0.02	2.46	2037	2.83	2129.35±874.91	4337495.5	5.73	2.02
L01DC01	Bleomycin	64	0.09	642.77±288.57	41137.44	0.05	0.61	43	0.06	900.99±795.56	38742.93	0.05	0.86
L02AE01	Buserelin	2	0.00	2852.17±0	5704.34	0.01	2.71	220	0.31	2908.94±388.83	639967.64	0.84	2.76
L01AB01	Busulphan	8	0.01	319.95±288.50	2559.61	0.00	0.30	6	0.01	74.60±23.25	447.59	0.00	0.07
L01BC06	Capecitabine	897	1.25	2505.66±1389.81	2247577.59	2.97	2.38	442	0.61	2846.30±1646.78	1258062.9	1.66	2.70
L01XA02	Carboplatin	674	0.94	711.37±347.88	479460.76	0.63	0.68	458	0.64	775.35±399.04	355109.16	0.47	0.74
L01AD01	Carmustine	14	0.02	909.00±379.79	12726.04	0.02	0.86	1	0.00	2908.32±0	2908.32	0.00	0.00
L01AA02	Chlorambucil	129	0.18	511.58±383.83	65994.06	0.09	0.49	167	0.23	493.67±352.87	82443.47	0.11	0.47
L01XA01	Cisplatin	241	0.33	266.27±169.91	64171.25	0.08	0.25	281	0.39	286.01±210.96	80368.32	0.11	0.27
L01AA01	Cyclophosphamide	1761	2.45	94.89±44.17	167096.72	0.22	0.09	538	0.75	121.02±81.29	65106.98	0.09	0.12
GO3HA01	Cyproterone	4783	6.65	223.15±105.59	1067337.00	1.41	0.21	481	0.67	844.67±689.84	406284.49	0.54	0.80
L01BC01	Cytarabine	35	0.05	1199.10±1440.16	41968.39	0.06	1.14	66	0.09	1707.86±2382.97	112719.04	0.15	1.62
L01AX04	Dacarbazine	80	0.11	767.51±279.47	61400.94	0.08	0.73	76	0.11	620.66±328.53	47170.10	0.06	0.59
L01DA01	Dactinomycin	8	0.01	90.41±0	723.28	0.00	0.09	10	0.01	288.24±63.11	2882.44	0.00	0.27
L01DB02	Daunorubicin							1	0.00	1059.08±0	1059.08	0.00	0.00
L01CD02	Docetaxel	913	1.27	5427.17±1534.53	4955010.67	6.54	5.16	542	0.75	5425.08±1737.43	2940394.90	3.88	5.16
L01DB01	Doxorubicin	715	0.99	1963.24±2069.72	1403718.16	1.85	1.87	240	0.33	1747.79±2016.27	419468.65	0.55	1.66
L01DB03	Epirubicin	1068	1.48	1140.38±670.85	1217929.30	1.61	1.08	232	0.32	958.25±551.71	222314.75	0.29	0.91
L01XX11	Estramustine	2	0.00	389.40±0	778.80	0.00	0.37	73	0.10	786.52±640.66	57415.77	0.08	0.75
L01CB01	Etoposide	154	0.21	1115.64±809.29	171808.80	0.23	1.06	233	0.32	1177.08±744.88	274259.50	0.36	1.12
L02BG06	Exemestane	421	0.58	1418.30±153.48	597103.85	0.79	1.35	3	0.00	972.27±767.68	2916.81	0.00	0.00
L01BB05	Fludarabine	72	0.10	3103.61±1821.67	223460.10	0.30	2.95	46	0.06	6056.55±1501.47	278601.26	0.37	5.76
L01BC02	Fluorouracil	1337	1.86	109.85±102.25	146871.01	0.19	0.10	557	0.77	173.13±123.32	96431.30	0.13	0.16
L02BB01	Flutamide	26	0.04	328.71±249.43	8546.54	0.01	0.31	298	0.41	847.30±295.55	252494.15	0.33	0.81
L01BC05	Gemcitabine	833	1.16	4335.20±2020.77	3611222.55	4.77	4.12	537	0.75	4086.87±1998.83	2194647.3	2.90	3.88
L02AE03	Goserelin	234	0.33	1818.52±846.31	425534.77	0.56	1.73	972	1.35	2841.76±629.86	2762195	3.65	2.70
L01XX05	Hydroxyurea	587	0.82	124.43±52.52	73038.66	0.10	0.12	275	0.38	148.50±57.14	40838.25	0.05	0.14
L01XX06	Ifosfamide	44	0.06	2051.38±1082.32	90260.81	0.12	1.95	90	0.13	1790.02±1857.90	161101.51	0.21	1.70
L01XE01	Imatinib	358	0.50	6935.38±1242.70	2482867.62	3.28	6.59	688	0.96	6550.19±1585.86	4506532.5	5.95	6.22
L03AB04	Interferon Alfa 2A	59	0.08	3397.72±1114.53	200465.50	0.26	3.23	102	0.14	3054.87±1915.01	311596.89	0.41	2.90
L03AB05	Interferon Alfa 2B	140	0.19	3611.89±2853.58	505665.16	0.67	3.43	165	0.23	2922.36±2391.88	482188.83	0.64	2.78
L01XX19	Irinotecan	371	0.52	4412.56±2223.44	1637060.64	2.16	4.19	384	0.53	4101.65±2391.88	1575034.4	2.08	3.90
L01XX02	L-asparaginase	4	0.01	3427.39±1788.28	13709.55	0.02	3.26						
L02AE02	Leuprolide	63	0.09	1324.39±849.68	83436.83	0.11	1.26	577	0.80	2677.00±891.24	1544631.6	2.04	2.54
L02AB02	Medroxyprogesterone	125	0.17	478.30±260.78	59787.02	0.08	0.45	4	0.01	656.93±375.88	2627.71	0.00	0.00
L01AA03	Melphalan	88	0.12	515.69±702.68	45380.42	0.06	0.49	98	0.14	592.49±760.82	58064.24	0.08	0.56
L01BB02	Mercaptopurine	65	0.09	1224.09±287.59	79565.93	0.11	1.16	88	0.12	885.44±459.87	77918.45	0.10	0.84
L01BA01	Methotrexate	17550	24.38	35.54±123.76	623766.66	0.82	0.03	6877	9.56	34.77±34.78	239081.42	0.32	0.03
L01DC03	Mitomycin	75	0.10	429.35±289.75	32201.04	0.04	0.41	32	0.04	860.04±1593.81	27521.39	0.04	0.82
L01DB07	Mitoxantrone	52	0.07	1845.25±465.92	95953.15	0.13	1.75	57	0.08	2061.59±410.84	117510.35	0.16	1.96
L01XA03	Oxaliplatin	67	0.09	4332.15±2341.16	290253.72	0.38	4.12	182	0.25	4763.12±2331.72	866887.06	1.14	4.53
L01CD01	Paclitaxil	701	0.97	4388.90±2321.06	3078621.23	4.06	4.17	204	0.28	3906.17±2295.19	796858.09	1.05	3.71
L01XC02	Rituximab	559	0.78	5118.06±2441.60	2860993.97	3.78	4.86	497	0.69	5687.65±2215.45	2826760.5	3.73	5.40

Table 4.62 Prevalence and cost of cancer medicine items according to gender in 2005 (continued)

ATC code	Active ingredient	Female						Male					
		Prev. (N)*	Prev. % ¹	Average cost (R)	Total cost (R)**	Cost % ²	CPI	Prev. (N)*	Prev. % ¹	Average cost (R)	Total cost (R)**	Cost % ²	CPI
L02BA01	Tamoxifen	11585	16.10	140.10±43.16	1623029.59	2.14	0.13	293	0.41	149.15±85.96	43700.05	0.06	0.14
L01AX03	Temozolomide	176	0.24	4175.22±2611.50	734838.37	0.97	3.97	212	0.29	4756.28±2102.07	1008332.3	1.33	4.52
L01BB03	Thioguanine	3	0.00	4605.23±2502.68	13815.68	0.02	4.38	8	0.01	1855.27±828.38	14842.19	0.02	1.76
L01XX17	Topotecan	25	0.03	5247.89±2320.03	131197.37	0.17	4.99	8	0.01	5074.24±1744.57	40593.88	0.05	4.82
L01XC03	Trastuzumab	624	0.87	6824.41±1641.70	4258432.53	5.62	6.49	5	0.01	2196.71±0	10983.55	0.01	2.09
L01CA01	Vinblastine	59	0.08	319.84±147.41	18870.63	0.02	0.30	63	0.09	482.25±304.69	30382.01	0.04	0.46
L01CA02	Vincristine	195	0.27	176.13±92.61	34345.36	0.05	0.17	206	0.29	175.86±76.70	36227.98	0.05	0.17
L01CA03	Vindesine	11	0.02	2070.76±5.74	22778.41	0.03	1.97	13	0.02	2292.21±0	29798.73	0.04	2.18
L01CA04	Vinorelbine	416	0.58	3677.22±1601.99	1529724.58	2.02	3.49	326	0.45	3224.49±1993.13	1051182.9	1.39	3.06
	TOTAL	51307	71		41820895	55		20200	28		33726265	45	

¹Prev. % was determined by dividing Prev. (N)* by the total number of cancer medicine items claimed in the specific study year (refer to table 4.2).

²Cost % was determined by dividing Total cost (R)** by the total cost of cancer medicine items claimed in the specific study year (refer to table 4.2).

Table 4.63 Prevalence and cost of cancer medicine items according to gender in 2006

ATC code	Active ingredient	Female						Male					
		Prev. (N)*	Prev. % ¹	Average cost (R)	Total cost (R)**	Cost % ²	CPI	Prev. (N)*	Prev. % ¹	Average cost (R)	Total cost (R)**	Cost % ²	CPI
L03AC01	Aldesleukin	14	0.02	5773.06±1123.04	80822.82	0.07	4.38	173	0.21	6110.64±689.60	1057140.00	0.97	4.64
L01XX14	All-Trans Retinoic Acid	1	0.00	7597.88±0	7597.88	0.01	5.77	3	0.00	1322.67±0	3968.01	0.00	0.00
L02BG03	Anastrozole	3990	4.83	1221.65±146.83	4874391.24	4.49	0.93	25	0.03	1183.18±117.71	29579.46	0.03	0.90
L01XC07	Bevacizumab	198	0.24	6637.06±2233.45	1314137.86	1.21	5.04	300	0.36	5988.75±2183.80	1796625.76	1.65	4.55
L02B803	Bicalutamide	13	0.02	1917.32±780.10	24925.18	0.02	1.46	2186	2.65	2277.37±932.80	4978331.80	4.58	1.73
L01DC01	Bleomycin	93	0.11	769.54±606.42	71571.34	0.07	0.58	95	0.12	1017.09±679.55	96623.92	0.09	0.77
L02AE01	Busarelin	4	0.00	2846.63±11.09	11386.51	0.01	2.16	392	0.48	2907.90±415.96	1139898.60	1.05	2.21
L01AB01	Busulphan	4	0.00	138.04±61.98	552.14	0.00	0.00	1	0.00	32.55±0	32.55	0.00	0.00
L01BC06	Capecitabine	886	1.07	2532.42±1261.57	2243728.26	2.06	1.92	503	0.61	2737.77±1493.07	1377098.58	1.27	2.08
L01XA02	Carboplatin	1022	1.24	717.78±329.73	733570.36	0.68	0.55	515	0.62	732.00±431.27	376982.08	0.35	0.56
L01AD01	Carmustine	5	0.01	1660.89±1051.15	8304.46	0.01	1.26	7	0.01	1953.01±1211.41	13671.08	0.01	1.48
L01AA02	Chlorambucil	153	0.19	387.98±265.87	59361.70	0.05	0.29	148	0.18	442.58±234.99	65502.32	0.06	0.34
L01XA01	Cisplatin	371	0.45	247.85±172.02	91951.02	0.08	0.19	284	0.34	295.31±202.60	83868.07	0.08	0.22
L01AA01	Cyclophosphamide	2130	2.58	99.35±64.32	211607.28	0.19	0.08	944	1.14	108.81±55.03	102720.50	0.09	0.08
G03HA01	Cyproterone	4621	5.60	224.68±107.34	1038236.34	0.96	0.17	483	0.59	665.87±573.64	321615.46	0.30	0.51
L01BC01	Cytarabine	61	0.07	2086.08±2029.15	127250.63	0.12	1.58	40	0.05	1285.18±2472.77	51407.16	0.05	0.98
L01AX04	Dacarbazine	81	0.10	785.64±268.83	63636.54	0.06	0.60	97	0.12	1060.11±434.03	102830.27	0.09	0.81
L01DA01	Dactinomycin	7	0.01	210.46±0	1473.22	0.00	0.00	4	0.00	368.68±135.62	1474.71	0.00	0.00
L01DB02	Daunorubicin	6	0.01	3225.63±1163.49	19353.79	0.02	2.45	1	0.00	4012.23±0	4012.23	0.00	3.05
L01CD02	Docetaxel	1114	1.35	5288.64±1540.05	5891550.24	5.42	4.02	615	0.75	5507.79±1568.18	3387288.75	3.12	4.18
L01DB01	Doxorubicin	913	1.11	1880.17±2620.37	1716597.80	1.58	1.43	453	0.55	2148.47±3161.89	973255.26	0.90	1.63
L01DB03	Epirubicin	1003	1.22	1077.54±621.78	1080776.05	0.99	0.82	182	0.22	1124.15±631.87	204595.40	0.19	0.85
L01XX11	Estramustine							47	0.06	1459.59±1254.16	68600.73	0.06	1.11
L01CB01	Etoposide	150	0.18	1036.41±780.11	155462.18	0.14	0.79	258	0.31	1501.85±788.22	387478.45	0.36	1.14
L02BG06	Exemestane	477	0.58	1435.96±212.10	684955.15	0.63	1.09						

Table 4.63 Prevalence and cost of cancer medicine items according to gender in 2006 (continued)

ATC code	Active ingredient	Female						Male					
		Prev. (N)*	Prev. % ¹	Average cost (R)	Total cost (R)**	Cost % ²	CPI	Prev. (N)*	Prev. % ¹	Average cost (R)	Total cost (R)**	Cost % ²	CPI
L01BB05	Fludarabine	40	0.05	6051.08±1100.61	242043.08	0.22	4.59	104	0.13	4732.42±2542.49	492171.67	0.45	3.59
L01BC02	Fluorouracil	1399	1.70	116.45±104.74	162906.88	0.15	0.09	795	0.96	188.75±130.56	150053.90	0.14	0.14
L02BB01	Flutamide	37	0.04	356.23±221.78	13180.37	0.01	0.27	258	0.31	787.47±279.89	203166.84	0.19	0.60
L01BC05	Gemcitabine	982	1.19	4204.20±1801.71	4128520.26	3.80	3.19	663	0.80	4713.75±1959.94	3125217.73	2.88	3.58
L02AE03	Goserelin	258	0.31	1764.21±830.45	455167.40	0.42	1.34	1034	1.25	2883.78±504.74	2981823.52	2.74	2.19
L01XX05	Hydroxyurea	722	0.87	131.93±55.52	95250.26	0.09	0.10	238	0.29	146.92±61.71	34966.98	0.03	0.11
L01XX06	Ifosfamide	107	0.13	1515.32±1602.76	162138.96	0.15	1.15	112	0.14	2207.55±1745.96	247245.36	0.23	1.68
L01XE01	Imatinib	412	0.50	6927.65±1307.68	2854191.60	2.63	5.26	1059	1.28	6485.43±1558.36	6868066.49	6.32	4.92
L03AB04	Interferon Alfa 2A	78	0.09	3861.73±1978.07	301215.14	0.28	2.93	84	0.10	3734.59±1696.12	313705.73	0.29	2.84
L03AB05	Interferon Alfa 2B	71	0.09	4476.33±3159.54	317819.23	0.29	3.40	108	0.13	3057.90±2638.18	330252.66	0.30	2.32
L01XX19	Irinotecan	323	0.39	3936.59±2470.80	1271518.25	1.17	2.99	426	0.52	4897.26±2534.49	2086232.93	1.92	3.72
L01XX02	L-asparaginase	3	0.00	4321.54±2477.93	12964.61	0.01	3.28						
L02AE02	Leuprolide	57	0.07	1116.39±585.09	63634.20	0.06	0.85	590	0.71	2665.21±867.07	1572474.01	1.45	2.02
L02AB02	Medroxyprogesterone	151	0.18	559.12±301.45	84427.76	0.08	0.42	5	0.01	345.97±127.83	1729.86	0.00	0.26
L01AA03	Melphalan	85	0.10	521.62±650.49	44338.09	0.04	0.40	93	0.11	418.75±516.46	38943.50	0.04	0.32
L01BB02	Mercaptopurine	88	0.11	978.92±335.40	86145.18	0.08	0.74	98	0.12	1149.72±690.45	112672.51	0.10	0.87
L01BA01	Methotrexate	19828	24.03	33.69±33.33	668083.30	0.61	0.03	7738	9.38	38.51±83.20	297964.97	0.27	0.03
L01DC03	Mitomycin	101	0.12	595.19±747.04	60113.95	0.06	0.45	34	0.04	567.42±415.49	19292.32	0.02	0.43
L01DB07	Mitoxantrone	40	0.05	2297.11±649.01	91884.34	0.08	1.74	82	0.10	2016.12±266.08	165322.06	0.15	1.53
L01XA03	Oxaliplatin	354	0.43	4700.48±2353.91	1663969.55	1.53	3.57	419	0.51	5562.88±2416.40	2330848.01	2.14	4.22
L01CD01	Paclitaxil	875	1.06	5341.49±2977.12	4673801.75	4.30	4.06	173	0.21	4686.93±2213.01	810838.73	0.75	3.56
L01XC02	Rituximab	912	1.11	6037.64±2113.50	5506323.35	5.07	4.58	944	1.14	6461.57±1951.28	6099721.99	5.61	4.91
L02BA01	Tamoxifen	10415	12.62	138.84±41.34	1446035.39	1.33	0.11	334	0.40	143.18±91.10	47823.42	0.04	0.11
L01AX03	Temozolomide	296	0.36	5279.54±2791.13	1562744.95	1.44	4.01	518	0.63	4910.80±2845.53	2543793.83	2.34	3.73
L01BB03	Thioguanine	16	0.02	1103.24±585.90	17651.78	0.02	0.84	8	0.01	1384.25±574.77	11074.03	0.01	1.05
L01XX17	Topotecan	13	0.02	4682.46±1733.85	60872.03	0.06	3.56	27	0.03	4590.72±2363.73	123949.35	0.11	3.49
L01XC03	Trastuzumab	1609	1.95	7063.74±2313.89	11365564.90	10.46	5.36						
L01CA01	Vinblastine	77	0.09	382.57±145.50	29457.98	0.03	0.29	85	0.10	431.60±221.82	36685.58	0.03	0.33
L01CA02	Vincristine	352	0.43	165.42±47.80	58227.14	0.05	0.13	387	0.47	181.72±85.82	70327.24	0.06	0.14
L01CA03	Vindesine												
L01CA04	Vinorelbine	621	0.75	3414.08±1699.86	2120140.61	1.95	2.59	151	0.18	3930.63±1610.94	593524.67	0.55	2.98
	TOTAL	57639	70		60133532	55		24323	29		48334491	44	

¹Prev. % was determined by dividing Prev. (N)* by the total number of cancer medicine items claimed in the specific study year (refer to table 4.2).

²Cost % was determined by dividing Total cost (R)** by the total cost of cancer medicine items claimed in the specific study year (refer to table 4.2).

4.6.3 Comparison between cancer medicine items according to gender

In this section the prevalence and cost of cancer medicine items claimed by female cancer patients and male cancer patients will be discussed. All data presented in table 4.64 – table 4.66 were extracted from table 4.62 – table 4.63.

4.6.3.1 Top five cancer medicine items for each gender according to prevalence and cost.

In table 4.64 and table 4.65 the top five cancer medicine items according to prevalence and cost claimed by females and males in both study years is presented.

Table 4.64 Top five cancer medicine items according to prevalence claimed by female and male cancer patients

	Females				Males			
	2005		2006		2005		2006	
		%*		%*		%*		%*
1	Methotrexate	24.38	Methotrexate	24.03	Methotrexate	9.56	Methotrexate	9.38
2	Tamoxifen	16.10	Tamoxifen	12.62	Bicalutamide	2.83	Bicalutamide	2.65
3	Cyproterone	6.65	Cyproterone	5.60	Goserelin	1.35	Imatinib	1.28
4	Anastrozole	3.74	Anastrozole	4.83	Imatinib	0.96	Goserelin	1.25
5	Cyclophosphamide	2.45	Cyclophosphamide	2.58	Leuprolide	0.80	Cyclophosphamide	1.14
		53.32		49.66		15.50		15.70

*Percentages shown in table 4.64 were taken from table 4.62 and 4.63.

**Refer to table 4.62 and table 4.63 for the number of cancer medicine items represented by the percentage given in table 4.64.

The top five cancer medicine items claimed by females comprised 53.32% (2005) and 49.66% (2006) of all cancer medicine items claimed by female cancer patients while the top five cancer medicine items claimed by males comprised only 15.50% (2005) and 15.70% (2006) of all cancer medicine items claimed by male cancer patients (refer to table 4.62 and 4.63).

Methotrexate was claimed the most by both females and males (refer to table 4.64). From table 4.25 it can be seen that methotrexate comprised 33.98% (2005) and 33.41% (2006) of all cancer medicine items claimed by all cancer patients, which was the highest percentage cancer medicine items claimed (refer to section 4.3.6 and section 4.4.4).

Methotrexate claimed by female cancer patients comprised 24.38% in 2005 and 24.03% in 2006 of all cancer medicine items claimed, while methotrexate claimed by male patients comprised 9.56% and 9.38% of all cancer medicine items claimed in 2005 and 2006 respectively (refer to table 4.62 and 4.63). It is thus evident that female patients claimed more methotrexate than male patients (females had 14.82% and 14.65% higher prevalence of methotrexate than males, in 2005 and 2006 respectively). Methotrexate is used in the management and treatment of acute

lymphoblastic leukaemia; as part of curative regimens of *choriocarcinoma* and other *gestational trophoblastic tumours*; as adjuvant therapy of *osteosarcoma* and *breast cancer*; and in a wide variety of neoplasms including tumours of the *head, neck, breast and bone* (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). Methotrexate is also indicated in other diseases such as *asthma* and *rheumatoid arthritis* (refer to section 4.3.6).

From the results in table 4.25, it can be seen that tamoxifen comprised 16.51% (2005) and 13.03% (2006) of all cancer medicine items. Of these percentages 16.10% (2005) and 12.62% (2006) was claimed by female cancer patients (refer to table 4.64). Tamoxifen is mainly used in females for breast cancer (refer to section 4.4.4) but was also claimed by male cancer patients in both 2005 and 2006. Tamoxifen claimed by male cancer patients comprised 0.41% (n=293) and 0.40% (n=334) of cancer medicine items claimed in 2005 and 2006 respectively. Breast cancer in males are very rare and less than 1 in 100 breast cancer cases are diagnosed in males, but this disease does occur in males (Cancerbackup, 2008). The most common hormone therapy used in male breast cancer is tamoxifen, and this may explain why tamoxifen was claimed a few times by male patients throughout 2005 and 2006 (Cancerhelp UK, 2008).

Bicalutamide (L02BB02) is part of the endocrine therapy (L02) and more specifically a non-steroidal anti-androgen (L02BB). Bicalutamide is used in advanced prostate carcinoma (similar to cyproterone), in combination or alone (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). The trade names containing bicalutamide are Casodex 50mg tablets® and Casodex 150mg tablets®.

Bicalutamide was mainly claimed by male cancer patients (refer to table 4.62 and table 4.63). In table 4.25 the total prevalence of bicalutamide was presented, which were 2.84% (n=2 044) of all cancer medicine items claimed in 2005 and in 2006, it was 2.66 (n=2 199). Of those percentages, 2.83% and 2.65% were claimed by male cancer patients (refer to table 4.63 and table 4.64). From table 4.28 and table 4.29 it can also be seen that bicalutamide were mostly claimed by patients 59 years of age and older (age group 5). Therefore, it can be said that bicalutamide was mostly claimed by male cancer patients in age group 5.

Aspects of cyproterone (G03HA01) were already discussed in section 4.4.4 and section 4.5.3.7. Cyproterone is indicated in palliative treatment of inoperable prostate carcinoma. Cyproterone may also be used for severe acne and hirsutism in woman as well as male sexual deviation.

From table 4.62 and table 4.63 it is evident that cyproterone was mainly claimed by female patients. Cyproterone comprised 7.32% (n=5 267) and 6.20% (n=5 120) of all cancer medicine items claimed in 2005 and 2006 respectively (refer to table 4.25). Cyproterone claimed by female patients encompassed 6.65% (n=4 783) in 2005 and 5.60% (n=4 621) in 2006. This indicates that cyproterone was not necessarily claimed for the treatment of cancer (prostatic carcinoma), but may have been prescribed for another disease, which can be treated with cyproterone.

It can be assumed that cyproterone claimed by male patients was mainly indicated for treating prostatic carcinoma. This was 0.67% (n=481) and 0.59% (n=483) of all cancer medicine items, which were claimed by male patients in 2005 and 2006 respectively.

Aspects of goserelin (L02AE03) have already been discussed in section 4.5.3.1. Goserelin is indicated in prostate cancer and hormone receptor-positive breast cancer in pre-menopausal woman (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008).

From table 4.62 and table 4.63 it is evident that goserelin was mostly claimed by male cancer patients. In 2005, goserelin claimed by male cancer patients comprised 1.35% (n=972) of all cancer medicine items claimed compared to 0.33% (n=234) claimed by female cancer patients in 2005. Goserelin claimed by male cancer patients in 2006 comprised 1.25% (n=1 034) of all cancer medicine items claimed compared to 0.31% (n=258) claimed by female patients. Table 4.28 and table 4.29 also shows that goserelin was largely claimed by age group 5 (patients 59 years of age and older). This emphasises in the use of goserelin is in the treatment of prostate cancer.

Aspects of anastrozole (L02BG03) have already been discussed in section 4.3.4. Anastrozole is used in hormone receptor-positive breast cancer in post-menopausal (or oophorectomised) woman (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). The trade name containing anastrozole is Arimidex 1mg tablets® (refer to Appendix B).

Anastrozole comprised 3.78% (n=2 724) and 4.87% (n=4 015) of all cancer medicine items claimed in 2005 and 2006 respectively (refer to table 4.25). Of these percentages, anastrozole claimed by female cancer patients comprised 3.74% (n=2 692) and 4.83% (n=3 990) in 2005 and 2006 respectively (refer to table 4.65).

Aspects of imatinib (L01XE01) have been discussed in section 4.3.1, section 4.4.4 and section 4.5.3.14. Imatinib is indicated for the *treatment of chronic myeloid leukaemia* in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). Imatinib is

the active ingredient in Gleevec 100mg capsules®, Gleevec 100mg tablets® and Gleevec 400mg tablets® (refer to appendix B).

According to table 4.25, imatinib comprised 1.46% (n= 1 051) and 1.78% (n=1 471) of all cancer medicine items claimed in 2005 and 2006 respectively. Male cancer patients claimed 0.96% (n=688) of all imatinib claimed in 2005 and 1.28% (n=1 059) in 2006. Imatinib claimed by female cancer patients comprised the remaining 0.50% (n=358) and 0.50% (n=412) in 2005 and 2006 respectively.

Cyclophosphamide (L01AA) is an antineoplastic agent (L02) and more specifically a nitrogen mustard analogue (L01AA). Cyclophosphamide is used to treat lymphomas, solid tumours and chronic lymphocytic leukaemia and may be used alone or in combination with other cancer drugs. It is also indicated in a variety of aggressive non-malignant diseases (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008).

Cyclophosphamide comprised 3.19% (n=2 299) of all cancer medicine items claimed in 2005 and 3.72% (n=3 074) in 2006 (refer to table 4.25). Of these, 2.45% (n=1 761) and 2.58% (n=2 130) were claimed by female cancer patients in 2005 and 2006 respectively. Cyclophosphamide claimed by male cancer patients comprised 0.75% (n=538) and 1.14% (n=944) in 2005 and 2006 respectively.

From table 4.28 and 4.29 it is evident that the use of cyclophosphamide increased with age. In 2005, the number of items (cyclophosphamide) increased from 2 (age group 1) to 1 067 (age group 5) while in 2006, the number of items (cyclophosphamide) increased from 2 (age group 1) to 1 538 (age group 5).

Aspects of leuprolide (L02AE02) have been discussed in section 4.5.3.3. Leuprolide is mainly indicated in palliative treatment of advanced prostatic cancer. It has also been used in central precocious puberty, in the management of endometriosis and uterine fibroids and in the treatment of breast cancer in pre-menopausal woman (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). The trade names on the database containing Leuprolide is Lucrin 2.8ml 5mg/ml®, the Lucrin depot injection 3.75mg® and the Lucrin depot injection 11.25mg/vial.

As seen in table 4.64, leuprolide is only included in the top 5 cancer medicine items in 2005, and were mainly claimed by male cancer patients. Leuprolide comprised 0.89% (n=640) and 0.78% (n=647) of all cancer medicine items. Leuprolide claimed by male cancer patients comprised 0.80% (n=577) and 0.71% (n=590) of the total prevalence of leuprolide in 2005 and 2006 respectively. The remaining 0.09% (n=63) and 0.07% (n=57) were claimed by female cancer patients.

The top five cancer medicine items according to cost claimed by females and males are presented in table 4.65.

Table 4.65 Top five cancer medicine items according to cost claimed by female and male cancer patients

	Females				Males			
	2005		2006		2005		2006	
		%*		%*		%*		%*
1	Docetaxel	6.54	Trastuzumab	10.46	Imatinib	5.95	Imatinib	6.32
2	Trastuzumab	5.62	Docetaxel	5.42	Bicalutamide	5.73	Rituximab	5.61
3	Anastrozole	4.38	Rituximab	5.07	Docetaxel	3.88	Bicalutamide	4.58
4	Gemcitabine	4.12	Anastrozole	4.49	Rituximab	3.73	Docetaxel	3.12
5	Paclitaxel	4.06	Paclitaxel	4.30	Goserelin	3.65	Gemcitabine	2.88
		24.72		29.74		22.94		22.51

* Percentages shown in table 4.65 were taken from table 4.62 and 6.63.

**Refer to table 4.62 and table 4.63 for the total cost of cancer medicine items represented by percentages given in table 4.65.

The top five cancer medicine items according to cost claimed by female cancer patients comprised 24.72% and 29.74% of the total cost of cancer medicine items claimed by female cancer patients in 2005 and 2006 respectively. The top five cancer medicine items according to cost claimed by male cancer patients comprised 22.94% and 22.51% of the total cost of cancer medicine items claimed by male cancer patients.

Docetaxel is indicated in the management of *advanced or metastatic breast, ovarian and non-small cell lung cancer* (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). Docetaxel is a more potent analogue of paclitaxel, which is the active ingredient in Taxol 100mg/vial and Taxol 300mg/5ml injections (refer to section 4.3.7). Docetaxel is the active ingredient in Taxotere 20mg/1.5ml injection and Taxotere 80mg injection (refer to Appendix B). Other aspects of docetaxel have been discussed in section 4.4.4 and section 4.5.3.18.

Docetaxel (L01CD02) comprised 10.42% (R7 895 405.57) and 8.54% (R9 278 838.99) of the total cost of cancer medicine items in 2005 and 2006 respectively. In 2005, docetaxel claimed by female cancer patients comprised 6.54% (R4 955 010.67) and male cancer patients comprised 3.88% (R2 940 394.90) of the total cost of docetaxel claimed (refer to table 4.66). The cost of docetaxel claimed by female cancer patients comprised 5.42% (R5 891 550.24) of the total cost of docetaxel

claimed in 2006, while docetaxel claimed by male cancer patients comprised 3.12% (R3 387 288.75) of the total cost of docetaxel in 2006 (refer to table 4.65).

Trastuzumab is indicated for metastatic breast cancer in patients with a tumour over expressing the human epidermal growth factor receptor 2 (HER2) (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). Aspects of trastuzumab have been discussed in section 4.3.2, section 4.4.4 and 4.5.3.16.

Trastuzumab (L01XC03) comprised 5.64% (R4 269 416.08) and 10.46% (R11 365 564.90) of the total cost of all cancer medicine items claimed in 2005 and 2006 respectively (refer to table 4.25). In 2005, only female patients claimed trastuzumab. In 2006, only 0.01% (R10 983.55) of the total cost of trastuzumab in 2006 had been claimed by male cancer patients (refer to table 4.62 and table 4.63).

Gemcitabine (L01BC05) is an antineoplastic agent (L01) and more specifically a pyrimidine analogue (L01BC). Gemcitabine is an analogue of cytarabine, which is discussed in section 4.3.8. Gemcitabine is used in the treatment of locally advanced or metastatic non-small cell lung, bladder, pancreatic and ovarian cancers (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). The trade name containing gemcitabine is the Gemzar injection 200mg® and Gemzar 1g/vial® (refer to Appendix B).

Gemcitabine comprised 7.67% (R5 805 869.89) and 6.67% (R7 253 737.99) of the total cost of cancer medicine items in 2005 and 2006 respectively (refer to table 4.25). Gemcitabine claimed by female cancer patients comprised 4.77% (R3 611 222.55) and 3.80% (R4 128 520.26) of the total cost of gemcitabine in 2005 and 2006 respectively. Gemcitabine claimed by male cancer patients comprised 2.90% (R2 194 647.30) and 2.88% (R3 125 217.73) of the total cost of gemcitabine in 2005 and 2006 respectively.

Aspects of paclitaxel (L01CD01) have been discussed in section 4.3.7. Paclitaxel is used and indicated for palliative treatment of stage 3 or 4 *advanced local carcinoma of the ovary* after surgical resection, in combination with cisplatin/carboplatin; palliative management of *metastatic carcinoma of the ovary* after failure of first line or subsequent chemotherapy; treatment of *metastatic carcinoma of the breast* after failure of combination chemotherapy or relapse within 6 months of adjuvant chemotherapy; palliative treatment of *advanced non-small cell lung cancer* in patients who are not candidates for potentially curative surgery and/or radiation (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). Paclitaxel is the active ingredient in Taxol 300mg/50ml® and the Taxol 100mg/vial® injection.

Paclitaxel comprised 5.11% (R3 873 479.32) and 5.05% (R5 484 640.48) of the total cost of all cancer medicine items in 2005 and 2006 respectively. Of this, paclitaxel claimed by female cancer comprised 3.78% (R2 860 993.97) and 4.30% (R4 673 801.75) in 2005 and 2006 respectively. Paclitaxel claimed by male cancer patients comprised 1.05% (R796 858.09) and 0.75% (R810 838.73) in 2005 and 2006 respectively (refer to table 4.62 and table 6.63).

In section 4.3.3, section 4.4.4 and section 4.5.3.17 some aspects of rituximab (L01XC02) have already been discussed. Rituximab is used in the treatment of *Non-Hodgkins lymphomas*. It can be used as mono-therapy in *relapsed or refractory low-grade or follicular lymphoma*, or as first-line treatment with combination therapy, such as CVP (cyclophosphamide, vincristine, and prednisolone) (Gibbon, 2008; SAEPI, 2008; Sweetman, 2008). Rituximab is the active ingredient in the Mabthera 100mg vial® and the Mabthera 500mg vial® (refer to Appendix B).

Rituximab comprised 7.51% (R5 687 754.46) and 10.68% (R11 606 045.00) of all cancer medicine items claimed in 2005 and 2006 respectively. In 2005, rituximab claimed by female cancer patients comprised 3.78% (R2 860 993.97) of the total cost of rituximab while rituximab claimed by male cancer patients comprised 3.73% (R2 826 760.50) (refer to table 4.62 and table 4.63). In 2006, rituximab claimed by female cancer patients comprised 5.07% (R5 506 323.35) of the total cost of rituximab. Rituximab claimed by male cancer patients in 2006 comprised 5.61% (R6 099 721.99) of the total cost of rituximab.

Anastrozole, imatinib, bicalutamide and goserelin were also part of the top five cancer medicine items according to prevalence (refer to table 4.64) as well as the top five cancer medicine items according to cost (refer to table 6.65) and will therefore only be discussed shortly below:

- The total cost of anastrozole (L02BG03) comprised 4.43% (R3 356 062.09) and 4.51% (R4 903 970.70) of all cancer medicine items (refer to table 4.25). Anastrozole claimed by female cancer patients comprised 4.38% (R3 317 211.65) and 4.49% (R4 874 391.24) of the total cost of anastrozole claimed by cancer patients in 2005 and 2006 respectively (refer to table 4.62, table 4.63 and table 4.64).
- The total cost of imatinib (L01XE01) comprised 9.26% (R7 016 518.26) and 8.95% (R9 722 258.09) of all cancer medicine items claimed (refer to table 4.25). In 2005, imatinib claimed by female cancer patients comprised 3.28% (R2 482 867.62) while male cancer patients comprised 5.95% (R4 506

532.50) of the total cost of imatinib claimed by cancer patients. In 2006, imatinib claimed by female cancer patients comprised 2.63% (R2 854 191.60) of the total cost of imatinib while male cancer patients comprised 6.32% (R6 868 066.49) (refer to table 4.65).

- The total cost of bicalutamide (L02BB03) comprised 5.75% (R4 355 611.96) and 4.60% (R5 003 256.98) of all cancer medicine items (refer to table 4.25). Bicalutamide claimed by male cancer patients comprised 5.73% (R4 337 495.50) and 4.58% (R4 978 331.80) of the total number of buserelin claimed by cancer patients in 2005 and 2006 respectively (refer to table 4.62, table 4.63 and table 4.65).
- The total cost of goserelin (L02AE03) comprised 4.21% (R3 187 729.74) and 3.16% (R3 436 990.92) of all cancer medicine items (refer to table 4.25). Goserelin claimed by male cancer patients comprised 3.65% (R2 762 195) and 2.74% (R2 981 823.52) of the number of buserelin claimed by cancer patients, in 2005 and 2006 respectively (refer to table 4.62, table 4.63 and table 4.65).

The five cancer medicine items with the highest average cost claimed by female and male cancer patients in 2005 and 2006 are presented in table 4.66.

Table 4.66 Top five average costs of cancer medicine items claimed by female and male cancer patients

Females					
Rank	2005		Rank	2006	
1	Imatinib	6935.38±1242.70	1	Trastuzumab	7063.74±2313.89
2	Trastuzumab	6824.41±1641.70	2	Imatinib	6927.65±1307.68
3	Bevacizumab	6722.92±2042.06	3	Bevacizumab	6637.06±2233.45
4	Aldesleukin	5863.09±1131.28	4	Fludarabine	6051.08±1100.61
5	Docetaxel	5427.17±1534.53	5	Rituximab	6037.64±2113.50
Males					
Rank	2005		Rank	2006	
1	Imatinib	6550.19±1585.86	1	Imatinib	6485.43±1558.36
2	Fludarabine	6056.55±1501.47	2	Rituximab	6461.57±1951.28
3	Bevacizumab	5933.32±1781.89	3	Aldesleukin	6110.64±689.60
4	Rituximab	5687.65±2215.45	4	Bevacizumab	5988.75±2183.80
5	Docetaxel	5425.08±1737.43	5	Oxaliplatin	5562.88±2416.40

*Average costs shown in table 4.66 was taken from table 4.62 – 4.63.

Imatinib was ranked first in 2005 for both female and male cancer patients, and it also had the highest average cost of all the cancer medicine items, as well as for

male cancer patients in 2006. The average cost for imatinib was higher for female cancer patients than for male patients in both 2005 and 2006.

The average cost of trastuzumab increased from 2005 ($R6824.41 \pm 1641.70$) to 2006 ($R7\ 063 \pm 2\ 313.89$). In 2006, trastuzumab had the highest average cost for female cancer patients.

The average cost of rituximab for male cancer patients increased with a relatively large margin (12%) from 2005 ($R5\ 687.65 \pm 2\ 215.45$) to 2006 ($R6\ 461.57 \pm 1\ 951.28$). In 2006, the average cost of rituximab for male cancer patients ($R6\ 461.57 \pm 1\ 951.28$) was 6.56% higher than the average cost of rituximab for female cancer patients ($6\ 037.64 \pm 2\ 113.50$).

Aldesleukin (L03AC01) is an immunostimulant (L03) and more specifically an interleukin (L013AC). The trade name containing aldesleukin is Chiron IL-2® (refer to Appendix B).

In 2005, aldesleukin had the 4th highest average cost ($R5\ 863.09 \pm 1\ 131.28$) in female cancer patients while in 2006, aldesleukin had the 3rd highest average cost ($R6\ 110.64 \pm 689.60$) in male cancer patients.

Bevacizumab (L01XC07) is an antineoplastic agent (L01) and more specifically a monoclonal antibody (L01XC). It is indicated in the treatment of metastatic colorectal cancer, in combination with fluoropyrimidine-based chemotherapy. Bevacizumab is the active ingredient in the Avastin 100mg/4ml infusion®; the Avastin 100mg/4ml vial®; the Avastin 400mg/16ml infusion® and the Avastin 400mg/16ml vial®.

The average cost of bevacizumab was higher for female cancer patients than for male cancer patients in both 2005 and 2006. In 2005, the average cost of bevacizumab was $R6\ 722.92 \pm 2\ 042.06$ for female cancer patients while for male cancer patients the average cost of bevacizumab was $R5\ 933.32 \pm 1\ 781.89$. In 2006, the average cost of bevacizumab for female cancer patients was $R6\ 637.06 \pm 2\ 233.45$ and for male cancer patients it was $R5\ 988.75 \pm 2\ 183.80$.

The five cancer medicine items with the highest average cost claimed by female cancer patients (refer to table 4.66) overall had higher average costs than those five cancer medicine items with the highest average cost claimed by male cancer patients (refer to table 4.66).

4.7 REGIMEN THERAPY FOR FIVE COMMON CANCERS IN A SECTION OF THE PRIVATE HEALTH CARE SECTOR IN SOUTH AFRICA.

In this section a combination therapy for the five common cancers in South Africa will be discussed. These cancers are: lung cancer, breast cancer, prostate cancer, colorectal cancer and lymphoma (refer to section 2.5).

For the purpose of this study, first-line cancer treatment regimens for each of these cancers were identified by a practicing oncologist, Dr. John Duminy (2007), supported by the oncology treatment guidelines of the South African Oncology Consortium (2006) (refer to section 2.7.3). This are only selected first-line regimens and does not include all combinations of therapy for each of these cancers. Treatment of cancer is complex and almost each scenario and patient differs, depending on various factors such as age of patient, stage of cancer, quality of life, financial impact and many more. Therefore only first-line treatments and the five most prevalent cancer treatment regimens, as suggested treatment regimens by Duminy (2007), were selected. This is for illustrative purposes only and does not represent the true usage patterns of these regimens or the true prevalence of the different cancers discussed.

From the results in table 4.67, it can be seen that these selected regimens comprised 1.74% and 2.14% of the total number of prescriptions claimed through the medicine claims database in 2005 and 2006 respectively. The total cost of these regimens comprised 6.92% (R5 243 458.64) and 7.12% (R7 736 115.80) of the total cost of all cancer medicine items claimed in 2005 and 2006 respectively.

4.7.1 Lung cancer

Prescriptions with the selected regimens for the treatment of lung cancer comprised 0.57% (n=333) and 0.52% (n=335) of the total number of prescriptions claimed in 2005 and 2006 respectively. The total cost of the selected regimens for lung cancer amounted to 2.17% (R1 643 760.92) and 1.75% (R1 907 001.10) of the total cost of all cancer medicine items claimed in 2005 and 2006 respectively.

Lung cancer can be divided into non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) (refer to section 2.5.1.1). Two first-line treatment regimens of each of these two types of lung cancer differ and will now be discussed separately.

4.7.1.1 Small cell lung cancer (SCLC)

Two medicine treatment regimens for SCLC have been identified.

SCLC: REGIMEN 1

Cyclophosphamide (L01AA01)

Doxorubicin (L01DB01)

Vincristine (L01CA02)

Regimen 1 for SCLC consists of cyclophosphamide, doxorubicin and vincristine. Cyclophosphamide is a nitrogen mustard analogue (L01AA), doxorubicin is a anthracycline (L01DB) and vincristine is a vinca alkaloid (L01CA) (refer to Appendix B).

Table 4.68 shows the prevalence and cost of this regimen, extracted from the cancer database in 2005 and 2006. According to the medicine claims database, this regimen comprised 0.09% (n=54) and 0.12% (n=79) of all prescriptions containing cancer medicine items claimed in 2005 and 2006 respectively. The total cost for this regimen in 2005 and 2006 respectively encompassed 0.08% (R56 908.88) and 0.08% (R87 941.11) of the total cost of cancer medicine items.

SCLC: REGIMEN 2

Cisplatin (L01XA01)

Etoposide (L01CB01)

Regimen 2 for SCLC consists of cisplatin, a platinum compound (L01XA) and etoposide, a podophyllotoxin derivate (L01CB). Table 4.67 shows the prevalence and cost of this regimen, extracted from the cancer database in 2005 and 2006. This regimen comprised 0.11% (n=67) in 2005 and 0.05% (n=34) of all prescriptions containing cancer medicine items. The total cost for this regimen encompassed 0.13% (R94 936.10) and 0.06% (R68 410.47) of the total cost of cancer medicine items in 2005 and 2006 respectively.

4.7.1.2 Non small cell lung cancer (NSCLC)

Two medicine treatment regimens for NSCLC have been identified.

NSCLC: REGIMEN 1

Cisplatin (L01XA01) Gemcitabine (L01BC05)
--

Regimen 1 for NSCLC consists of cisplatin, a platinum compound (L01XA01) and Gemcitabine (L01BC05), a pyrimidine analogue. Table 4.67 shows the prevalence and cost of this regimen, extracted from the cancer database in 2005 and 2006. According to the medicine claims database, this regimen comprised 0.28% (n=162) and 0.24% (n=157) of all prescriptions containing cancer medicine items claimed in 2005 and 2006 respectively. The total cost for this regimen in 2005 and 2006 respectively encompassed 1.69% (R1 279 394.63) and 1.34% (R1 461 259.50) of the total cost of cancer medicine items.

NSCLC: REGIMEN 2

Cisplatin (L01XA01) Vinorelbine (L01CA04)
--

Regimen 2 for NSCLC consists of cisplatin, a platinum compound (L01XA01) and vinorelbine, a vinca alkaloid (L01CA). Table 4.67 shows the prevalence and cost of this regimen, extracted from the cancer database in 2005 and 2006. This regimen comprised 0.09% (n=50) and 0.10% (n=65) of all prescriptions containing cancer medicine items claimed in 2005 and 2006 respectively. The total cost for this regimen in 2005 and 2006 respectively encompassed 0.28% (R212 521.31) and 0.27% (R289 390.02) of the total cost of cancer medicine items.

4.7.2 Breast cancer

The selected regimens comprised 0.39% (n=229) and 0.45% (n=292) of all prescriptions claimed in 2005 and 2006 respectively. The total cost of these regimens comprised 0.51% (R385 681.50) and 0.32% (R342 971.03) (refer to table 4.67).

Three regimens for the first-line treatment of breast cancer have been identified. Regimen 3 is classified as hormone therapy and consists of cancer medicine items from the subgroup L02 (endocrine therapy).

Breast cancer: REGIMEN 1

Doxorubicin (L01DB01)

Cyclophosphamide (L01AA01)

Regimen 1 for the treatment of breast cancer consists of doxorubicin, which is an anthracycline (L01DB) and cyclophosphamide, which is a nitrogen mustard analogue (L01AA). Table 4.67 shows the prevalence and cost of this regimen, taken from the cancer database in 2005 and 2006. According to the medicine claims database, this regimen comprised 0.18% (n=107) and 0.30% (n=196) of all prescriptions containing cancer medicine items claimed in 2005 and 2006 respectively. The total cost for this regimen in 2005 and 2006 respectively encompassed 0.34% (R257 164.93) and 0.21% (R228 937.05) of the total cost of cancer medicine items.

Breast cancer: REGIMEN 2

Doxorubicin (L01DB01)

Cyclophosphamide (L01AA01)

Fluorouracil (L01BC02)

Regimen 2 for the treatment of breast cancer consists of doxorubicin, which is an anthracycline (L01DB), cyclophosphamide, a nitrogen mustard analogue (L01AA) and fluorouracil, which is a pyrimidine analogue (L01BC). Table 4.67 shows the prevalence and cost of this regimen, taken from the cancer database in 2005 and 2006. This regimen comprised 0.21% (n=121) and 0.13% (n=87) of all prescriptions containing cancer medicine items claimed in 2005 and 2006 respectively. The total

cost for this regimen in 2005 and 2006 respectively encompassed 0.17% (R127 163.12) and 0.09% (R101 869.81) of the total cost of cancer medicine items (refer to table 4.67).

Breast cancer: REGIMEN 3 (hormonal)

Anastrozole (L02BG03)

Goserelin (L02AE03)

Regimen 3 is classified as endocrine (hormonal) therapy for the treatment of breast cancer and consists of anastrozole, an aromatase inhibitor (L02BG) and Goserelin (L02AE03). Table 4.67 shows the prevalence and cost of this regimen, taken from the cancer database in 2005 and 2006. This regimen comprised 0.01% (n=5) of all prescriptions containing cancer medicine items in 2005 and in 2006, and this regimen was only claimed 2 times (n=2). Other medicine items that can also be used with anastrozole include Buserelin (L02AE01) and Leuprolide (L02AE02), which are also gonatropin releasing hormone analogues (L02AE).

4.7.3 Prostate cancer

Two regimens were identified for the purpose of this study for the treatment of prostate cancer. These regimens are also endocrine (hormonal) therapy.

Prostate cancer: REGIMEN 1

Buserelin (L02AE01)

Bicalutamide (L02BB03)

Regimen 1 for the treatment of prostate cancer consists of buserelin, a gonadotropin-releasing hormone (GnRH) analogue (L02AE) and bicalutamide, which is an anti-androgen (L02BB). Table 4.67 shows the prevalence and cost of this regimen, taken from the cancer database in 2005 and 2006. This regimen was only present on 6 prescriptions in 2005 while in 2006, 0.01% (n=9) of the prescriptions contained this regimen. The total cost of this regimen comprised 0.03% (R26 153.94) and 0.04% (R46 993.17) of the total cost of all cancer medicine items.

Prostate cancer: REGIMEN 2**Goserelin (L02AE03)****Bicalutamide (L02BB03)**

Regimen 2 for the treatment of prostate cancer consists of goserelin, a gonadotropin-releasing hormone (GnRH) analogue (L02AE) and bicalutamide, which is an anti-androgen (L02BB). Table 4.67 shows the prevalence and cost of this regimen, taken from the cancer database in 2005 and 2006. This regimen comprised 0.13% (n=76) and 0.16% (n=102) of the total number of prescriptions claimed in 2005 and 2006 respectively. The total cost of this regimen comprised 0.52% (R390 833.76) and 0.47% (R507 675.03) of the total cost of all cancer medicine items claimed in 2005 and 2006.

4.7.4 Colorectal cancer

The chosen regimens used in colorectal cancer comprised 0.52% (n=305) and 0.77% (n=497) of the total number of prescriptions claimed in 2005 and 2006 respectively. The total cost of these regimens comprised 3.50% (R2 649 023.81) and 3.42% (R3 721 504.87) of the total cost of all cancer medicine items claimed in 2005 and 2006 respectively.

Two regimens were identified for the treatment of colorectal cancer and will now be discussed.

Colorectal cancer: REGIMEN 1**Fluorouracil (L01BC02)****Irinotecan (L01XX19)*****Folinic acid** (V03AF04)**

Regimen 1 for the treatment of colorectal cancer consists of fluorouracil, a pyrimidine analogue (L01BC) and irinotecan, classified as an "other antineoplastic agent" (L01XX). Also included in this regimen, is *Folinic acid** (V03AF04). This drug was excluded from the cancer database because it is not essentially used in cancer

treatment and is used as a complementary drug in cancer treatment. Folinic acid was taken note of but for the purpose of this study will not be included in further discussion.

Table 4.67 shows the prevalence and cost of this regimen, extracted from the cancer database in 2005 and 2006. This regimen comprised 0.46% (n=271) and 0.45% (n=292) of the total number of prescriptions claimed through the medicine claims database in 2005 and 2006 respectively. The total cost of these regimens comprised 3.14% (R2 375 550.89) and 2.02% (R2 194 983.31) of the total cost of all cancer medicine items.

Colorectal cancer: REGIMEN 2

Fluorouracil (L01BC02)

Oxaliplatin (L01XA03)

Folinic acid* (V03AF04)

Regimen 2 for the treatment of colorectal cancer consists of fluorouracil, a pyrimidine analogue (L01BC) and oxaliplatin, a platinum compound (L01XA). Folinic acid is also included in this regimen (refer to Colorectal cancer: regimen 1). Table 4.67 shows the prevalence and cost of this regimen, taken from the cancer database in 2005 and 2006. The number of prescriptions containing this regimen comprised 0.06% (n=34) and 0.32% (n=205) of the total number of prescriptions claimed in 2005 and 2006 respectively. The total cost of this regimen comprised 0.36% (R273 472.92) and 1.40% (R1 526 521.56) of the total cost of all cancer medicine items in 2005 and 2006 respectively.

4.7.5 Lymphoma

The number of prescriptions containing the selected regimens for the treatment of lymphoma comprised 0.11% (n=67) and 0.25% (n=164) of the total number of prescriptions claimed. The total cost of these regimens comprised 0.17% (R130 085.80) and 1.11% (R1 215 503.04) of the total cost of all cancer medicine items claimed in 2005 and 2006 respectively.

This disease (Lymphoma) can be divided into two main groups: Hodgkin's disease (HD) and Non-Hodgkin's lymphoma (NHL) (also refer to section 2.5.5).

4.7.5.1 Non-Hodgkin's Lymphoma (NHL)

NHL: REGIMEN 1

Cyclophosphamide (L01AA01) Doxorubicin (L01DB01) Vincristin (L01CA02) Rituximab (L01XC02) Prednisone (H02AB07)

Regimen 1 for the treatment of NHL consists of cyclophosphamide, a mustard nitrogen analogue (L01AA), doxorubicin, which is an anthracycline (L01DB), vincristine (L01CA), a vinca alkaloid and rituximab, which is a monoclonal antibody (L01XC02). Prednisone, a glucocorticoid (H02AB07), is also prescribed with this regimen.

Table 4.67 shows the prevalence and cost of this regimen, extracted from the cancer database in 2005 and 2006. The number of prescriptions containing the selected regimen comprised 0.02% (n=10) and 0.10% (n=62) of the total number of prescriptions claimed during 2005 and 2006 respectively. The total cost of this regimen comprised 0.12% (R88 237.90) and 0.93% (R1 015 427.72) of the total cost of all cancer medicine items in 2005 and 2006 respectively.

NHL: REGIMEN 2

Cyclophosphamide (L01AA01) Vincristin (L01CA02) Prednisone (H02AB07)

Regimen 2 for the treatment of NHL consists of cyclophosphamide, a mustard nitrogen analogue (L01AA) and vincristine (L01CA), a vinca alkaloid. Prednisone, a glucocorticoid, is also prescribed with this regimen.

Table 4.67 shows the prevalence and cost of this regimen, extracted from the cancer database in 2005 and 2006. The number of prescriptions containing this regimen

comprised 0.08% (n=49) and 0.08% (n=50) of the total number of prescriptions claimed in 2005 and 2006 respectively. The total cost of this regimen comprised 0.02% (R15 183.09) and 0.01% (R15 918.71) of the total cost of all cancer medicine items in 2005 and 2006 respectively.

4.7.5.2 Hodgkin's disease (HD)

NHL: REGIMEN 1

Doxorubicin (L01DB01)

Bleomycin (L01DC01)

Vinblastin (L01CA01)

Dacarbazine (L01XA04)

Regimen 1 for the treatment of HD consists of doxorubicin, an anthracycline (L01DB), bleomycin, classified as a "other cytotoxic antibiotic" (L01DC), vinblastine, a vinca alkaloid (L01CA) and dacarbazine, which is an "other alkylating agent" (L01XA). Table 4.67 shows the prevalence and cost of this regimen, taken from the cancer database in 2005 and 2006. The number of prescriptions claimed comprised 0.01% (n=8) and 0.08% (n=52) of the total number of prescriptions claimed in 2005 and 2006 respectively. The total cost of this regimen comprised 0.17% (R130 085.80) and 1.11% (R1 215 503.04) of the total cost of all cancer medicine items in 2005 and 2006 respectively.

Table 4.67 Cancer treatment regimens for five common cancers in a section of the private health care sector in South Africa

			2005				2006			
Cancer site	Regimen		Prevalence ¹ (N) (a)	% (b)	Total cost (R) (c)	% (d)	Prevalence ¹ (N) (a)	% (b)	Total cost (R) (c)	% (d)
Lung cancer										
SCLC	REGIMEN 1	Cyclophosphamide	54	0.09	56 908.88	0.08	79	0.12	87 941.11	0.08
		Doxorubicin								
		Vincristine								
	REGIMEN 2	Cisplatin	67	0.11	94 936.10	0.13	34	0.05	68 410.47	0.06
		Etoposide								
NSCLC	REGIMEN 1	Cisplatin	162	0.28	1 279 394.63	1.69	157	0.24	1 461 259.50	1.34
		Gemcitabine								
	REGIMEN 2	Cisplatin	50	0.09	212 521.31	0.28	65	0.10	289 390.02	0.27
		Vinorelbine								
TOTAL			333	0.57	1 643 760.92	2.17	335	0.52	1 907 001.10	1.75
Breast cancer										
	REGIMEN 1	Docetaxel	107	0.18	257 164.93	0.34	196	0.30	228 937.05	0.21
		Cyclophosphamide								
	REGIMEN 2	Docetaxel	121	0.21	127 163.12	0.17	87	0.13	101 869.81	0.09
		Cyclophosphamide								
		Fluorouracil								
	REGIMEN 3	Anastrozole	5	0.01	19 272.36	0.03	2	0.00	6 631.73	0.01
		Goserelin								
TOTAL			233	0.40	403 600.41	0.54	285	0.43	337 438.59	0.31
Prostate cancer										
	REGIMEN 1	Buserelin	6	0.01	26 153.94	0.03	9	0.01	46 993.17	0.04
		Bicalutamide								
	REGIMEN 2	Goserelin	76	0.13	390 833.76	0.52	102	0.16	507 675.03	0.47
		Bicalutamide								
TOTAL			82	0.14	416 987.70	0.55	111	0.17	554 668.20	0.51

Table 4.68 Cancer treatment regimens for five common cancers in the private health care sector in South Africa (continued)

			2005			2006				
Cancer site	Regimen		Prevalence ¹ (N)	%*	Total cost (R)	%**	Prevalence ¹ (N)	%*	Total cost (R)	%**
Colorectal cancer										
	REGIMEN 1	Fluorouracil	271	0.46	2 375 550.89	3.14	292	0.45	2 194 983.31	2.02
		Irinotecan								
		Levamisole								
	REGIMEN 2	Fluorouracil	34	0.06	273 472.92	0.36	205	0.32	1 526 521.56	1.40
		Oxaliplatin								
		Levamisole								
TOTAL			305	0.52	2 649 023.81	3.50	497	0.77	3 721 504.87	3.42
Lymphoma										
NHL	REGIMEN 1	Cyclophosphamide	10	0.02	88 237.90	0.12	62	0.10	1 015 427.72	0.93
		Doxorubicin								
		Vincristine								
		Rituximab								
		Prednisone								
	REGIMEN 2	Cyclophosphamide	49	0.08	15 183.09	0.02	50	0.08	15 918.71	0.01
		Vincristine								
		Prednisone								
HD	REGIMEN 1	Doxorubicin	8	0.01	26 664.81	0.04	52	0.08	184 156.61	0.17
		Bleomycin								
		Vinblastine								
		Dacarbazine								
TOTAL			67	0.11	130 085.80	0.17	164	0.25	1 215 503.04	1.11
Total of five cancers			1020	1.74	5 243 458.64	6.92	1392	2.14	7 736 115.80	7.12

¹Prevalence indicates the number of prescriptions containing the specific medicine treatment regimen.

*Percentage (b) is calculated by dividing (a) by the total number of prescriptions containing one or more cancer medicine item claimed in 2005 (n=58 682) and 2006 (n=64 919) respectively (refer to table 4.2)

**Percentage (d) is calculated by dividing (c) by the total cost of all prescriptions/cancer medicine items claimed in 2005 (R75 736 630.77) and 2006 (R108 675 842) respectively (refer to table 4.2)

4.8 SUMMARY

In this chapter, the results of the empirical investigation have been discussed. Cancer medicine items have been analysed by means of a classification (ATC classification – Appendix A), an in-depth analysis of the prevalence of cancer medicine items as well as the costs associated with cancer medicine items. The use of generic, no-generic and original cancer medicine items, the use of cancer medicine items in different age groups and genders have been examined.

The conclusions and recommendations, based on the empirical investigation, will be formulated and discussed in chapter five.

CHAPTER 5

Conclusions, limitations and recommendations

5.1 INTRODUCTION

In this chapter the conclusions, based on the results of the literature review and the empirical investigation will be presented (in a summary format) as well as the limitations encountered during this study. Certain recommendations to this study will also be made.

5.2 CONCLUSIONS

In order to ensure that the study has succeeded in achieving the specific aims that were set, the conclusions drawn for each aim will be summarised briefly:

Specific research objectives from the literature study:

- The **first** specific aim was to define cancer and put the disease in perspective, both internationally and nationally (refer to section 2.2 – 2.3).

This was done through a broad overview of the literature on cancer. Cancer and oncology was defined and the statistics of cancer prevalence and cancer deaths was investigated, both internationally and in South Africa.

It was concluded that cancer can be described as a deadly disease with widespread effects and can affect people from all over the world, no matter what race, society or age. Although there is great progress in the development of new cancer drugs, cancer can be, in comparison with other major diseases, seen as minimally controlled by modern medicine (Varmus, 2006:1162) and is quickly becoming a mortality force to reckon with (Ma & Yu, 2006:85).

In South Africa, it seems cancer research is not enjoying enough attention and is in need of major improvement and also adequate funding. The statistics available is insufficient to accurately estimate the real burden of cancer in South Africa. There is

numerous problems with the National Cancer Registry and all other cancer registries in South Africa are not mandated by law and therefore cancer is not a reportable disease (Albrecht, 2006:4).

In 2002, the International Agency for Research on Cancer (Parkin *et al.*, 2004) listed prostate cancer, cervix cancer, lung cancer, breast cancer, oesophagus cancer and colorectal cancer as some of the major cancers in South Africa. This estimation was done by using the available data in South Africa and scaling it to incidence (refer to section 2.3.5.1).

- The **second** specific aim was to investigate the different cancer treatment approaches. (refer to section 2.4)

This aim was approached through an overview of the literature on cancer. The conventional treatment of cancer includes different approaches e.g. chemotherapy, radiotherapy and surgery. Chemotherapy is used i.e. in effecting cure in some cancers, reducing a tumour size before surgery/radiotherapy, eliminating remaining disease after surgery/radiotherapy and in palliative treatment. There are different uses for radiotherapy and it may be used alone or in combination with chemotherapy and/or surgery, depending on certain guidelines. Surgery is the oldest form of treating cancer and also has different uses e.g. definitive surgery, staging surgery, curative surgery, palliative surgery or combination surgery. These traditional methods are still widely used and effective but new development to control cancer has become increasingly important over the past few years. The major aim of new cancer treatments and strategies is to convert cancer into a chronic, controllable illness (Bosanquet & Sikora, 2006a:7, 123). New cancer treatment approaches reviewed in this study included gene therapy, monoclonal antibodies, small molecules and vaccines.

- The **third** specific aim was to describe different cancers in particular lung cancer, breast cancer, prostate cancer, colorectal cancer and lymphoma (HD and NHL). (refer to section 2.5).

Five cancers commonly diagnosed in the private health care sector of South Africa was chosen and discussed (refer to section 2.5). These are lung cancer, breast cancer, prostate cancer, colorectal cancer and lymphoma (Hodgkin's disease and Non-Hodgkin's lymphoma). These cancers were defined and the available incidence and mortality rates were studied. A review of the signs and symptoms as well as early detection and risk factors involved in each cancer were discussed.

Lung cancer is the most frequently found cancer worldwide (Mqoqi *et al.*, 2004:36-37) and only 15% of lung cancer cases are found in the early stages of the disease (Health Alliance Cancer Services, 2006:1). Cigarette smoking remains the most important risk factor for lung cancer (American Cancer Society, 2008c:14). Breast cancer is the leading cancer in woman worldwide (Parton *et al.*, 2001:1528) and breast self-examination is a very important factor in early detection (Bryant, 1995:407). Some of the biggest risk factors for breast cancer are age, family history and previous benign disease (refer to table 2.12). Prostate cancer is the second most common cancer in men worldwide and the most common cancer in men in South Africa. Age is the major risk factor for prostate cancer (Prostate cancer Foundation, 2004) and early detection of prostate cancer is very important (refer to section 2.5.3.4). Colorectal cancer is a common cancer in both males and females. Early detection of this cancer increases the possibility of cure dramatically (Barkun & Flegel, 2007:545). Risk factors include diet, lifestyle, family history and age. Lymphoma can be divided into Hodgkin's disease (HD) and non-Hodgkin's lymphoma (NHL). The differences between these two diseases is summarised in table 2.15. Incidence of HD has decreased in men and slightly increased in woman while the incidence of NHL almost doubled over the past 30 years because of the pandemic spread of HIV and AIDS – resulting in AIDS-related NHL. Risk factors for both these diseases include age, gender, family factors and exposure to chemicals.

- The **fourth** specific aim was to define and briefly describe the concepts: *managed care, pharmacoeconomics and drug utilisation review*. (refer to section 2.7, section 2.9 and section 2.13).

An overview of the concepts of managed care, pharmacoeconomics and drug utilisation review was provided. These terms were defined and applied to South Africa and cancer treatments where possible. Types of managed care plans were briefly discussed and the South African Oncology Consortium (SAOC) was identified as a managed health care organisation in South Africa. Cost-benefit analysis, cost-effectiveness analysis, cost-minimisation analysis, cost-utility analysis and cost-of-illness studies were discussed and examples of cancer studies done in the past were given. Through this study it is evident that pharmacoeconomics can and should play a major role in the treatment decisions of cancer treatment. The relatively high cost of cancer care (refer to section 2.10.1) shows the need to ensure cost-effective cancer treatment plans using different pharmacoeconomic methodologies (refer to section 2.9.3).

- The **fifth** specific aim was to briefly investigate the approach to cancer of some medical schemes in South Africa (refer to section 2.8).

This was done through a brief overview of the literature. Different medical schemes in South Africa was summarised and the concept prescribed minimum benefits were discussed briefly. The approach to cancer treatment of three major medical schemes in South Africa was summarised and briefly discussed. There were definite guidelines stipulated by each of these medical schemes for the treatment of cancer. Specifically, following the recent controversy over Herceptin® (refer to 2.8.2.1, p.68), treatment guidelines for the use of Herceptin® were specified by Discovery Health.

- The **sixth** specific aim was to have a closer look at the economics of cancer (refer to section 2.10).

The cost of cancer treatment and cancer drugs is currently of high interest to the mainstream health economics field and according to Bosanquet and Sikora (2006:1) it needs much more attention and development. Novel cancer therapies is causing a steep increase in cost of cancer care (Niezen *et al.*, 2006:2887) and progress made in the diagnosing, screening and treatment of cancer patients has played a major factor in this increase of cancer treatment cost. Economic modelling of cancer treatment have become more relevant and important because this brings together all available data on the relevant factors such as effectiveness, costs, outcomes and alternative courses of action (Phillips, 2008:8). Two types of economic modelling, i.e. decision tree models and Markov models have been discussed and can be very useful in the evaluation of cancer treatment.

- The **seventh** specific aim was to investigate some methods that may be used to evaluate value and quality of life of cancer patients. (refer to section 2.11 and section 2.12).

Some aspects of value of life and quality of life in cancer patients were identified through an overview of the literature. Both value of life and quality of life is difficult to measure and very important in cancer care because of the extensive impact cancer can have on one's life. Two methods to determine value of life were briefly overviewed i.e. the human capital approach and the willingness-to-pay approach. The different aspects of quality of life, such as physical concerns, functional ability, emotional wellbeing etc., can be measured and assessed by means of different instruments. These instruments include FACT, FLIC, EORTC QLQ-36 and other quality of life measurement instruments (refer to section 2.12.2).

Specific research objectives from the empirical investigation

- The **first** specific aim was to determine the prevalence, cost and usage patterns of antineoplastic and immunomodulating agents in comparison with medicine in general (refer to section 4.2 and section 4.3).

From the results it could be seen that the number of cancer patients, the number of prescriptions containing one or more cancer drug and the number of cancer medicine items respectively comprised less than 1% of the total number of patients, prescriptions and medicine items recorded in the total database. To the contrary, the total cost of cancer medicine items comprised 4.00% and 5.31% of the total cost of all medicine items (total database). This indicates the *relatively high cost of cancer medicine items*.

On the total database, *generic medicine items* was claimed the most in both study years while on the cancer database, *original cancer medicine items* was claimed the most (refer to section 4.2.1.1 and table 4.1.1). The usage of generic substitution for cancer medicine items was evidently relatively low in 2005 and 2006 (refer to section 4.2.1.1 and figure 4.1.1). This may be because of two main reasons, namely no generic medicine items were available for the majority of cancer drugs (no-generic cancer medicine items) or due to the prescription preferences.

The *cost of no-generic medicine items* was the *highest* on both the total database and the cancer database. This is because no-generic medicine items are either still under patent protection or no generic medicine item has been developed after the patent protection of the specific drug expired (refer to section 3.2 and section 3.8.3.3). The relatively high cost of no-generic medicine items (on both total and cancer database) is also indicated by the calculated d-values in table 4.4.

The largest percentage of patients on the total database was patients between the ages of 19 and 45 years of age (age group 3). On the cancer database, the largest percentage of patients were 59 years or older (age group 5). This supports the statement made in the literature that most cancers are age related (refer to section 2.5.2.5, section 2.5.2.5, section 2.5.3.5, section 2.5.4.5 and section 2.5.5.5.2).

Results in table 4.8 revealed that cancer medicine items claimed by male cancer patients are relatively expensive, more so than cancer medicine items claimed by female cancer patients as well as medicine items claimed by all patients on the total database, without taking the value or extent of cancer treatment into consideration. Trends of a high effect sizes (d-values) in cancer medicine items claimed by male cancer patients were also encountered as presented in table 4.9.

Co-payments (levies) paid by patients on the total database and cancer database did not vary much, ranging from R26.33 ± 102.69 to R36.55 ± 479.95 in both study years. Medical schemes (third party payers) were responsible for more than 97% of the total cost of all cancer medicine items claimed for both study years.

- The **second** specific aim was to analyse the prescribing patterns for the top twenty cancer products according to highest total cost, highest average cost and highest prevalence. (refer to section 4.3).

The top twenty cancer products according to highest total cost, highest average cost and highest prevalence was extracted from Appendix B and summarised in table 4.11 – 4.13. Seven cancer products were identified according to specific criteria, concerning total cost, prevalence, average cost and CPI. These cancer products were Gleevec 100mg capsules®, Herceptin®, the Mabthera 500mg vial®, Arimidex 1mg tablets®, Eloxatin 100mg IV®, Methotrexate 2.5mg tablets and the Taxol 300mg/50ml injection® / Taxol 100mg/vial injection (refer to section 4.3.1-4.3.8).

- The **third** specific aim was to determine the prevalence and cost associated with original, non-original and generic forms of cancer medicine items in the top twenty cancer products according to highest total cost, highest average cost and highest prevalence (refer to section 4.3.9.2 and section 4.2.1.1).

The cancer medicine items in the top twenty cancer medicine items according to *highest total cost* were mostly no-generic cancer products (90% in both years). These includes cancer medicine items such as Gleevec 100mg capsules®, Mabthera 500mg vial®, Gemzar 1000mg injection®, etc. (refer to table 4.11). As seen in the previous objective, the cost of no-generic cancer medicine items was the highest overall for both the total database and the cancer database in both study years. No-generic cancer medicine items also had the highest percentage top twenty cancer products according to average cost (75% in both years) (includes cancer products such as Herceptin®, Gleevec 400mg tablets®, Avastin 400mg/16ml vial® etc.) and in the top twenty cancer products according to prevalence (65% in both years) (includes cancer medicine items such as Arimidex 1mg tablets®, Herceptin® and others).

Generic cancer medicine items were not included in the top twenty cancer products according to total cost. This may be because generic medicine items are usually more inexpensive than original and no-generic medicine items and therefore would not have such high total cost (refer to section 3.8.3.3). Generic cancer medicine items were included in the top twenty cancer medicine items according to prevalence. Generic cancer medicine items such as Neophedan 20mg tablets® and

Kessar 20mg tablets® were included in the top three cancer medicine items according to prevalence in both study years (refer to table 4.13).

- The **fourth** specific aim was the classification of cancer medicine items according to the different therapeutic, pharmacological and chemical subgroups. (refer to section 1.2, section 3.8.2.2 and Appendix A)

All the cancer medicine items on the medicine claims database for 2005 and 2006 was classified by means of the ATC classification system of the WHO. Cancer medicine items are classified as "Antineoplastic and immunomodulating agents" and falls under the classification code "L".

- The **fifth** specific aim was to determine the prevalence and cost of cancer medicine items in the different therapeutic, pharmacological and chemical subgroups.

From the results (presented in section 4.4), it is evident that cancer medicine items from the therapeutic subgroup L01 (antineoplastic agents) were claimed most frequently and comprised the largest cost percentage of cancer medicine items in both study years. The therapeutic subgroup L03 (immunostimulants) had the highest average cost and a CPI >3 in both study years as well as effect sizes >0.8, and this indicate the relatively *high cost* of cancer medicine items in this therapeutic subgroup. Endocrine therapy had the lowest average cost and a CPI <1, and it can therefore be deducted that endocrine therapy (L02) was *relatively inexpensive* while antineoplastic agents (L01) and immunostimulants (L03) were *relatively expensive* cancer treatments in 2005 and 2006 (refer to section 4.4.1).

The pharmacological subgroups L01B (anti-metabolites) and L02B (hormone antagonists and related hormones) had the highest prevalence percentages whilst the pharmacological subgroups L01X (other antineoplastic agents) and L01C (plant alkaloids and other natural products) had the highest cost percentages (refer to section 4.4.2).

Five of the chemical subgroups (L01BA, L02BA, L02AA, L02BC, L02BG – refer to Appendix A) comprised more than 60% of the prevalence of all cancer medicine items in both study years respectively (refer to section 4.4.3.1). Also, five of the chemical subgroups (L01CD, L01XC, L01BC, L01XE, L02AE – refer to appendix A) comprised about 60% of the total cost of all cancer medicine items claimed in both study years respectively (refer to section 4.4.3.2).

In both study years, more than 50% of the cancer medicine items (active ingredients) had CPI values higher than 1 and therefore it can be said that more than half of cancer medicine treatments prescribed in 2005 and 2006 were relatively expensive (refer to table 4.19). Some active ingredients were discussed in detail in section 4.4.4 according to their relatively high prevalence, high cost or high CPI values. These active ingredients were trastuzumab, imatinib, cyproterone, methotrexate, tamoxifen, docetaxel and rituximab. A cost-minimisation analysis was performed on the original trade name of tamoxifen, Nolvadex D 20mg tablets. It was deducted that a cost saving of between R59 531.75 – R83 727.06 was possible if Nolvadex D 20mg tablets® was substituted by the generic products, Kessar 20mg tablets® or Neophedan 20mg tablets® (refer to section 4.4.4).

- *The **sixth** specific aim was to determine the prevalence and cost of cancer agents associated with the different patient age groups (refer to section 4.5).*

Almost 50% of all cancer patients are 59 years of age or older (age group 5) (refer to figure 4.8). The most cancer medicine items were also claimed by this age group (≥ 59 years of age) (refer to section 4.5.1) and the total cost of cancer medicine items claimed by patients 59 years or older comprised almost 60% of the total cost of all cancer medicine items claimed during the two study years respectively (refer to section 4.5.2 and figures 4.9 and 4.10). Cancer medicine items claimed for the treatment of childhood cancers (age group 1 and 2 combined) comprised only 2% of all cancer medicine items claimed in both study years and less than 1% of the total cost of all cancer medicine items. Cancer medicine items claimed by patients in age group 3 comprised 17.36% and 16.54% of the total number of cancer medicine items in 2005 and 2006 respectively. The cost of cancer medicine items claimed by patients in age group 3 comprised 13.31% and 11.21% of the total cost of all cancer medicine items. Cancer medicine items claimed by patients in age group 4 encompassed 27.96% and 28.26% of the total number of cancer medicine items while the cost of cancer medicine items for this specific age group comprised 27.50% and 29.62% of the total cost of all cancer medicine items (refer to section 4.5.1 and 4.5.2). In section 4.5.3 some of the cancer medicine items claimed by the different age groups were discussed. These cancer medicine items were goserelin, L-asparaginase, leuprolide, mercaptopurine, methotrexate, cyproterone, tamoxifen, imatinib, trastuzumab, rituximab and docetaxel.

- The **seventh** specific aim was to determine the prevalence and cost of cancer agents according to the gender of the patient (refer to section 4.6).

More than 70% of all cancer patients in 2005 and 2006 were females whilst male cancer patients comprised about 30% of all cancer patients claiming through the medicine claims database (refer to figure 4.11). As expected, the number of cancer medicine items claimed by female cancer patients also comprised more than 70% of the total number of cancer medicine items claimed in 2005 and 2006 while the remaining cancer medicine items were claimed by male cancer patients. Contrary to expectation, the total cost of cancer medicine items was divided almost evenly between male and female cancer patients for both study years. The total cost of cancer medicine items claimed by female cancer patients comprised 55% of the total cost of all cancer medicine items claimed in both study years whilst cancer medicine items claimed by male cancer patients comprised about 45%. This supports the statement made (see objective one, section 4.2.3.2, table 4.8, table 4.9) that cancer medicine items claimed by male cancer patients are relatively more expensive than those claimed by female cancer patients.

The top five cancer medicine items according to prevalence, total cost and average cost claimed by each gender were discussed in section 4.8.3. In female patients, the top five cancer medicine items claimed by female cancer patients were methotrexate, tamoxifen, cyproterone, anastrozole and cyclophosphamide. In males, the cancer medicine items claimed the most were methotrexate, bicalutamide, goserelin, imatinib and leuprolide (refer to table 4.63). The medicine items with the highest cost in female cancer patients were docetaxel, trastuzumab, anastrozole, gemcitabine and paclitaxel in 2005. In 2006, it was trastuzumab, docetaxel, rituximab, anastrozole and paclitaxel. The cost for cancer medicine items in males in 2005 was the highest for imatinib, bicalutamide, docetaxel, rituximab and goserelin. In 2006, it was imatinib, rituximab, bicalutamide, docetaxel and gemcitabine (refer to table 4.64).

- The **eight** specific aim was to determine and analyse the prevalence and total cost of selected regimen therapies prescribed for five common types of cancer in a section of the private health care sector of South Africa. (refer to section 4.7)

Selected first-line regimens for five common cancers (discussed in section 2.5) as suggested by Duminy (2007) were extracted from the medicine claims database for illustrative purposes only. The prevalence and total cost of these regimens were determined and discussed. According to the data obtained, the regimens for the

treatment of lung cancer had the highest frequency, followed by colorectal cancer, breast cancer, prostate cancer and then lymphoma. The cost of the medicine treatment regimens for colorectal cancer was the highest, followed by lung cancer, prostate cancer and breast cancer whilst lymphoma also had the lowest cost (in accordance with the low prevalence).

5.3 LIMITATIONS

Based on the results and discussion in chapter four, certain limitations were identified, which could restrict or limit the scope of this study:

- All the information concerning medicine usage and the cost of medicine usage obtained from the medicine claims database, that was utilised as a data source in this study, was considered to be accurate and correct (refer to section 3.9). The researcher was not involved in compiling the database or manipulating the data.
- No demographic or clinical data concerning the diagnosis of the study population were available on the database, therefore the relevance of some of the utilisation patterns could not be determined e.g. medicine items such as methotrexate and cyproterone.
- The number of newly diagnosed patients could not be determined because patient information was confidential.
- Treatment periods e.g. weekly, monthly as well as dosages of cancer medicine items were not included in the cost calculations of the data (refer to section 4.1.2).
- All cost aspects and implications of cancer treatment such as radiation, surgery, direct and indirect costs and other fees were not taken in account in this study.
- Treatment outcomes of cancer treatments could not be determined because this study was limited to the medicine usage and prescribing patterns of cancer medicine items (refer to section 4.1.2).
- Some of the cancer medicine items used in this study (i.e. methotrexate and cyproterone) are also used in the treatment of other diseases. The ICD10 diagnosis is not complete and therefore the prevalence and cost of these

cancer medicine items do not exclusively represent the usage of these medicine items in cancer treatment.

- The results of this study are only valid for the specific medicine claims database that was utilised for the purpose of this study. Therefore, it cannot be used as a true indication of the usage patterns of cancer medicine items nor will it reflect the true costs of cancer medicine items in the whole of South Africa.
- The criteria set for the classification of cancer medicine items according to original/generic/no-generic cancer medicine items were designed specifically for the purpose of this study and may thus differ from original/generic/no-generic classification systems currently available in the literature.
- The average cost per medicine item for specific trade names/active ingredients were calculated as it were prescribed without further analysis regarding the average number of capsules/tablets/vials prescribed (refer to section 4.2.1).

5.4 RECOMMENDATIONS

On completion of the research study the following recommendations can be made:

- A proper cancer surveillance infrastructure and a Cancer Control Programme should urgently be implemented in South Africa and cancer research should receive more attention and funding. A reliable information database regarding cancer prevalence, nature and extend of cancer treatments should form an important part of such a control programme. This is necessary to provide health policy workers and decision makers with the correct and scientific information to ensure cost effective cancer treatments.
- The indication of clinical data, e.g. stage of cancer, type of cancer, active or palliative treatment, of the study population should also be taken in consideration in future studies, and not only cost aspects.
- The development of a sustainable pharmacoeconomic model(s) to address the cost-effectiveness of specific cancer treatment(s) must be investigated.
- Quality of life and value of life aspects and perceptions of cancer patients during and after treatment should be investigated in more detail.

- The development and use of less expensive generic cancer medicine items should be investigated in future studies.
- Cost-of-illness, cost-benefit and cost minimisation studies on the treatment of cancer are strongly recommended.
- An in-depth investigation should be performed, using appropriate methods or instruments to determine cost-effective treatments, addressing the cost and prevalence of cancer medicine items used in the treatment of a specific cancer type such as lung cancer, breast cancer and colorectal cancer.
- High standard deviations encountered in this study indicates that, in future studies the number of tablets/capsules/vials/IVs prescribed, as well as treatment periods should be taken into consideration in cost analysis of cancer medicine items.
- Further research should be done regarding the role age plays in the cost of cancer medicine items (refer to section 4.5.3.1, 4.5.3.6, 4.5.3.7, 4.5.3.8).

5.5 SUMMARY

In this chapter the conclusions of the specific objectives were drawn and discussed. The limitations that were encountered during the course of the study, as well as the recommendations that were derived in completion of this study were discussed.

APPENDIX A: ATC CLASSIFICATION OF ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS

Therapeutic group		Pharmacological subgroup		Chemical subgroup		Active ingredient	
L01	Antineoplastic agents	L01A	Alkylating agents	L01AA	Nitrogen mustard analogues	L01AA01	Cyclophosphamide
						L01AA02	Chorambucil
						L01AA03	Melphalan
						L01AA05	Chlormethine
						L01AA06	Ifosfamide
						L01AA07	Trofosfamide
						L01AA08	Prednimustine
				L01AB	Alkyl sulfonates	L01AB01	Busulphan
						L01AB02	Treosulphan
						L01AB03	Mannosulphan
				L01AC	Ethylene imines	L01AC01	Thiotepa
						L01AC02	Triaziquone
						L01AC03	Carboquone
				L01AD	Nitrosoureas	L01AD01	Carmustine
						L01AD02	Lomustine
						L01AD03	Semustine
						L01AD04	Streptozocin
						L01AD05	Fotemustine
						L01AD06	Nimustine
						L01AD07	Ranimustine
				L01AG	Epoxides	L01AG01	Etoglucid
				L01AX	Other alkylating agents	L01AX01	Mitobronitol
						L01AX02	Pipobroman
						L01AX03	Temozolomide
						L01AX04	Dacarbazine
		L01B	Anti metabolites	L01BA	Folic acid analogues	L01BA01	Methotrexate
						L01BA03	Ralitrexed
						L01BA04	Pemetrexed
				L01BB	Purine analogues	L01BB02	Mercaptopurine
						L01BB03	Tioguanine
						L01BB04	Cladribine
						L01BB05	Fludarabine

Therapeutic group		Pharmacological subgroup		Chemical subgroup		Active ingredient	
				L01BC	Purimidine analogues	L01BC01	Cytarabine
						L01BC02	Fluorouracil
		L01B	Anti metabolites	L01BC	Purimidine analogues	L01BC03	Tegafur
						L01BC04	Carmofur
						L01BC05	Gemcitabine
						L01BC06	Capecitabine
						L01BC52	Fluorouracil, combinations
						L01BC53	Tegafur, combinations
		L01C	Plant alkaloids&other natural products	L01CA	Vinca alkaloids and analogues	L01CA01	Vinblastine
						L01CA02	Vincristine
						L01CA03	Vindesine
						L01CA04	Vinorelbine
				L01CB	Podophyllotoxin derivatives	L01CB01	Etoposide
						L01CB02	Teniposide
				L01CC	Colchicine derivatives	L01CC01	Demecolcine
				L01CD	Taxanes	L01CD01	Paclitaxel
						L01CD02	Docetaxel
				L01CX	Other plant alkaloids&natural products	L01CX01	Trabectedin
		L01D	Cytotoxic antibiotics & related substances	L01DA	Actinomycines	L01DA01	Dactinomycin
				L01DB	Anthracyclines&related substances	L01DB01	Doxorubicin
						L01DB02	Daunorubicin
						L01DB03	Epirubicin
						L01DB04	Aclarubicin
						L01DB05	Zorubicin
						L01DB06	Idarubicin
						L01DB07	Mitoxantrone
						L01DB08	Pirarubicin
						L01DB09	Valrubicin
				L01DC	Other cytotoxic antibiotics	L01DC01	Bleomycin
						L01DC02	Plicamycin
						L01DC03	Mitomycin
		L01X	Other antineoplastic agents	L01XA	Platinum compounds	L01XA01	Cisplatin
						L01XA02	Carboplatin
						L01XA03	Oxaliplatin
				L01XB	Methylhydrazines	L01XB01	Procarbazine

Appendix A

Therapeutic group		Pharmacological subgroup		Chemical subgroup		Active ingredient	
				L01XC	Monoclonal antibodies	L01XC01	Edrecolomab
						L01XC02	Rituximab
						L01XC03	Trastuzumab
		L01X	Other antineoplastic agents	L01XC	Monoclonal antibodies	L01XC04	Alemtuzumab
						L01XC05	Gemtuzumab
						L01XC06	Cetuximab
						L01XC07	Bevacizumab
				L01XD	Agents used in photodynamic therapy	L01XD01	Porfimer sodium
						L01XD02	Verteporfin
						L01XD03	Methyl aminolevulinate
						L01XD04	Aminolevulinic acid
						L01XD05	Temoporfin
				L01XX	Other antineoplastic agents	L01XX01	Amsacrine
						L01XX02	Asparaginase
						L01XX03	Altretamine
						L01XX05	Hydroxycarbamide
						L01XX07	Lonidamine
						L01XX08	Pentostatin
						L01XX09	Miltefosine
						L01XX10	Masoprocol
						L01XX11	Estramustine
						L01XX14	Tretinoin
						L01XX16	Mitoguazone
						L01XX17	Topotecan
						L01XX18	Tiazofurine
						L01XX19	Irinotecan
						L01XX22	Alitretinoin
						L01XX23	Mitotane
						L01XX24	Pegaspargase
						L01XX25	Bexarotene
						L01XX27	Arsenic trioxide
						L01XX29	Denileukin diftitox
						L01XX32	Bortezomib
						L01XX33	Celecoxib
						L01XX35	Anagrelide

Therapeutic group		Pharmacological subgroup		Chemical subgroup		Active ingredient	
		L01X	Other antineoplastic agents	L01XX	Other antineoplastic agents	L01XX36	Oblimersen
						L01XX37	Sitimagene ceradenovec
				L01XE	Protein kinase inhibitors	L01XE01	Imatinib
						L01XE03	Erlotinib
						L01XE04	Sunitinib
						L01XE05	Sorafenib
						L01XE06	Dasatinib
						L01XE07	Lapatinib
						L01XE08	Nilotinib
L02	Endocrine therapy	L02A	Hormones and related agents	L02AA	Estrogens	L02AA01	Diethylstilbestrol
						L02AA02	Polyestradiol phosphate
						L02AA03	Ethinylestradiol
						L02AA04	Fosfestrol
				L02AB	Progestogens	L02AB01	Megestrol
						L02AB02	Medroxyprogesterone
						L02AB03	Gestonorone
				L02AE	Gonadotropin releasing hormone analogues	L02AE01	Buserelin
						L02AE02	Leuprolin
						L02AE03	Goserelin
						L02AE04	Triptorelin
				L02AX	Other hormones	L02AX	
		L02B	Hormones antagonists&related agents	L02BA	Anti-estrogens	L02BA01	Tamoxifen
						L02BA02	Toremifene
						L02BA03	Fulvestrant
				L02BB	Anti-androgens	L02BB01	Flutamide
						L02BB02	Nilutamide
						L02BB03	Bicalutamide
				L02BG	Enzyme inhibitors	L02BG01	Aminogluthetimide
						L02BG02	Formestane
						L02BG03	Anastrozole
						L02BG04	Letrozole
						L02BG05	Vorozole
						L02BG06	Exemestane
				L02BX	Other hormone antagonists&related agents	L02BX01	Abarelix
L03	Immunostimulants	L03A	Immunostimulants	L03AA	Colony stimulating factors	L03AA02	Filgrastim

Therapeutic group		Pharmacological subgroup		Chemical subgroup		Active ingredient	
L03	Immunostimulants	L03A	Immunostimulants	L03AA	Colony stimulating factors	L03AA03	Molgramostim
						L03AA09	Sargramostim
						L03AA10	Lenograstim
						L03AA13	Pegfilgrastim
				L03AB	Interferons	L03AB01	Interferon alfa natural
						L03AB02	Interferon beta natural
						L03AB03	Interferon gamma
						L03AB04	Interferon alfa-2a
						L03AB05	Interferon alfa-2b
						L03AB06	Interferon alfa-n1
						L03AB07	Interferon beta-1a
						L03AB08	Interferon beta-1b
						L03AB09	Interferon alfacon-1
						L03AB10	Peginterferon alfa-2b
						L03AB11	Peginterferon alfa-2a
				L03AC	Interleukins	L03AC01	Aldesleukin
						L03AC02	Oprelvekin
				L03AX	Other cytokines&immunomodulators	L03AX01	Lentinan
						L03AX02	Roquinimex
						L03AX03	BCG vaccine
						L03AX04	Pegademase
						L03AX05	Pidotimod
						L03AX07	Poly I:C
						L03AX08	Poly ICLC
						L03AX09	Thymopentin
						L03AX10	Immunocyanin
						L03AX11	Tasonermin
						L03AX12	Melanoma vaccine
						L03AX13	Glatiramer acetate

APPENDIX B: PREVALENCE AND COST OF INDIVIDUAL CANCER MEDICINE TRADENAMES

Active Ingredient	ATO code	Generic Indication	Trade name	2005						2006					
				Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	CPI	Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	CPI
All-Trans Retinoic Acid (Tretinoin)	L01XX14	N	Vesanlod-Roc 10mg cap	3	0.00	2608.21 ± 66.04	7824.64	0.01	0.00	4	0.00	2891.47 ± 3137.61	11565.89	0.01	2.20
Bevacizumab	L01XC07	N	Avastin 100mg/4ml Inf.							83	0.10	6813.68 ± 3290.78	565535.06	0.52	5.17
	L01XC07	N	Avastin 100mg/4ml vial	96	0.13	5978.80 ± 2196.55	573964.71	0.76	0.09	64	0.08	4564.71 ± 2232.25	292141.49	0.27	3.47
	L01XC07	N	Avastin 400mg/16ml Inf							157	0.19	6130.75 ± 2214.41	962528.06	0.89	4.66
	L01XC07	N	Avastin 400mg/16ml vial	77	0.11	6584.18 ± 1461.97	506981.67	0.67	0.03	194	0.24	6652.37 ± 1138.32	1290559.01	1.19	5.05
Bleomycin	L01DC01	N	Blenoxane 15IU/Vial	4	0.01	653.46 ± 534.70	2613.84	0.00	0.00						
	L01DC01	O	Blenoxane 15IU/Vial	75	0.10	770.70 ± 595.53	57802.27	0.08	0.08	156	0.19	840.31 ± 596.40	131088.98	0.12	0.64
	L01DC01	Y	Blenamax 15 IU/Vial							3	0.00	549.48 ± 0	1648.44	0.00	0.42
	L01DC01	Y	Bleolem	28	0.04	695.15 ± 482.62	19464.26	0.03	0.03	29	0.04	1222.68 ± 867.01	35457.84	0.03	0.93
Busulphan	L01AB01	N	Myleran 2mg tab	14	0.02	214.80 ± 246.78	3007.20	0.00	0.00	5	0.01	116.94 ± 71.46	584.69	0.00	0.09
Capecitabine	L01BC06	N	Xeloda 150	334	0.46	463.90 ± 168.23	154941.08	0.20	0.20	293	0.36	484.73 ± 174.01	142026.84	0.13	0.37
	L01BC06	N	Xeloda 500	1005	1.40	3334.03 ± 939.66	3350699.37	4.42	0.24	1096	1.33	3174.09 ± 886.30	3478800.00	3.20	2.41
Carboplatin	L01XA02	N	Carbosin 150mg/15ml Inj.	235	0.33	565.56 ± 442.38	132906.26	0.18	0.18	120	0.15	530.03 ± 381.80	63604.05	0.06	0.40
	L01XA02	N	Carbosin 450mg/10ml Sol for Inj.	10	0.01	805.99 ± 223.94	8059.80	0.01	0.01						
	L01XA02	N	Carbosin 500mg/50ml Inj.	277	0.38	869.22 ± 239.85	240773.67	0.32	0.32	143	0.17	932.98 ± 287.42	133416.48	0.12	0.71
	L01XA02	O	Paraplatin RTU 150mg Inj.	84	0.12	1078.89 ± 626.59	90627.13	0.12	0.00	97	0.12	1007.14 ± 532.84	97693.06	0.09	0.76
	L01XA02	O	Paraplatin RTU 450mg Inj.	32	0.04	1177.76 ± 0	37688.32	0.05	0.01	69	0.08	1178.56 ± 6.64	81320.49	0.07	0.89
	L01XA02	Y	Abic Carboplatin 150	2	0.00	725.04 ± 0	1450.08	0.00	0.00						
	L01XA02	Y	Abic Carboplatin Sol 150	159	0.22	479.08 ± 289.16	76174.48	0.10	0.10	261	0.32	448.09 ± 288.31	116951.79	0.11	0.34
	L01XA02	Y	Abic Carboplatin Sol 450	215	0.30	763.10 ± 92.31	164065.63	0.22	0.22	428	0.52	776.75 ± 177.52	332450.77	0.31	0.59
	L01XA02	Y	Carbosin 450mg/10ml Sol for Inj.							7	0.01	725.04 ± 0	5075.28	0.00	0.55
	L01XA02	Y	P&U Carboplatin 150mg	43	0.06	607.87 ± 371.04	26138.44	0.03	0.03	166	0.20	442.24 ± 195.24	73412.51	0.07	0.34
	L01XA02	Y	P&U Carboplatin 450mg	75	0.10	755.81 ± 82.75	56686.11	0.07	0.07	246	0.30	839.95 ± 397.17	206628.01	0.19	0.64

Appendix B

Active Ingredient	ATC code	Generic Indication	Tradename	2005						2006					
				Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	CPI	Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	CPI
Carmustine	L01AD01	N	Bicnu 100mg Inj.	15	0.02	1042.29 ± 632.79	15634.36	0.02	0.02	12	0.01	1831.30 ± 1106.74	21975.54	0.02	1.39
Chlorambucil	L01AA02	N	Leukeran 2mg tab	296	0.41	501.48 ± 366.15	148437.53	0.20	0.20	301	0.36	414.83 ± 266.40	124864.02	0.11	0.32
Cisplatin	L01XA01	N	Cisplatin-Faulding 10ml vial	24	0.03	140.82 ± 41.75	3379.63	0.00	0.00						
	L01XA01	N	P&U Cisplatin 10mg/10ml	42	0.06	272.97 ± 129.45	11448.39	0.02	0.02						
	L01XA01	O	Abiplatin Pwd. 10mg Inj.	135	0.19	231.53 ± 239.52	31256.54	0.04	0.04	210	0.25	236.68 ± 215.35	49702.40	0.05	0.18
	L01XA01	O	Abiplatin Pwd. 50mg Inj.	293	0.41	413.11 ± 198.71	121042.03	0.16	0.16	328	0.40	468.21 ± 191.46	153574.38	0.14	0.36
	L01XA01	O	Abiplatin Sol. 10mg/20ml	1	0.00	14.32 ± 0	14.32	0.00	0.00						
	L01XA01	O	P&U Cisplatin 10mg/10ml	25	0.03	377.24 ± 308.84	9430.90	0.01	0.01	124	0.15	182.30 ± 121.81	22605.68	0.02	0.14
	L01XA01	O	P&U Cisplatin 50mg/50ml	182	0.25	277.26 ± 124.71	50460.93	0.07	0.07	229	0.28		69203.71	0.06	0.23
	L01XA01	Y	Cisplatin-Faulding 10ml vial	20	0.03	169.97 ± 38.41	3399.31	0.00	0.00	17	0.02	104.99 ± 69.62	1784.87	0.00	0.08
	L01XA01	Y	Cisplatin-Faulding 50ml vial	29	0.04	175.61 ± 113.07	5092.81	0.01	0.01	16	0.02	200.31 ± 137.86	3204.90	0.00	0.15
	L01XA01	Y	Platosin RTU 10-20 20ml	81	0.11	151.99 ± 182.09	12311.54	0.02	0.02	98	0.12	113.12 ± 110.80	11085.33	0.01	0.09
	L01XA01	Y	Platosin 50-100 100ml	119	0.17	411.9 ± 185.97	49016.06	0.06	0.06	171	0.21	397.28 ± 227.67	67934.60	0.06	0.30
Cyclophosphamide	L01AA01	N	Endoxan 50mg Tab	387	0.54	125.43 ± 65.05	48541.93	0.06	0.06						
	L01AA01	O	Endoxan 50mg Tab	188	0.26	138.47 ± 68.93	26031.65	0.03	0.03	576	0.70	141.77 ± 62.57	81661.47	0.08	0.11
	L01AA01	O	Endoxan 1000mg Inj.	1089	1.51	105.81 ± 44.95	115227.56	0.15	0.15	1384	1.68	108.51 ± 60.19	150178.89	0.14	0.08
	L01AA01	O	Endoxan 200mg Inj.	441	0.61	55.19 ± 41.39	24336.67	0.03	0.03	711	0.86	64.11 ± 41.27	45584.59	0.04	0.05
	L01AA01	O	Endoxan 500mg Inj.	194	0.27	93.12 ± 41.46	18065.89	0.02	0.02	403	0.49	91.57 ± 55.07	36902.83	0.03	0.07
Cytarabine	L01BC01	N	Cytarabine-Faulding 5ml Inj.	40	0.06	1790.21 ± 2154.97	71608.32	0.09	0.04	22	0.03	4099.99 ± 2953.11	90199.73	0.08	3.11
	L01BC01	N	Cytosar 100mg Inj.	24	0.03	263.15 ± 238.34	6315.70	0.01	0.01	35	0.04	380.45 ± 536.33	13315.92	0.01	0.29
	L01BC01	Y	Cytarabine-Faulding 5ml Inj.	2	0.00	236.17 ± 0	472.34	0.00	0.00	2	0.00	830.46 ± 261.35	1660.91	0.00	0.63
	L01BC01	Y	Cytosar 500mg 10ml Inj.	26	0.04	2237.3 ± 1895.31	58169.91	0.08	0.00	21	0.03	2892.43 ± 1617.88	60741.08	0.06	2.20
	L01BC01	Y	P&U Cytarabine CSV 25ml	2	0.00	8562.96 ± 1774.7	17125.92	0.02	0.00	8	0.01	1448.85 ± 625.22	11590.80	0.01	1.10
	L01BC01	Y	P&U Cytarabine CSV Inj. 5ml	7	0.01	142.17 ± 173.69	995.24	0.00	0.00	13	0.02	88.41 ± 98.52	1149.35	0.00	0.07
Dacarbazine	L01AX04	O	DTic-Dome 200mg Inj.	156	0.22	695.97 ± 312.18	108571.04	0.14	0.14	178	0.22	935.21 ± 391.95	166466.81	0.15	0.71

Appendix B

Active Ingredient	ATC code	Generic Indication	Tradename	2005						2006					
				Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	CPI	Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	CPI
Dactinomycin	L01DA01	N	Cosmegen 3ml 0.5mg Inj.	18	0.03	200.32±111.1	3605.72	0.00	0.00	11	0.01	267.99±109.04	2947.93	0.00	0.20
Daunorubicin	L01DB02	Y	Daunoblastin 20mg Inj.	1	0.00	1059.08±0	1059.08	0.00	0.00	7	0.01	3338.00±1102.94	23366.02	0.02	2.53
Docetaxel	L01CD02	N	Taxotere 20mg/1.5ml Inj.	826	1.15	4979.19±1626.04	4112813.30	5.43	4.73	849	1.03	4680.60±1514.10	3973833.21	3.66	3.55
	L01CD02	N	Taxotere 80mg Inj.	629	0.87	6013.66±1392.21	3782592.27	4.99	5.71	880	1.07	6028.42±1279.80	5305005.78	4.88	4.58
Doxorubicin	L01DB01	O	Adriblastina 10mg Inj							8	0.01	252.11±41.95	2016.87	0.00	0.19
	L01DB01	O	Adriblastina 50mg Inj.							11	0.01	421.80±138.99	4639.82	0.00	0.32
	L01DB01	O	Adriblastina CSV 10mg	26	0.04	320.55±69.3	8334.34	0.01	0.01	12	0.01	320.57±179.94	3846.78	0.00	0.24
	L01DB01	O	Adriblastina CSV 50mg	24	0.03	629.29±158.61	15102.84	0.02	0.02	11	0.01	658.37±102.90	7242.12	0.01	0.50
	L01DB01	O	Caelyx 20mg/10ml	317	0.44	4693.72±991.27	1487909.88	1.96	0.20	310	0.38	6881.05	2071126.39	1.91	5.07
	L01DB01	Y	Doxorubicin HCL Faulding pwd.	9	0.01	775.73±132.27	6981.58	0.01	0.01						
	L01DB01	Y	Doxorubicin PCH 10	38	0.05	256.27±99.53	9738.20	0.01	0.01	113	0.14	343.30±204.26	38793.18	0.04	0.26
	L01DB01	Y	Doxorubicin PCH 50	30	0.04	601.64±312.4	18049.08	0.02	0.02	148	0.18	815.33±332.07	120669.43	0.11	0.62
	L01DB01	Y	Doxorubicin RTU 10-5 5ml	200	0.28	290.23±129.53	58046.29	0.08	0.08	296	0.36	329.36±218.03	97491.01	0.09	0.25
	L01DB01	Y	Doxorubicin RTU 50-25 25ml	311	0.43	704.26±223.1	219024.60	0.29	0.29	457	0.55	752.80±246.43	344027.46	0.32	0.57
Epirubicin	L01DB03	N	Farvorubicin 10mg Inj.	197	0.27	400.95±137.25	78986.89	0.10	0.10	197	0.24	558.20±420.07	109966.00	0.10	0.42
	L01DB03	N	Farvorubicin 50mg Inj.	356	0.49	1571.8±526.72	559561.06	0.74	0.24	288	0.35	1421.65±437.28	409434.48	0.38	1.06
	L01DB03	N	Farvorubicin CSV 10mg/5ml	255	0.35	468.96±363.88	119585.60	0.16	0.16	255	0.31	472.76±238.98	120554.52	0.11	0.36
	L01DB03	N	Farvorubicin CSV 50mg/25ml	492	0.68	1386.4±459.5	682110.50	0.90	0.22	445	0.54	1450.37±506.08	645416.45	0.59	1.10
Estramustine Phosphate	L01XX11	N	Estracyl 140mg cap	75	0.10	775.93±635.4	58194.57	0.08	0.08	47	0.06	1459.59±1254.16	68600.73	0.06	1.11
Etoposide	L01CB01	N	Etopophos 100mg Inj.	2	0.00	4681.3±0	9362.60	0.01	0.00	3	0.00	2415.11±413.17	7245.32	0.01	1.83
	L01CB01	N	Vepesid 100mg cap	40	0.06	1582.78±846.92	63311.27	0.08	0.03	67	0.08	1986.13±909.96	133070.68	0.12	1.51
	L01CB01	N	Vepesid 50mg cap	58	0.08	1796.5±630.51	104196.81	0.14	0.06	61	0.07	1608.82±952.32	98137.83	0.09	1.22
	L01CB01	O	Vepesid 100mg Inj. 5ml	88	0.12	1152.48±706.59	101418.38	0.13	0.01	39	0.05	1908.36±688.33	74425.88	0.07	1.45
	L01CB01	Y	Eposin 100mg/5ml	95	0.13	658.66±453.29	62572.48	0.08	0.08	126	0.15	880.02±493.17	110882.42	0.10	0.67
	L01CB01	Y	Etoposide 100mg Inj.	1	0.00	4313.71±0	4313.71	0.01	0.00						
	L01CB01	Y	P&U Etoposide 100mg Inj.	103	0.14	979.54±477.83	100893.05	0.13	0.13	112	0.14	1064.09±515.45	119178.50	0.11	0.81

Appendix B

Active Ingredient	ATC code	Generic indication	Trade name	2005						2006					
				Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	GPI	Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	GPI
Fludarabine	L01BB05	Y	Fludara IV 50mg Inj.	118	0.16	4254.76±2229.96	502061.36	0.66	0.01	144	0.17	5098.71±2310.35	734214.75	0.68	3.87
Fluorouracil	L01BC02	O	Fluoroblastin 500mg/10ml	740	1.03	171.87±127.99	127185.80	0.17	0.17	515	0.62	166.15±129.94	85567.33	0.08	0.13
	L01BC02	Y	Abic Fluorouracil 500mg/10ml	919	1.28	118.46±93.72	108867.29	0.14	0.14	1294	1.57	163.92±115.31	212117.32	0.20	0.12
	L01BC02	Y	Abic Fluorouracil 50mg/ml	227	0.32	29.67±19.88	6734.82	0.01	0.01	378	0.46	36.98±26.28	13979.28	0.01	0.03
	L01BC02	Y	Fluorouracil-Faulding 10ml	5	0.01	50.52±0.31	252.60	0.00	0.00	6	0.01	103.85±33.28	623.11	0.00	0.08
	L01BC02	Y	Fluorouracil-Faulding 5ml	3	0.00	87.27±31.34	261.80	0.00	0.00	1	0.00	673.74±0	673.74	0.00	0.51
	L01BC02	N	Fluracetyl 5000mg/20ml Inj.							2	0.00	298.28±0	596.56	0.00	0.00
Gemcitabine	L01BC05	N	Gemzar 200mg Inj.	520	0.72	2649.09±1488.29	1377526.50	1.82	0.37	570	0.69	2907.12±1471.04	1657057.32	1.52	2.21
	L01BC05	N	Gemzar 1000mg Inj.	850	1.18	5209.82±1643.76	4428343.39	5.85	1.12	1075	1.30	5206.21±1477.94	5596680.67	5.15	3.95
Hydroxyurea	L01XX05	N	Hydrea 500mg cap	862	1.20	132.11±55.16	113876.91	0.15	0.15	960	1.16	135.64±57.45	130217.24	0.12	0.10
Ifosfamide	L01AA05	N	Holoxan 1000mg Inj.	33	0.05	968.77±673.43	31969.57	0.04	0.04	77	0.09	1757.25±1843.53	135308.04	0.12	1.33
	L01AA05	N	Holoxan 2000mg Inj.	67	0.09	2782.13±1868.04	186402.50	0.25	0.06	98	0.12	2376.60±1785.48	232906.84	0.21	1.80
	L01AA05	N	Holoxan 500mg Inj.	34	0.05	970.3±377.86	32990.25	0.04	0.04	44	0.05	935.67±334.96	41169.44	0.04	0.71
Imatinib	L01XE01	N	Gleevec 100mg cap	1051	1.46	6676.04±1495.82	7016518.26	9.26	0.50	320	0.39	6512.94±1354.92	2084140.40	1.92	4.95
	L01XE01	N	Gleevec 100mg Tab							163	0.20	5265.99±1123.22	858355.59	0.79	4.00
	L01XE01	N	Gleevec 400mg Tab.							988	1.20	6862.11±1486.14	6779762.10	6.24	5.21
Irinotecan	L01XX19	N	Campto 2ml 20mg/ml Inj.	281	0.39	2222.87±1784.74	624625.28	0.82	0.04	254	0.31	2192.36±1582.67	556859.54	0.51	1.66
	L01XX19	N	Campto 5ml 20mg/ml Inj.	474	0.66	5458.8±1657.45	2587469.78	3.42	0.12	495	0.60	5658.37±2117.52	2800891.64	2.58	4.30
L-asparaginase (asparaginase/amidohydrolase)	L01XX02	N	Laspar Inj.	4	0.01	3427.39±1788.28	13709.55	0.02	0.00	3	0.00	4321.54±2477.93	12964.61	0.01	3.28
Melfalan	L01AA03	N	Alkeran 2mg Tab.	175	0.24	376.56±126.26	65897.86	0.09	0.09	171	0.21	355.38±136.27	60770.72	0.06	0.27
	L01AA03	N	Alkeran 50mg Inj.	11	0.02	3413.35±340.71	37546.80	0.05	0.00	7	0.01	3215.84±628.86	22510.87	0.02	2.44
Mercaptopurine	L01BB02	N	Puri-Nethol 50mg tab	153	0.21	41.36±75.22	157484.38	0.21	0.21	186	0.23	1068.91±556.93	198817.69	0.18	0.81
Methotrexate	L01BA01	N	Abitrexate 1000mg/10ml	8	0.01	672.6±268.52	5380.74	0.01	0.01	15	0.02	425.45±0	6381.75	0.01	0.32
	L01BA01	N	Abitrexate 5g/50ml	10	0.01	4433.22±1849.26	44332.20	0.06	0.00	16	0.02	1884.81±495.50	30156.88	0.03	1.43
	L01BA01	O	Methotrexate 2.5mg Tab	23856	33.15	31.36±14.31	748132.75	0.99	0.99	26697	32.35	31.54±14.06	841923.49	0.77	0.02
	L01BA01	Y	Abitrexate 500mg/20ml							19	0.02	278.62±0	5293.78	0.00	0.21
	L01BA01	Y	Abitrexate 50mg/2ml	103	0.14	109.9±56.39	11319.90	0.01	0.01	114	0.14	150.49±84.25	17155.72	0.02	0.11

Appendix B

Active Ingredient	ATC code	Generic Indication	Trade name	2005						2006					
				Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	CPI	Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	CPI
Methotrexate (continued)	L01BA01	Y	Emthexate RTU 50-2 2ml Inj.	287	0.40	58.66±33.02	16834.45	0.02	0.02	432	0.52	64.66±30.09	27934.36	0.03	0.05
	L01BA01	Y	Emthexate RTU 500-20 20ml	18	0.03	620.81±198.39	11174.51	0.01	0.01	21	0.03	343.16±184.44	7206.43	0.01	0.26
	L01BA01	Y	P&U Methotrexate 500mg	2	0.00	4182.03±0	8364.06	0.01	0.00	1	0.00	336.22±0	336.22	0.00	0.26
	L01BA01	Y	P&U Methotrexate 50mg/2ml	169	0.23	107.67±51.81	18195.46	0.02	0.02	258	0.31	115.99±53.01	29924.70	0.03	0.09
Mitomycin	L01DC03	N	Mitomycin-C 10mg Inj.	51	0.07	904.17±1238.53	46112.84	0.06	0.06	74	0.09	864.43±860.68	63967.85	0.06	0.66
	L01DC03	N	Mitomycin-C 2mg Inj.	56	0.08	243.03±117.2	13609.59	0.02	0.02	61	0.07	253.09±101.28	15438.42	0.01	0.19
Mitoxantrone	L01DB07	N	Novantrone 10mg/5ml Inj.	22	0.03	1253.15±108.97	27589.28	0.04	0.01	11	0.01	1305.09±9.48	14355.95	0.01	0.99
	L01DB07	N	Novantrone 20mg/10ml Inj.	87	0.12	2136.72±301.9	185894.22	0.25	0.00	111	0.13	2187.84±387.12	242850.45	0.22	1.66
Oxaliplatin	L01XA03	N	Eloxatin (Sect 21) 100mg/20ml							182	0.22	6097.25±2112.90	1109700.00	1.02	4.63
	L01XA03	N	Eloxatin (sect 21) 50mg/10ml							98	0.12	2545.22±889.32	249431.95	0.23	1.93
	L01XA03	N	Eloxatin 100mg IV	169	0.23	5677.28±2102.7	959460.57	1.27	0.09	286	0.35	6405.73±1946.03	1832038.57	1.69	4.86
	L01XA03	N	Eloxatin 100mg/200ml Inf.							71	0.09	6188.21±1965.92	439363.22	0.40	4.70
	L01XA03	N	Eloxatin 50mg IV	80	0.11	2471±826.37	197680.21	0.26	0.04	109	0.13	2698.70±943.26	294158.70	0.27	2.05
	L01XA03	N	Eloxatin 50mg/ml Inf.							27	0.03	2597.23±925.07	70125.12	0.06	1.97
Paclitaxel	L01CD01	O	Taxol 100mg/vial Inj.	525	0.73	5308.89±2055.55	2787165.62	3.68	0.03	364	0.44	7066.53±2267.54	2572215.53	2.37	5.37
	L01CD01	O	Taxol 30mg/5ml Inj.	259	0.36	2236.48±1248.62	579248.97	0.76	0.05	244	0.30	2986.04±1733.33	728593.29	0.67	2.27
	L01CD01	Y	Anzatax 150mg/25ml	21	0.03	5315.36±2154.88	111622.57	0.15	0.00	72	0.09	5730.13±1627.85	412569.27	0.38	4.35
	L01CD01	Y	Anzatax 30mg/5ml	5	0.01	1962.71±1324.19	9813.54	0.01	0.01	44	0.05	1280.28±744.87	56332.51	0.05	0.97
	L01CD01	Y	Biolyse Paclitaxel for Injection 5ml	14	0.02	5750.44±1452.54	80506.21	0.11	0.01	43	0.05	5818.21±2829.87	250183.00	0.23	4.42
	L01CD01	O	Taxol 300mg/50ml	23	0.03	5553.65±1631.13	127733.85	0.17	0.01	81	0.10	8746.48±1607.57	708465.02	0.65	6.64
	L01CD01	Y	Teva-Paclitaxel 100mg/16.7ml	20	0.03	3439.2±1711.2	68783.97	0.09	0.01	62	0.08	4437.36±1366.11	275116.38	0.25	3.37
	L01CD01	Y	Teva-Paclitaxel 300mg/50ml	18	0.03	4572.51±2021.37	82305.18	0.11	0.01	76	0.09	4786.89±1352.21	363803.55	0.33	3.64
	L01CD01	Y	Teva-Paclitaxel 30mg/5ml	20	0.03	1314.97±475.76	26299.41	0.03	0.01	62	0.08	1892.93±1440.48	117361.93	0.11	1.44
Rituximab	L01XC02	N	Mabithera 100mg vial	407	0.57	5072.99±1576.61	2064707.17	2.73	0.46	668	0.81	553.84±1960.39	3709962.66	3.41	4.22
	L01XC02	N	Mabithera 500mg vial	649	0.90	5582.51±2713.76	3623047.29	4.78	0.28	1188	1.44	6646.53±1983.34	7896082.68	7.27	5.05

Appendix B

Active Ingredient	ATC code	Generic Indication	Trade Name	2005						2006					
				Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	GPI	Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	GPI
Temozolomide	L01AX03	N	Temodal 100mg	297	0.41	5110.51±2042.17	1517822.83	2.00	0.35	568	0.69	6259.02±2215.20	3555125.11	3.27	4.75
	L01AX03	N	Temodal 20mg	76	0.11	2720.55±2272.19	206762.07	0.27	0.06	214	0.26	2358.06±1978.73	504624.16	0.46	1.79
	L01AX03	N	Temodal 5mg	16	0.02	1685.4±2215.21	26966.32	0.04	0.01	32	0.04	1462.17±1802.50	46789.51	0.04	1.11
Thioguanine	L01BB03	N	Larvis 40mg tab	11	0.02	2605.26±1839.29	28657.87	0.04	0.01	24	0.03	1196.91±585.44	26725.81	0.03	0.91
Topotecan	L01XX17	N	Hycamtin Inf. 5ml	33	0.05	5205.8±2169.88	171791.25	0.23	0.04	40	0.05	4620.53±2156.78	184821.38	0.17	3.51
Trastuzumab	L01XC03	N	Herceptin	629	0.87	6787.62±1686.08	4269416.08	5.64	0.39	1609	1.95	7063.74±2313.89	11365564.90	10.46	5.36
Vinblastine	L01CA01	O	Vinblastine RTU 10-10ml	120	0.17	393.49±243.49	47218.66	0.06	0.06	162	0.20	408.29±190.44	66143.56	0.06	0.31
	L01CA01	Y	Vinblastine-Faulding 1mg/ml Inj.	2	0.00	1016.99±0	2033.98	0.00	0.00						
Vincristine	L01CA02	O	Oncovin 1mg/ml Sol.	39	0.05	314.39±67.76	12261.28	0.02	0.02	5	0.01	296.66±34.94	1483.32	0.00	0.23
	L01CA02	Y	Abic Vincristine 1mg/ml Inj.	28	0.04	90.41±4.54	2531.56	0.00	0.00	70	0.08	246.35±165.39	17244.47	0.02	0.19
	L01CA02	Y	Abic Vincristine 2mg/2ml Inj.	156	0.22	198.93±66.58	31033.85	0.04	0.04	414	0.50	187.86±33.78	77773.78	0.07	0.14
	L01CA02	Y	P&U Vincristine 1mg	14	0.02	243.5±79.82	3408.94	0.00	0.00	33	0.04	177.21±75.34	5848.02	0.01	0.13
	L01CA02	Y	P&U Vincristine 2mg	160	0.22	130.2±54.77	20832.55	0.03	0.03	217	0.26	120.76±7.46	26204.79	0.02	0.09
	L01CA02	Y	Vincristine PFI 1mg	3	0.00	125.07±47.68	375.20	0.00	0.00						
	L01CA02	Y	Vincristine PFI 2mg	1	0.00	129.96±0	129.96	0.00	0.00						
Vindesine	L01CA03	N	Eldisine 5mg/vial	24	0.03	2190.71±112.77	52577.14	0.07	0.00						
Vinorelbine	L01CA04	N	Navelbine 10mg Inj.	171	0.24	2028.6±1256.87	346890.05	0.46	0.22	162	0.20	2960.69±1426.04	479631.27	0.44	2.25
	L01CA04	N	Navelbine 20mg Cap	91	0.13	2393.06±1699.08	217768.49	0.29	0.03	104	0.13	2234.16±1423.55	232352.91	0.21	1.70
	L01CA04	N	Navelbine 30mg Cap	194	0.27	4818.26±1767.83	934743.31	1.23	0.16	156	0.19	4096.85±2269.08	639109.29	0.59	3.11
	L01CA04	N	Navelbine 50mg Inj.	286	0.40	3781.49±1215.21	1081505.62	1.43	0.24	350	0.42	3893.06±1261.92	1362571.81	1.25	2.96
Anastrozole	L02BG03	N	Arimidex 1mg Tab	2724	3.78	1232.03±178.45	3356062.09	4.43	1.17	4015	4.87	1221.41±146.69	4903970.7	4.51	0.93
Bicalutamide	L02BB03	N	Casodex 50mg Tab.	1376	1.91	1551.58±290.22	2134970.55	2.82	1.47	1291	1.56	1554.35±312.44	2006662.43	1.85	1.18
	L02BB03	N	Casodex 150mg Tab.	668	0.93	3324.31±245.04	2220641.41	2.93	3.16	908	1.10	3300.21±419.22	2996594.55	2.76	2.51
Buserelin	L02AE01	N	Suprefact 3 Month Depot	222	0.31	2908.43±387.10	645671.98	0.85	2.76	396	0.48	2907.29±413.90	1151285.11	1.06	2.21

Appendix B

Active ingredient	ATC code	Generic Indication	Trade name	2005						2006					
				Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	CPI	Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	CPI
Cyproterone	G03HA01	N	Androcure 100mg Tab	189		1419.21±695.08	268230.02			184		992.38±691.23	183598.60		
	G03HA01	N	Androcure 10mg Tab.	2683	0.26	246.7±65.47	661902.06	0.35	1.35	2630	0.22	243.33±75.26	639953.05	0.17	0.76
	G03HA01	N	Androcure Depot 1000mg/ml Inj.	75	3.73	269.67±128.27	20225.55	0.87	0.23	76	3.19	220.53±106.11	16760.65	0.59	0.18
	G03HA01	O	Androcure 50mg Tab.	613	0.10	339.54±255.96	208135.6	0.03	0.26	593	0.09	339.28±280.52	201193.29	0.02	0.17
	G03HA01	O	Androcure 50mg Tab.	613	0.85	339.54±255.96	208135.6	0.27	0.32	593	0.72	339.28±280.52	201193.29	0.19	0.26
	G03HA01	Y	Cipla Cyproterone acetate	1675	2.33	184.39±154.14	308849.15	0.41	0.18	1490	1.81	199.02±154.40	296537.12	0.27	0.15
Exemestane	L02BG06	N	Aromasin 25mg	424		1415.14±166.06	600020.66			477		1435.96±212.10	684955.15		
	L02BG06	N	Aromasin 25mg	424	0.59	1415.14±166.06	600020.66	0.79	1.34	477	0.58	1435.96±212.10	684955.15	0.63	1.09
	L02BB01	O	Eulexin 250mg Tab	205	0.28	909.75±339.75	186497.78	0.25	0.86	141	0.17	879.40±346.73	123995.26	0.11	0.67
	L02BB01	Y	Flutahexal 250mg	90	0.13	589.03±207.03	53012.98	0.07	0.56	138	0.17	590.75±188.04	81523.41	0.08	0.45
	L02BB01	Y	Flutaplex 250	29	0.04	742.41±16.41	21529.93	0.03	0.71	16	0.02	676.78±159.36	10828.54	0.01	0.51
	L02AE03	N	Zoladex-Depot 10.8mg Inj.	943	1.31	3043.84±235.36	2870343.62	3.79	2.89	1029	1.25	3029.53±92.42	3117388.14	2.87	2.30
Leuprolide	L02AE03	N	Zoladex-Depot 3.6mg Inj.	263	0.37	1206.79±113.58	317386.12	0.42	1.15	263	0.32	1215.22±59.87	319602.78	0.29	0.92
	L02AE02	N	Lucrin 2.8ml 5mg/ml	30	0.04	701.05±216.34	21031.53	0.03	0.67	30	0.04	758.50±238.79	22755.10	0.02	0.58
	L02AE02	N	Lucrin Depot 11.25 Inj.	421	0.58	3221.91±175.78	1356424.79	1.79	3.06	424	0.51	3208.89±65.76	1360567.41	1.25	2.44
	L02AE02	N	Lucrin Depot 3.75mg Inj.	189	0.26	1325.99±292.69	250612.07	0.33	1.26	193	0.23	1309.77±180.64	252785.70	0.23	0.99
	L02AB02	O	Provera 100mg Tab	99	0.14	490.9±299.88	48599.13	0.06	0.47	106	0.13	535.73±282.34	56787.56	0.05	0.41
	L02AB02	O	Provera 500mg							31	0.04	669.18±385.47	20744.58	0.02	0.51
Medroxypro-gesterone	L02AB02	Y	Provera 500mg	30	0.04	460.52±70.96	13815.6	0.02	0.44	19	0.02	453.97±158.51	8625.48	0.01	0.34
	L02BA01	O	Nolvadex 10 mg Tab.	2	0.00	197.29±79.03	394.58	0.00	0.19						
	L02BA01	O	Nolvadex D 20 mg Tab.	369	0.51	345.91±52.44	127641.75	0.17	0.33	299	0.36	346.78±54.91	103688.07	0.10	0.26
	L02BA01	Y	Kessar 10mg Tab.	250	0.35	98.11±34.38	24527.37	0.03	0.09	264	0.32	107.64±38.54	28417.69	0.03	0.08
	L02BA01	Y	Kessar 20mg Tab.	5148	7.15	119.01±12.90	612677.12	0.81	0.11	4634	5.62	117.64±13.96	545158.74	0.50	0.09
	L02BA01	Y	Neophedan 10mg Tab.	575	0.80	142.47±41.11	81921.74	0.11	0.14	472	0.57	140.61±41.49	66367.02	0.06	0.11
Tamoxifen	L02BA01	Y	Neophedan 20mg Tab.	5535	7.69	148.09±18.53	819660.39	1.08	0.14	5080	6.16	147.68±19.33	750227.29	0.69	0.11

Appendix B

Active ingredient	ATC code	Generic Indication	Trade name	2005						2006					
				Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	CPI	Prev. (N)	Prev. %	Average cost (R)	Total cost (R)	Cost %	CPI
Aldesleukin	L03AC01	N	Chiron IL-2 vial	113	0.16	5426.49±1509.36	613193.92	0.81	5.2	187	0.23	6085.37±732.01	1137963.67	1.05	4.62
Interferon Alfa 2A	L03AB04	N	Roferon A 0.6ml penfill	26	0.04	4640.55±1647.72	120654.36	0.16	4.4	55	0.07	5642.30±1411.39	310326.34	0.29	4.28
	L03AB04	N	Roferon A prefill 3000000	32	0.04	1863.41±558.82	59629.17	0.08	1.8	42	0.05	1971.33±470.07	82795.91	0.08	1.50
	L03AB04	N	Roferon A prefill 4500000	25	0.03	2593.2±646.98	64829.99	0.09	2.5	37	0.04	2788.71±961.32	103182.20	0.09	2.12
	L03AB04	N	Roferon A prefill 6000000	40	0.06	3640.34±569.02	145613.59	0.19	3.5	18	0.02	462.25±3575.28	65832.08	0.06	2.78
	L03AB04	N	Roferon A prefill 9000000	38	0.05	3193.03±2430.55	121335.28	0.16	3	10	0.01	5278.43±0.019	52784.34	0.05	4.01
Interferon Alfa 2B	L03AB05	N	Intron A 10 000 000 Inj.	9	0.01	2683.59±1303.49	24152.31	0.03	2.6	30	0.04	4502.37±2471.47	135071.02	0.12	3.42
	L03AB05	N	Intron A 5 000 000 Inj.	45	0.06	138.67±6.25	6240.01	0.01	0.1	36	0.04	86.64±94.56	3119.14	0.00	0.07
	L03AB05	N	Intron A HSA-free 10ml	6	0.01	5724.6±1604.11	34347.58	0.05	5.4						
	L03AB05	N	Intron A HSA-free redipen m/do	245	0.34	3767.81±2502.47	923114.09	1.22	3.6	113	0.14	4512.23±2654.99	509881.73	0.47	3.43

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