The Potential for Cost Savings by extensively using Generics for Chronic Conditions in South Africa

by

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DECLARATION

The analyses in this thesis were conducted under the direct supervision of Ms Gill Manion and Mr Andy Gray at the University of KwaZulu-Natal, Durban, during 2006. No work represented in this dissertation has been submitted to any other tertiary institution, either in part or full. The opinions and views expressed in this dissertation are those of the author, and do not necessarily reflect those of the University of KwaZulu-Natal.

E. Nicolosi

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DEDICATION

I dedicate this work to my family, who have always encouraged me to better myself. I thank my husband Alessandro and my sons, Gianluigi and Nicola, for their support, encouragement and understanding. I would also like to thank my mother, Evelyn Thom, for her belief in me, and the conviction that success is always attainable, regardless of how daunting the prospect may initially appear to be.

ABSTRACT

Economic factors are a major constraint to quality health care in Africa. One of the aims of the Department of Health in South Africa is to increase availability and affordability of medicine. One way of reducing the cost of drugs is by introducing legislation to control the price of drugs and by the promotion of generics (interchangeable multisource medicines which are cheaper copies of the original brand name drug). Protocols for the Prescribed Minimum Benefits (PMBs) for the 27 conditions on the Chronic Disease List as published in the Government Gazette in 2003, were legally binding from 1 January 2004 and these conditions must be covered by all medical schemes. Medication prescribed for these conditions may have one or more generic substitutes and Government has allowed certain measures to be introduced by the medical schemes in order to contain costs. This study investigates the potential savings if generics are extensively used for these chronic conditions.

A census was conducted on the 25 chronic diseases for which algorithms are available. The empirical quantitative data collected was calculated to quantify potential costs savings in respect of each algorithm.

The major findings show that there are large cost differentials between originator drugs and their generic equivalents (97% in the case of prednisone) and smaller cost differentials between generics themselves (54.6% in the case of formoterol). This study also shows that there is a correlation between the number of generic equivalents an originator drug has and the percentage cost differential. A total of 67.5% of all cost differentials between originator and generics are greater than the Department of Health's proposed 40% benchmark pricing. The results support the recommendations that government needs to implement various measures to encourage increased use of generics in this country and to look at realistic benchmark price controls.

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ABBREVIATIONS

ACE	Angiotensin-Converting Enzyme
BIO	Biotechnology Industry Organisation
CDL	Chronic Disease List
CMS	Council of Medical Schemes
DDD	Defined Daily Dose
DMARD	Disease Modifying Anti-Rheumatic Drug
EDL	Essential Drug List
FDA	Food and Drug Agency
GEMS	Government Employees Medical Scheme
GP	General Practitioners
GSK	GlaxoSmithKline
LIMS	Low Income Medical Scheme
MCC	Medicines Control Council
MIMS	Monthly Index of Medical Specialties
NDP	National Drug Policy
NHIS	National Health Insurance Scheme
NSAID	Non-Steroidal Anti-Inflammatory Drug
PMB	Prescribed Minimum Benefit
R&D	Research and Design
SAMF	South African Medicines Formulary
SEP	Single Exit Price
SEPV	Single Exit Price inclusive VAT
SHI	Social Health Insurance
STG	Standard Treatment Guideline
WHO	World Health Organisation

CHAPTER 1 : INTRODUCTION

1.1 Introduction

Medicines make up an important part of the costs of any health system. Medicines account for about 10% of recurrent costs in the South African public sector, second only to personnel costs (Council for Medical Schemes, 2005). In the South African private sector, the higher percentage of costs attributable to medicines – variably estimated at 30-40% - has in the past attracted the attention of regulators and legislators. Together with private hospitals and medical specialists, medicines have in the past been responsible for more than 75% of all medical scheme payments (Council for Medical Schemes, 2005).

In 2005, numbers of principal members and beneficiaries belonging to a medical scheme increased by 3.5% and 2.6% respectively from 2004. A total of R45,8 billion was paid out in claims by registered medical schemes in South Africa in 2005 (Council for Medical Schemes, 2005). This included hospital services, visits to medical / dental specialists, general practitioners, medicines dispensed and visits to supplementary and allied health professionals. Although there was a significant decline in expenditure (down 8.8% from 2004) in the value of medicines dispensed by pharmacists and providers other than hospitals, R7.2 billion (15.7% of the total benefits) were paid out by medical schemes. However, benefits paid to medical specialists, general practitioners and dental specialists increased by an average of 17% (Council for Medical Schemes, 2005). Medical schemes encourage their members to manage their own health care benefits more closely, not only for the members to achieve optimal use but for the medical schemes to remain sustainable. One of the ways members may achieve this is by substituting generics (interchangeable multisource medicines which are cheaper copies of the original brand name drug) for brand name drugs, where possible.

1.2 Background

Medicines are not regarded as ordinary articles of trade, but are instead subject to a variety of regulatory systems and interventions by government. This section

covers the basic controls over medicines in the South African setting and also deals with the policy developments in relation to the use of generic medicines. The promotion of generics by the South African Government is seen as a welcome and vital step to reducing health care costs in South Africa. The promotion of generics has long been supported by the World Health Organisation (WHO) and intervention by the South African Government has seen an overhaul of the system in recent times (World Health Organisation, 2004).

The Medicines Control Council (MCC) of South Africa was established in 1965 as a statutory body in terms of the Medicines and Related Substances Control Act (1965) (Medicines and Related Substances Act, 1965). Through its main function of overseeing the regulation of medicines, more than 20 000 medicines have been approved, applications for more than 11 800 complementary medicines have been submitted for evaluation and 280 clinical trials have been approved annually (Medicines Control Council, 2006). The prescribing and dispensing of medicines is controlled through the determination of schedules for various medicines and substances. The MCC operates through non-governmental external experts who are members of the Council's Committee structures. Dossiers, submitted by the pharmaceutical industry for purposes of registration, are evaluated by the experts who are mainly from academic institutions e.g. medical and pharmacy schools.

The Department of Health aims to promote the health of all people in South Africa and one of Government's aims is to increase availability of medicine. Government's broad policy in this regard was spelled out in the 1996 National Drug Policy (NDP) (Department of Health, 1996). Although Cabinet approved at the time, the NDP was also given additional formal status by being included as an appendix to the White Paper on the Transformation of the Health System in South Africa, issued in 1997.

The NDP outlines three sets of objectives:

- Health objectives
- Economic objectives and
- National development objectives.

There are specific broad aims for each:

- Health objectives
    - to ensure the availability and accessibility of essential drugs to all citizens
    - to ensure the safety, efficacy and quality of drugs
    - to ensure good dispensing and prescribing practices
    - to promote the rational use of drugs by prescribers, dispensers and patients through provision of the necessary training, education and information
    - to promote the concept of individual responsibility for health, preventive care and informed decision making.

- Economic objectives
    - to lower the cost of drugs in both the private and public sectors
    - to promote the cost-effective and rational use of drugs
    - to establish a complementary partnership between Government bodies and private providers in the pharmaceutical sector
    - to optimize the use of scarce resources through cooperation with international and regional agencies

- National development objectives
    - to improve the knowledge, efficiency and management skills of pharmaceutical personnel
    - to re-orientate medical, paramedical and pharmaceutical education towards the principles underlying the National Drug Policy
    - to support the development of the local pharmaceutical industry and the local production of essential drugs
    - to promote the acquisition, documentation and sharing of knowledge and experience through the establishment of advisory groups in rational drug use, pharmacoeconomics and other areas of the pharmaceutical sector.

    (Department of Health, 1996).

A number of these objectives deal with access to affordable medicines, strengthening medicines selection process, greater use of economic techniques and data and reorientation of professional attitudes. They also include potentially conflicting provisions, such as the aim to not only reduce medicine prices but also to stimulate the local industry. In a sense, they also represent the realization that economic factors are a major constraint to access of quality health in South Africa, as in the rest of Africa. It has been noted, for example, that 65% of drug expenditure in sub-Saharan Africa is 'out of pocket' expenses (Gray and Matsebula, 2000). 'Out of pocket' expenses refer to the actual expenses made by patients themselves as opposed to the health system. One way of reducing the cost of drugs is by introducing legislation to control the price of drugs. When an Essential Drug List (EDL) is compiled, cost is a factor which is taken into consideration when determining the inclusion or exclusion of a drug (Gray and Matsebula, 2000).

Under a less regulated policy environment before 1994, the minimum benefits provided by medical schemes in South Africa were gradually whittled away. This was largely reversed with the passage of the Medical Schemes Act (1998), which offered greater protection for consumers (Department of Health, 1998B). The Act provided for the definition of Prescribed Minimum Benefits (PMB), which stipulate a package of services or care a medical scheme must provide for in its benefit design. A very important result of the Act was that medical schemes were not able to discriminate on the basis of age, medical history and health status. A patient could not be held to a 'waiting period' when joining a medical scheme, if s/he had been a member of a medical scheme for the previous two years. Contributions could only be determined on the basis of income and number of dependents. This has resulted in more affordable options available to members of medical schemes. Following the same principle, the PMB package was extended with the introduction of a Chronic Disease List (CDL). Not only were the conditions listed, but Professor Jan van der Merwe (from the University of Pretoria and a member of the Council for Medical Schemes) was asked by the Department of Health to draft protocols for the 25 original conditions on this list (SASP, 2004). The Council for Medical Schemes is a statutory body, established by the Act to provide supervision over medical schemes. The final algorithms for the 25 conditions on the CDL were

published in the Government Gazette at the beginning of August 2003 and were legally binding from 1 January 2004. Since that time Government has increased the number of chronic conditions to 27, including HIV/Aids and Bipolar Mood Disorder. However no algorithms have been drawn up for these latest two conditions. In terms of HIV/AIDS, the injunction is that a medical scheme should provide at least those services and treatments that are provided by the State (Department of Health, 1998B).

Under the Medical Schemes Act (1998) the current 27 chronic conditions must be covered by medical schemes. Medical Schemes have to provide benefits for the treatment and medicines and pay for the full management of the 27 conditions with no co-payments. Medication prescribed for the 27 chronic conditions may have a generic substitute and in many conditions more than one substitute may be available. By making these benefits mandatory, the government hopes to curtail attempts by schemes to rate members on the financial risk they pose to the scheme because of the state of their health. Medical Schemes had previously made chronic benefits available only on options with higher contribution levels. In this way, people with chronic conditions were effectively being risk-rated and forced to pay higher amounts for their cover.

In order to contain the costs incurred by providing PMBs for the chronic conditions and to ensure that schemes can financially cover their members who need this benefit, the Regulations to the Medical Schemes Act (1998) have allowed certain measures to be introduced by the medical schemes. One of these measures is that the medical scheme may draw up a list of safe and effective medicines prescribed to treat certain conditions, known as a formulary. The scheme may state in its rules that it will only cover the member if a doctor prescribes a medicine on their formulary. Many of these medicines are generics and if a brand name medicine is prescribed and dispensed, the scheme has the right to refuse to either cover it completely or will only pay the equivalent of the generic up to a fixed monthly medicine limit (Department of Health, 1998B).

The Government is also looking at creating a medical scheme for low income earners, who at present are excluded from private medical aids due to the high

premiums. A Government Employees Medical Scheme (GEMS) was introduced in January 2006 for public service employees. There are also calls for a National Health Insurance System, or at least a Social Health Insurance option, which will include all employed South Africans. The next phase of policy development will see schemes required to develop a minimum package of services that will be made available to all members. The Minister intends to table an Amendment Bill to this effect in early 2007 (National Health Act, 2004).

1.3 Motivation for the Research

As everyone is affected by the high cost of medicines, this is an area of wide interest to researchers. The ways in which the government has intervened in the health sector are the subject of considerable media and public interest. During the past few years there has been a lot of publicity with regard to medical schemes, and in particular how they can remain viable while providing cover for the wider population, whilst complying with the requirements of the Medical Schemes Act (1998). One way they can do this is by reducing the costs of medicines claimed. Whilst the current formularies set out by medical schemes encourage the use of generics, their use is not universal, nor do they have the weight of law, as do the PMB treatment algorithms. It is envisioned this study will determine whether there is the potential for cost saving if the use of such products is maximized and if so to what extent. This could provide the motivation for more explicit legal and policy interventions in this area.

1.4 Value of the Project

The potential for cost savings, in the South African context, that could be achieved in relation to the Council for Medical Schemes' 27 chronic conditions has not been studied. Although it is understood that a cost differential between originator and generic drugs exists, it is hoped that this study will quantify the scale of cost differentials with specific reference to those drugs used in chronic diseases listed by the Council for Medical Schemes. Not only is there a benefit in prescribing a generic over a brand name but, with an increase in knowledge of the different generics available, there will be a saving depending on which generic is

prescribed. Recommendations will be made to implement these findings for the benefit of the patient and medical schemes.

1.5 Problem Statement

In general, the Formularies set by medical schemes encourage the use of generics and should help make coverage of the Prescribed Minimum Benefit chronic disease list more affordable. This is, however, not true in every case. There is also minimal co-ordination between this private sector system and the Essential Drug List (EDL) and Standard Treatment Guidelines (STG) applied in the public sector.

There are sufficient generic equivalents available to meet the prescriptions of the treatment algorithms for chronic medical conditions, included as Prescribed Minimum Benefits for medical schemes in South Africa and if use of these is maximised, cost savings will accrue.

1.6 Objectives

The objective of this study is to determine the extent to which a new policy approach, in terms of generic medicines use in the private sector, can be applied.

Specifically, this study will focus on the Chronic Disease List that has been added to the Prescribed Minimum Benefits prescribed in terms of the Medical Schemes Act (1998). In each case:

- the number of generics available for the treatment of each chronic condition will be established;
- the single exit price (SEP) and the Defined Daily Dose (DDD) of each drug will be used to compare monthly treatment costs;
- the existing cost differentials, on an acquisition cost basis, will be determined, between generic medicines themselves as well as between the generic and the brand name drug;

- the prescribed algorithms will be compared with the equivalent Standard Treatment Guidelines/Essential Drugs List, where possible.

The research conducted and the results obtained will show whether, within a number of different generics and brand name drug for a single chronic condition there is the potential for further cost savings. This information will be useful to medical schemes as it will enable them to re-evaluate their formularies. Patients aware of the drugs available on the formularies, will be in a stronger position to decide whether to substitute a prescribed brand name drug with a generic and, if information is available, which one. The algorithms prescribed by Government may be too broad and through the data gathered recommendations may be made to enhance the algorithms to make them more cost effective for all.

As reliable prevalence data for all 27 Chronic diseases for the entire country, or even for the private sector in particular, are not available, no net potential cost savings can be computed.

1.7 Limitations to the Project

The South African pharmaceutical market is a dynamic one, and is subject to large numbers of changes every month. New medicines are registered and become available, whereas manufacturers may make decisions to withdraw certain products from the market, for largely commercial reasons (Global Health Watch, 2005).

The following potential limitations have been identified, and the action indicated has been taken to reduce, as far as possible, the impact of each limitation on the validity of the research results:

- The actual cost to the patient is greater than the SEP, and includes a variety of dispensing fees, delivery fees and other professional charges. This is an area of considerable contention and has been the subject of several court actions (e.g. New Clicks and Others v. Minister of Health and Others, Cape High Court. 2005) during the past two years (Minister of

Health and Another v New Clicks South Africa (Pty) Ltd and Others, 2005). In order to keep to a consistent method, only the acquisition cost – the SEP – was used in this study.

- Originator (branded) medicines and generic medicines are often presented in a variety of strengths, which may cost different amounts per unit of active ingredient. Different doses may also be used for the same indication. In order to be consistent about the doses and hence the quantities compared, it was decided to use a standardized, internationally-acceptable measure of utilization, the defined daily dose (DDD) (World Health Organisation, 2006). This dose may not represent a clinically-relevant dose, and may in fact be a dose that is never used, and that is not possible to obtain with existing formulations and strengths. However, by using the lowest cost within the available strengths for a particular medicine, consistency could be achieved. In addition, only adult formulations were considered, as these would constitute the vast majority of chronic disease patients covered by any one medical scheme.

- The range of generic medicines available varies from month to month, and is not always easily accessible. In order to be consistent, the most widely consulted reference used by medical practitioners was relied upon to identify generic medicines. This is the Monthly Index of Medical Specialties (MIMS), which is published monthly. Price information was also obtained from a single source, the online Blue Book. Where a medicine class rather than a specific medicine was listed in the algorithm, the members of that class that are used in South Africa were identified from a single source, the South African Medicines Formulary (2005).

- The public sector treatment guidelines vary to some degree between provinces and over time. In order to maintain consistency, only the relevant guidelines from the 2003 Primary Health Care and the 1998 Hospital level national guidelines were used (Department of Health, 1998A).

- As mentioned above accurate prevalence data for each of the 27 chronic diseases are not easily obtainable. In addition, the management of each

disease may involve one or more of the listed drugs and at varying doses. Determining a cost per patient is thus difficult without knowing more about the spread of the severity of the diseases and prescribing patterns. These may also vary over time. A dynamic model taking into effect all of these factors is beyond the scope of this project.

1.8 Structure of the Study

Chapter One : Introduction

The background and motivation for this study is discussed providing the history and regulatory framework. The aims and objectives of this study are included in this chapter.

Chapter Two : Literature Review

In this chapter a discussion of the theory of generic substitution is covered. Among the topics looked at are consumer perceptions, brand loyalty, and the benefits of generics. A review of current literature is presented and the importance of the cost savings potential is explained. An insight into how other people have approached their research is also provided. A look at the current situation in South Africa with regard to this topic is included. The basis is laid for the exploration of the relationship between what is reviewed and what the study determines.

Chapter Three : Methodology

The theory of the research methodology is discussed and identification of the data required is presented in this chapter. This chapter explains, step by step, the methods used to obtain this data. Various methods of data collection are possible, and these are discussed in some detail with an explanation of the decision taken with regard to the path this study followed in respect of data collection.

Chapter Four : Results and Discussion

The analyses of data take the form of Excel spreadsheets, tables and graphs. A comparison of medicine acquisition costs is used to show the potential cost differentials between originator drugs and their generic equivalents. It is shown that certain patterns appear, highlighting a range of cost differentials between different generics within a particular class and condition.

Chapter Five : Recommendations and Conclusions

This chapter uses the results of the data analyses in Chapter Four to present conclusions and recommendations. In chronic conditions with generic equivalents available, there is potential for large cost differentials between the originator drugs and the generics.

1.9 Conclusion

This chapter has introduced the subject for this dissertation and provides the background, motivation, value and limitations. This study only looks at 25 of the 27 (excluding HIV/Aids and Bipolar Mood Disorder) chronic conditions presently covered by medical schemes. The results of this study will enable various stakeholders, including the Council for Medical Schemes, to review each algorithm, note the cost differentials reported and if necessary adjust the algorithm. Prescribers will also have more knowledge of the cost implications for the patient of prescribing generics as opposed to brand name drugs. The next chapter discusses the related literature examined prior to embarking on this study.

CHAPTER 2 : LITERATURE REVIEW

2.1 Introduction

This chapter discusses the high cost of medicines and the various reasons. Different pricing policies are reviewed and discussed with analyses of research on existing examples. A look at other research studies into the potential savings of using generics is also discussed.

Strategies that affect the life of brand-name drugs is noted and branding in the pharmaceutical industry is looked at, discussing whether this will change consumers or practitioners habits.

2.2 Importance of controlling drug prices

South Africa is one of the many countries faced with high and increasing health care spending. The high rate of HIV/Aids among the population including those on private medical schemes has placed an increasing burden upon private medical schemes and patients. The cost of medical schemes are prohibitively high and only about 7 million people in South Africa (approximately 16% of the population) belong to them. These 7 million people however, contribute to more than 50% of the total cost of healthcare in this country (Cullinan, 2003). High pharmaceutical costs are a major contributing factor to the increase in health care spending. R5.5 billion is spent on medicines in the private sector in South Africa every year, compared to R2.5 billion in the government sector (Enslin, 2003) and drug costs are the single biggest cost driver. According to the South African Health Review 2000, 27% of the money paid out by medical schemes in 1998 was for medicines while medicines accounted for 28.5% of payments made to private hospitals (Gray and Matsebula, 2000). There is a need to reduce the drug expenditure in the private sector as in 1998 per capita expenditure of drugs in the public sector was R59 compared to R641 to R800 in the private sector. Although much has changed in the last decade, these were the last figures from comparable surveys in both sectors, performed as a part of the National Health Accounts Project 1998 (Muirhead and Thomas, 2000; Cornell *et al.*, 2001).

Approximately 17.75% of the South African population have a disease on the Chronic Disease List (CDL) (Bester *et al.*, 2005). Total chronic medicine expenditure, including the CDL diseases, makes up 44% of total medicine expenditure. Figure 2.1 shows that the 27 CDL diseases are responsible for 23% of total medicine expenditure (Bester *et al.*, 2005).

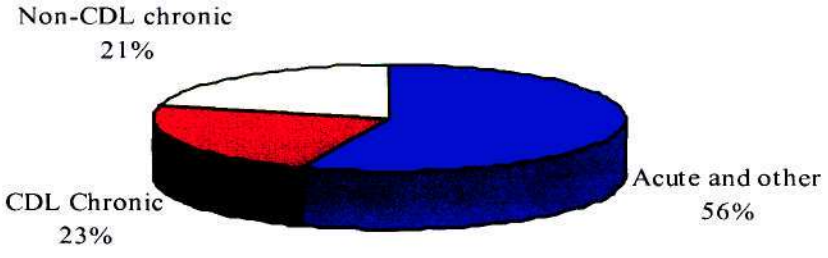

Figure 2.1 CDL expenditure as a percentage of total medicine expenditure, Q4 2005 (Source: Mediscor Medicines Review 2005)

The higher the prevalence of the disease, the greater the percentage towards the total CDL gross cost.

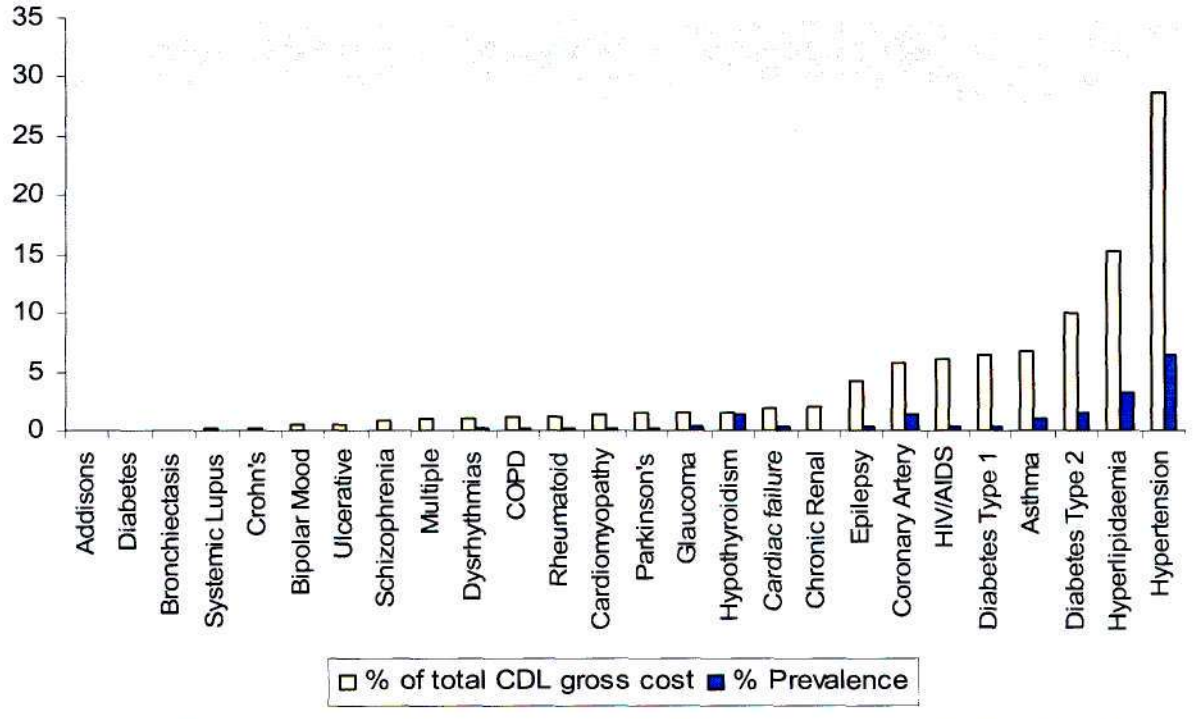

Figure 2.2 Percentage prevalence vs. percentage total cost of each CDL disease (Source: Mediscor Medicines Review 2005)

It should be noted that these prevalence figures are only for beneficiaries of schemes administered by Mediscor. They can be extrapolated to the entire private sector with any degree of certainty.

Taking into consideration distribution costs, retail mark-up and dispensing fees in South Africa, the producer's exit cost still accounts for the highest proportion of the actual drug costs, approximately 60%, while 40% is constituted by the distribution chain costs (Gray and Matsebula, 2000). The retailer in the pharmaceutical industry is either a pharmacist in a retail pharmacy or private hospital or a dispensing doctor (Fig 2.3).

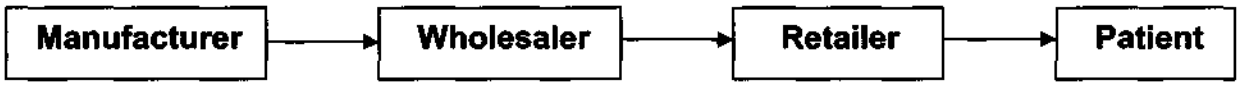

Figure 2.3 Traditional distribution chain for medicines (Source: South African Health Review 2000. Drug Pricing)

However, in a study comparing similar products in other markets, South Africa had 38 out of the 42 generic medicines studied with lower exit prices. In only one case was the South African generic more expensive (Bodhania, 2005). The aim of the National Drug Policy (1996) (Department of Health, 1996) is to promote the availability of safe and effective drugs at the lowest possible cost. South Africa looked at various policy options to reduce the price of drugs (Gray and Matsebula, 2000):

- Direct price control. This refers to the direct intervention of Government on fixing prices. This is not conducive to good trade practice as it is open to abuse.

- Reference pricing. A national authority sets the lowest price for a drug by comparison with similar therapeutic drugs. Government and Medical Schemes will only agree to pay the reference price and the patient will

have to cover the shortfall if a branded drug is chosen. The price set may be decided on in different ways:

  - Making it equal to the cost of the lowest priced drug in the group.
  - By comparing prices of a 'basket' of drugs with same in other countries of similar economic standing as South Africa.
  - Averaging the price of the drugs available within that group and either setting the average price or stipulating a price lower than that.

- Equity pricing. Under this option producers would subsidise the prices of drugs to developing countries by levying higher prices in non-developing countries. However, there is always the possibility that the subsidized prices come with pre-conditions.

- Promotion of generic use. This option promotes competition which brings a reduction in prices.

An Equity pricing policy, where developing countries are sold medicines at a 'discount' while non-developing countries pay a premium, may not suit a developing country as it may be – or perceived to be – less reliable and hence less appropriate for basing a sustainable strategy. The main reason is that they may feel that it puts them in a very weak position regarding their negotiating capacity on other issues. In other words the 'discounted' medicines may come with 'conditions' (Rovira, 2003). However, developing countries who are battling with a large percentage of their population infected with HIV/Aids are receiving antiretrovirals at a lower price. Another problem with Equity pricing is that cheaper drugs may end up being re-routed and sold at a higher price to non-developing countries for profit (T Hoen, 2001).

Germany introduced reference pricing for prescription drugs in 1989, followed by the Netherlands in 1991, Denmark and Sweden in 1993, Spain in 2000, and Belgium and Italy in 2001. Norway, having adopted reference pricing in 1993,

dropped it in 2001 after the expected savings did not materialise (Kanavos and Reinhardt, 2003). In New Zealand, reference pricing was introduced in 1994. H_2 antagonists were the first drugs to come under this policy and savings of $NZ 27.6 million had been realised as of June 30, 1995 (Moore, 1995). However, reference pricing may not benefit all countries. In a highly competitive market, for example the United States, it may force the price of patented drugs down, reducing profits and limiting the introduction of new drugs (Danzon and Ketcham, 2003).

South Africa is in the process of implementing a pricing policy, the results of which are expected to be implemented in January 2007 but are again a subject of a court action. It is expected that South Africa will follow a reference pricing option as it is one of the easiest to implement and monitor (Department of Health, 1996). The Government will set a 'reference price' based on comparing prices of an identical 'basket' of drugs from countries of a similar economic standing. Medical Schemes may then choose to reimburse the cost of medicines in various ways. They may require the patients to pay the full difference between the retail price and the stipulated reference price or they may only reimburse a percentage of the reference price to keep the volume of drugs used down.

An effect of controlling drug prices is the decrease in expected profit for a drug company who has invested in the research and design (R&D) of the drug. In an article by Giaccotto (2005), it is stated the introduction of price controls may have a negative effect on the amount of investment a company commits to R&D. Giaccotto (2005) goes on to estimate that a decline in drug prices of 10% or 50% would cause a decrease in R&D investment of approximately 6% and 29% respectively (Giaccotto *et al.*, 2005). The lack of innovation (e.g. improved routes of administration or better dosages) by pharmaceutical companies will be detrimental to the patient in the long term. Another effect of price controls is a traditional demand and supply one. If the price of a drug is decreased, more people can now afford it and the demand increases. When the demand for a

particular item increases, the price of this item along with its quantity goes up as well. However, with price control, the quantity demanded still goes up, but the price is capped and therefore cannot rise above its restricted level. The price ceiling therefore generates a shortage for the particular good and patients are adversely affected (Gannon *et al.*, 2006).

The South African Government and private medical aids are very active in promoting the use of generics. It has been shown that generics can play an important role as an alternative to brand medicines in treating diseases and that more expensive medicines do not necessarily translate into better healthcare (Hassali *et al.*, 2004). Along with this important role is the saving that results from the use of generics. Generic forms are typically less expensive than brand-name drugs due to the fact that the large financial cost of research and development of brand name medicines is not applicable to the production of generics.

However there is current debate over the actual cost of developing and introducing a brand name drug on to the market. According to the Tufts Centre for the Study of Drug Development it costs on average US$800 million to put a new brand-name drug on the shelf (DiMasi *et al.*, 2003). The Tufts Centre is funded by the pharmaceutical industry and would obviously show what these pharmaceutical companies would like the public to believe i.e. that the industry is very competitive and, therefore, a high-risk one. The image they would also like to portray is one of an industry only just breaking even after research and development costs while still bringing innovative medicines to the public.

Public Citizen, a consumer organization, conducted a detailed study of the figure above and determined that the US$800 million was inflated by about 75% (Global Health Watch, 2005).

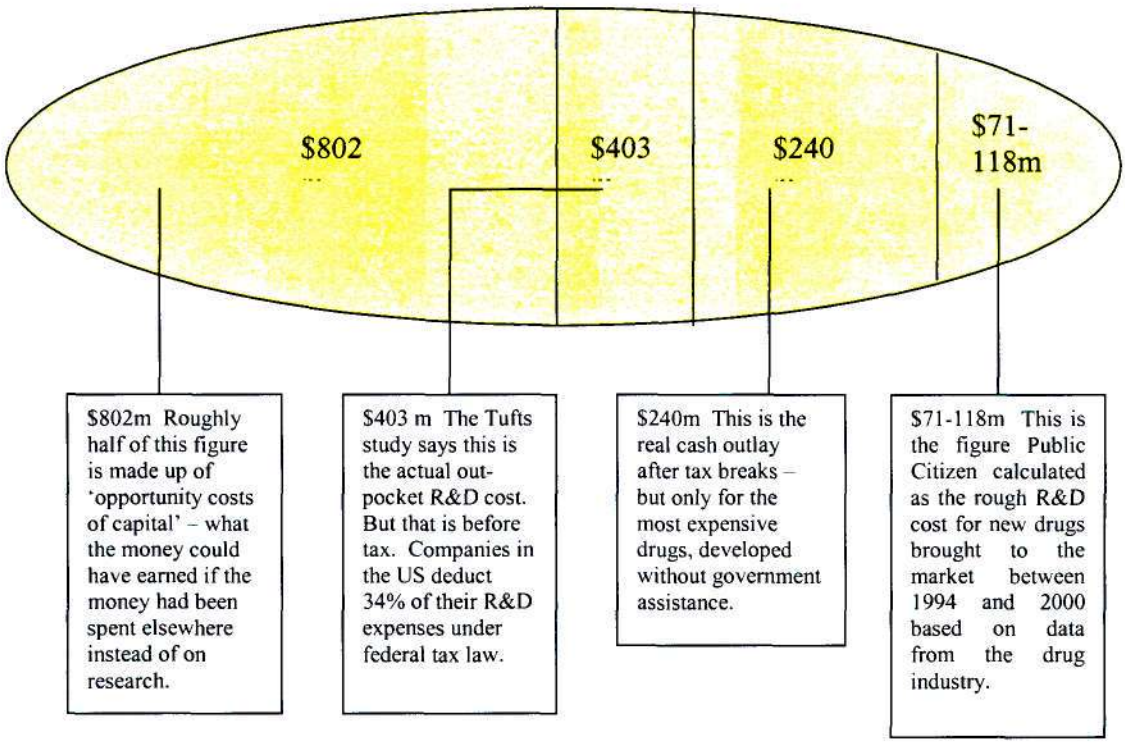

Figure 2.4 How much does it cost to develop a new medicine? (Source: Global Health Watch 2005)

The difference in calculation between the Tufts Centre and the consumer organisation, Public Citizen, is shown in Fig. 2.4. There are different views on the actual cost of R&D, which from a manufacturers point of view is passed on to the consumer. It is believed that it would be extremely valuable if the actual costs of R&D could be clearly established. However, this is beyond the ambit of this study.

According to an article by Welch (2005) medicine prices rose on average 7.1% above inflation in the USA in 2004. This was more than twice the general inflation rate in that country (Welch, 2005). Unfortunately, South Africa has also had higher than inflation rate increases in drugs resulting in prohibitively high costs prompting patients and medical schemes to look at ways of reducing this cost. Government and private medical schemes are urging their patients, doctors and pharmacists to use generics more often to cut costs. However,

according to Freudenheim (2002) costs of generics are increasing twice as much as brand-name drugs. This would appear to run counter to the expected pricing behaviour. When a patent expires on a brand-name drug the initial generic has 'exclusive rights' for a certain period, usually six months. This initial generic comes on the market at a higher than normal introductory cost. The price of the initial generic drops after the exclusive right period ceases and more generics come onto the market. Another reason for the sharp increase in generic prices is that the generic manufacturers are joining together, leaving fewer companies and therefore less competition. This can be counterproductive in that the lower prices translate into lower profits forcing smaller companies to withdraw from the market and prices start to increase again (Freudenheim, 2002).

Prices of brand name drugs do not decrease when a generic is introduced into the market. If the generic is manufactured by the same company that made the brand name drug, there was no difference in the way the company viewed their pricing strategy. Many Canadian private medical schemes do not require nor promote generic substitution and, therefore, pharmaceutical companies do not feel the need to decrease their prices, in fact price increases sometimes occur to offset the decrease in volume sales (Lexchin, 2004). In Canada, since the Ontario Drug Benefit Formulary was introduced, the initial generic must be priced at no more than 70% of the brand name drug and subsequent generics must be 10% less than the initial one (Lexchin, 2004).

2.3 Potential Savings

In 1996 the potential savings by using generics in South Africa was studied by analyzing generic prescribing by doctors and generic substitution by pharmacists. The methodology used was to analyse prescriptions gathered from pharmacists and compare with what was actually dispensed. Only 13.9% of pharmacists substituted generics for brand-name drugs which saved the patient 1.4% of the original cost of the prescription. It was found that a further 6.8% could have been saved by total generic substitution and 9.9% by total

generic prescribing (Karim *et al.*, 1996). A similar study was conducted in America. A random sample of adults who had used at least one outpatient drug that had a generic was taken from a government survey conducted from 1997 to 2000. The survey included medical and health data including insurance coverage and amount spent on each brand-name drug. The potential savings of replacing brand-name drugs with generics were then calculated. Although 56% of the prescribed drugs had a generic substitute, patients used the generic form in only 61% of these cases. It was calculated that if generics had been used in all cases a savings of US$46 per person under 65 years would have resulted while in those over 65 the savings would have been US$78. Taken overall this would have given a national savings of US$5.9 billion in the younger group and US$2.9 billion in the older group. The reason for the difference in savings for the ages is that older patients tend to require more medication but constitute a smaller percentage of the population (Haas *et al.*, 2001).

In a recent study conducted in South Africa by Djolov (2003), the top 200 drugs by sales value (which represents 53% of prescription drugs) were taken and compared to their bioequivalent generic (if available). Prices obtained through the Monthly Index of Medical Specialities (MIMS) were used to calculate savings by comparing the price of the brand name drug to the cheapest available generic. It was shown that a total savings of 6.1% could be achieved by generic substitution. Interestingly, 4.14% savings was achieved in the top 100 and only 1.96% in the next 100 drugs. If 1,96% is taken as the average for the remaining 47% of drugs, a total savings of R407 million could be achieved (Djolov, 2003). By looking at drug prescribing in the elderly using two groups, one with a private medical aid and the other with the government medical care programme there seems to be a higher potential for savings in the first group than in the second. This could be explained by the fact that the restrictions on the excess spending on brand name drugs which is already in place by the government medical programme may be working. There are large savings that could be realised by private medical schemes if the use of generics were encouraged more actively (Fischer and Avorn, 2004).

Competition among manufacturers can force prices of generic drugs to decrease more than the brand-name drug, resulting in a low ratio between the two prices. However, as can be seen in Table 2.1 the smallest ratio was only 0.39 which still points at a large price gap between the generic and brand-name drug (Cook, 1998).

Table 2.1 Price Comparison of generic and brand-name drugs, by number of manufacturers, 1994 (Source: Cooke, 1998)

No. of manufacturers selling generic copies of brand-name drug	No. of brand-name drugs	Ave. prescription price of generic drugs in category (US$)	Ave. prescription price of brand-name drugs in category (US$)	Ave. ratio of generic price to brand-name price
1 – 5	34	23.40	37.20	0.61
6 – 10	26	26.40	42.60	0.61
11 – 15	29	20.90	50.20	0.42
16 – 20	19	19.90	45.00	0.46
21 – 24	4	11.50	33.90	0.39
Average		22.40	43.00	0.53

2.4 Consumer Behaviour and Decision Making

Figure 2.5 shows that there are four types of consumer buying behaviour (Kotler, 2003: 201).

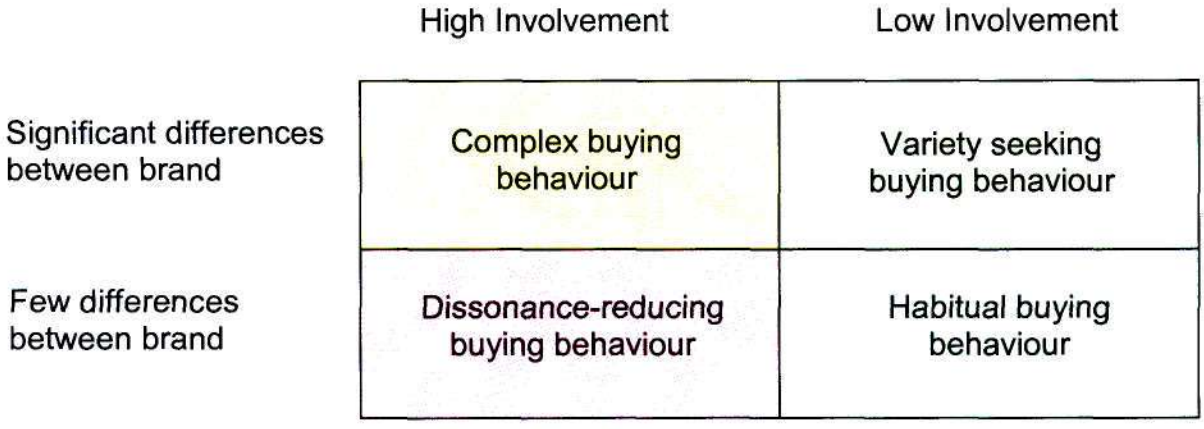

Figure 2.5 Consumer behaviour (Kotler, 2003: 201)

Most medicines are prescribed by doctors and the 'buying decision' has effectively already been taken away from the consumer. The consumer cannot choose the type of medicine prescribed but can ask and decide whether to use a generic. The only difference between the originator and a generic is the price. As there is very low involvement in making the buying decision a consumer displays habitual buying behaviour. Consumers displaying this buying behaviour are usually passive recipients of advertisements which may only reinforce brand familiarity rather than brand conviction. Thus the consumer does not search extensively for information, evaluate characteristics and make a decision. The lack of television and print advertisements reflects this aspect of habitual buying behaviour. The two factors which can influence a consumer between the time of intention to purchase and the actual purchase i.e. attitude of others and unanticipated situational factors, does not normally apply to the purchase of essential goods such as medicines (Kotler, 2003: 207).

As generics are chemically identical to the originator drugs their pharmacological effects are exactly the same. However, there have been reports of generics not working (e.g. patients taking the generic of clozapine have reported a deterioration of their condition) (Mofsen and Balter, 2001). This lends itself to the negative perception that patients often associate with generics. Lost sales driven by brand switching and negative word of mouth are estimated at US$15 – 20 billion annually (Manchanda *et al.*, 2005). However, consumers today have greater access to more and detailed information on diseases which changes them from being passive consumers to taking a more active part in the decision-making process of their health care, even to question and override doctors decisions (Merino-Castello, 2003). Unfortunately, Formularies put forward by medical schemes may affect consumers and prescribers decision process by limiting the choice of medicines that medical schemes will fully cover for chronic diseases.

In a study by Wosinska (2005: 323-332), on the effect of direct-to-consumer advertising, it was discovered that advertising had a more positive effect on compliance for patients taking the competitor drug and a negative effect (non-compliance) in patients taking the advertised drug. She hypothesises that this could be due to the fact that the advertising involves not only promoting the benefits of the drug but also the possible side effects (Wosinska, 2005). There is another danger to pharmaceutical advertising in that a consumer may identify with the symptoms portrayed in the advert and will visit a doctor requesting that particular drug. There is a 70% chance that the doctor will comply with the request. The reason for this is that doctors are exposed to drug advertising by pharmaceutical companies through medical journals, drug representatives, drug companies and pharmacists (Veracity, 2005).

In a short study conducted by Govender *et al.* (1999) it was shown consumers were more wary about taking or substituting a generic as the perceived seriousness of their disorder increased. In many patients cost savings will not

out weigh therapeutic benefits and many will still demand brand name drugs if this is in doubt (Govender *et al.*, 1999).

2.5 Prescriber behaviour

After the generic drug scandal in the USA in 1989, where Food and Drug Agency (FDA) officials were paid to speed up the approval of generic medicines, many pharmacists lost confidence in generics themselves and decreased generic substitution on prescriptions (Gupta, 1996). However, ten years later in a 2006 survey of 425 physicians in the USA, 78% favour substituting generics for brand-name drugs in most cases with five per cent who say it is never appropriate to substitute a generic for a branded drug. Doctors feel confident that they have the correct information to make an informed decision and to discuss this with their patients. The AARP (2006) report notes that 80% of the doctors surveyed receive weekly visits by representatives of brand-name manufacturers and 75% of these doctors have never received a visit from a generic drug representative (AARP, 2006). Pressure to prescribe generics come from patients themselves or medical schemes.

2.6 Branding and Brand Loyalty

Attributes and benefits are an integral part of the overall levels of meaning of a brand (Kotler, 2003: 418). However, they are the most important for consumers with regard to medicines. Keller (2000) states that "What distinguishes a brand from its unbranded commodity counterparts is the consumers' perceptions and feelings about the product's attributes and how they perform".

A patent may run for 20 years during which time the originator drug is the only brand on the market and has a unique opportunity to position itself in the consumers mind. The attributes and benefits of that drug once a patent expires does not change. However, the factor that does change is that the consumer now has the choice of the same attributes and benefits but at a lower price.

Brand loyalty is not very strong among patients whose only interest is in the cost savings they may achieve. If the patient is made aware that a generic will give them exactly the same benefits as a brand-name drug at a lower cost they will more likely change to the generic. The reason for the lack of brand loyalty is that drugs normally compete with each other on their functional attributes and not emotional attributes. The functional attributes which concern the pharmaceutical companies are (Suchanti, 2005):

- Efficacy - the drug has the ability to prevent or cure an illness.
- Safety - the drug is safe to use with no side-effects.
- Convenience - it is easy/pleasant to take with regard to dosage requirements.
- Cost-effectiveness – the drug is affordable.

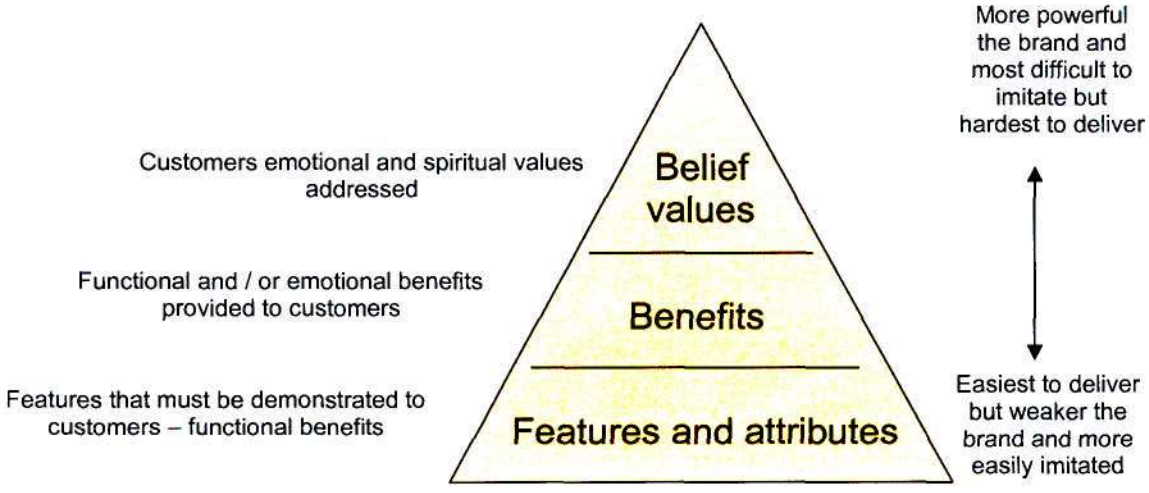

Figure 2.6 Brand Value Pyramid (adapted from Davis 2000)

Davis (2000) states that the higher up the pyramid a product is, the stronger the brand recognition, the harder it is to imitate and therefore, less competition occurs. The lower a product is down the pyramid, the weaker the brand and the easier it is for generics to enter the market. The emotional attributes are rarely promoted in drugs although there have been exceptions which are referred to

as 'blockbuster' drugs (e.g. Prozac and Viagra). For a product to succeed these days, companies must prove that the drug is innovative compared with potential branded and generic competition. Due to the high profits obtained from patent drugs, pharmaceutical companies have concentrated more on patenting than on creating brand loyalty. Although profits are not the only reason behind patenting this is regarded by the pharmaceutical industry as an essential component of their business model, as seen by the vigorous way in which they promote and protect intellectual property rights.

2.7 Strategies To Protect Patent of Brand-Name Drugs

A brand-name drug is patented from the time of first research and development. The total time can be as high as 20 years. During this time no generic may be introduced onto the market in competition with the brand-name drug. If the figures reported in the Tufts Centre for the Study of Drug Development (see Figure 2.4) are a true reflection of costs it is not surprising that pharmaceutical companies have come up with strategies to prolong or prevent the introduction of generics once patents expire. In the case of GlaxoSmithKline, their patented drug Zantac (an anti-ulcer drug) was worth approximately two to three thousand pounds in profits to them for every single day that it lasted (Graham, 2001). Three of the most common strategies to prolong the introduction of generics are (Pearce, 2006):

- Pre-emptive launch of generics. A pharmaceutical company is allowed to introduce their own generic before the patent expires on their own brand-name drug (this is called an 'authorised' generic or 'ultrageneric'). This may be done under license by another company on their behalf or through a subsidiary. This 'ultrageneric' is often launched on the same day as the first generic competitor ensuring that profits for the originator manufacturer are maximised by claiming market share for the generics too. Introducing two identical generics effectively cancels the first six months exclusive rights normally due to the first generic. Another benefit of a brand-name manufacturer producing their own generic is that they have the ability to

market a generic drug by offering to supply it at a reduced rate for a specific contract period which usually goes beyond the patent expiry date. Although losing on profits from the brand-name drug they halve their competitors profits and lock in patients with their generic at a higher price.

- Layering innovation. This is created by layering patents one upon another by patenting an innovation on a base product to maintain the patent. This results in an 'enhanced product' by means of alterations in the active ingredients, strength, dosage form, route of administration etc.

- Line extensions. This involves changing the use or extending the use into another market e.g. Merck's prostate drug Proscar® was remarketed to help hair loss in men, under a new name Propecia® (Pearce, 2006). This saves the patent and creates a new additional market with increased profits. Another example is GlaxoSmithKline's (GSK) Zyban® which was originally developed as an antidepressant drug. However one of the side effects noticed was that the nicotine craving diminished when taking it and patients gave up smoking. It has since been remarketed as a drug used in nicotine dependence.

2.7.1 Porters Five Forces

Porter's Five Forces model is an important tool for analysing an organisation's industry structure which is essential when making strategic decisions. In the traditional economic model, competition among rival firms would normally drive profits down. However, competition is never perfect and companies do not sit back passively and allow this to happen but rather try to find a competitive advantage over their rivals (Thompson, 2001).

As patents expire and generics reduce the profits of pharmaceutical companies, diverse innovation is required. The success of biotechnology in recent years (Schmid *et al.*, 2002) has forced the pharmaceutical companies to be proactive.

According to the Biotechnology Industry Organisation (BIO), pharmaceutical companies increased their licensing and investment deals within the biotechnology industry in 2004 by 44% compared to 2003 (Frost and Sullivan, 2005). This strategy of forming alliances is important for the pharmaceutical companies to maintain their large (and sometimes unjustifiable) profits. Figure 2.7 shows that although the pharmaceutical industry is highly competitive and profitable, there are other forces that affect and influence their decisions. The Power of the Buyers is weak as they have no bargaining power compared to the Power of the Suppliers who are few in number making it difficult for consumers to shop around for an alternative and cheaper medicine.

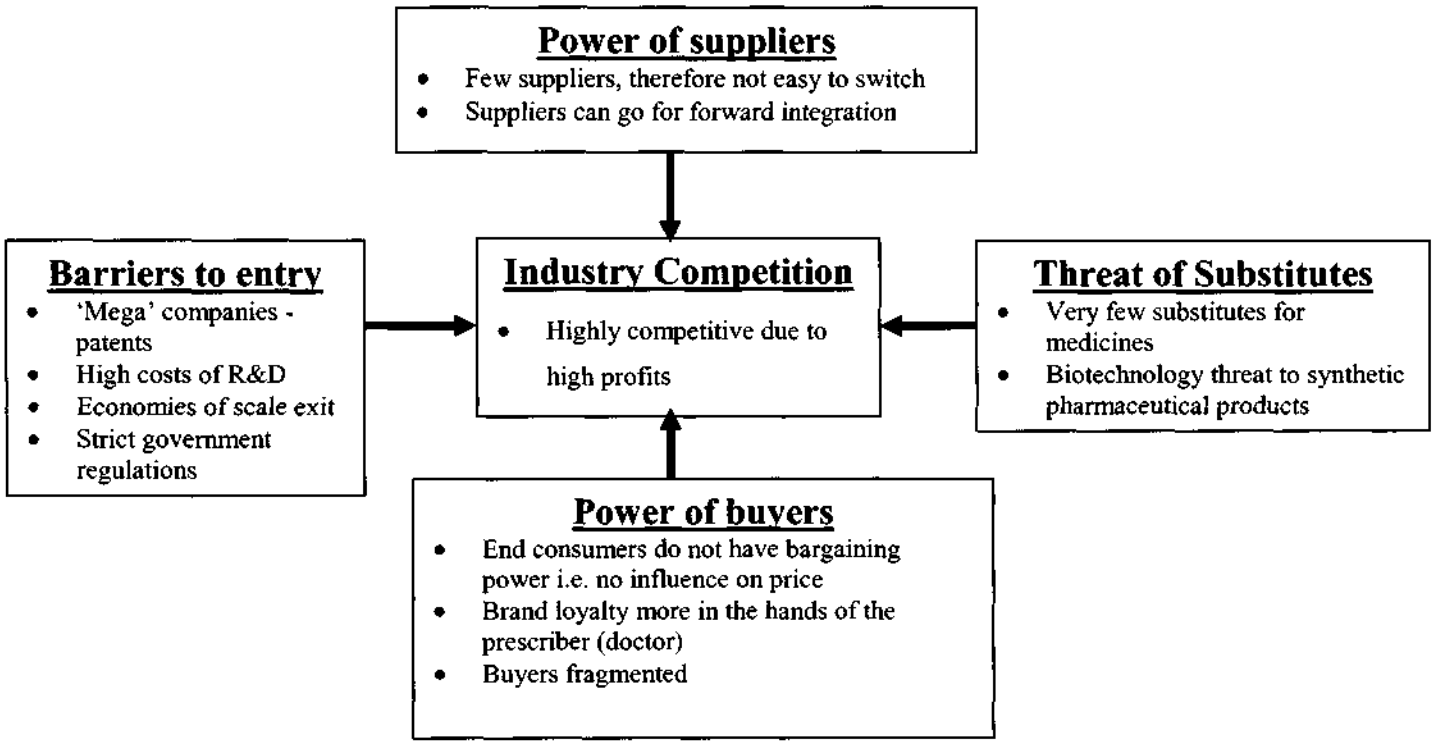

Figure 2.7 Porters Five Forces for the pharmaceutical industry

2.8 Me-Too Drugs

Generics, which are chemically equivalent to patented brand name drugs, are not the only form of competition to the original drug. A patent may be taken on a new drug within a particular class which is slightly different and is marketed as having a better therapeutic effect or a different mechanism of action. These drugs are called 'Me-too' drugs and are usually just as expensive or marginally lower in cost than the original class drug. An example of this are Angiotensin-Converting Enzyme (ACE) inhibitors where numerous 'Me-too' drugs exist e.g. Captopril, Enalapril and Lisinopril. There are usually more "Me-too' drugs the more prevalent a disease and manufacturers hope that these drugs will capture part of a lucrative market. However, many of these drugs have no extra benefit and are at best equivalent in efficacy, but more expensive than the original drug (Garattini, 1997). Me-too drugs are also taking the place of the cheaper cost effective generics within that class.

2.9 Government initiatives for low income earners

The Government introduced the Government Employees Medical Scheme (GEMS) in January 2006 for low income workers who are employed in public service. The scheme is 75% - 100% subsidised by Government, depending on annual salary. The lowest package on this scheme offers essential day-to-day benefits. The scheme now has 50 000 members, 40% who were previously not covered by any medical scheme. These people are now not eligible for free state care and their membership has helped reduce patient load at Government hospitals (Erasmus, 2006B). However, not everyone is happy with the GEMS. Unions feel this is another way of privatising healthcare and of downgrading the public health system (Bell, 2006).

According to a survey conducted in 2005 by the Low Income Medical Schemes (LIMS) Committee, low income households with no cover spend on average R105 per month on private General Practitioner (GP) visits (Erasmus, 2006A).

The survey also found that only 12% of individuals earning between R2 501 and R6 000 were covered while 20% earning between R4 501 and R6 000 were covered. GPs, medicines, dental services and optometrists were found to be high on the preference list of low income households. It was felt that if premiums were equal to their 'out-of-pocket' expenses low income earners would join a LIMS. Means of reducing premiums further could include employer subsidies, treasury subsidies, reduction of health care benefits and a reduction in the actual cost of healthcare (Erasmus, 2006A).

The LIMS is in effect a form of Social Health Insurance (SHI) as contributions from individuals, employers and even government would be included. This nation-wide medical insurance scheme would be for all employed people based on their ability to pay (using a sliding scale). The uninsured would benefit as they would be entitled to the standard health care in the public sector which is now better funded. Those who are insured would have various levels of health care packages available to them including private health care at an extra cost. However, this is also a step closer towards Government introducing a National Health Insurance Scheme (NHIS). This scheme would be financed by tax payments and everyone would receive the same level of coverage regardless of their ability to pay, their level of taxation or risk factors. A Reform Strategy and Approximate Timeline towards the implementation of a NHIS was recommended in a report by the Department of Health in 2002 and is shown in Figure 2.8 (Department of Health, 2002).

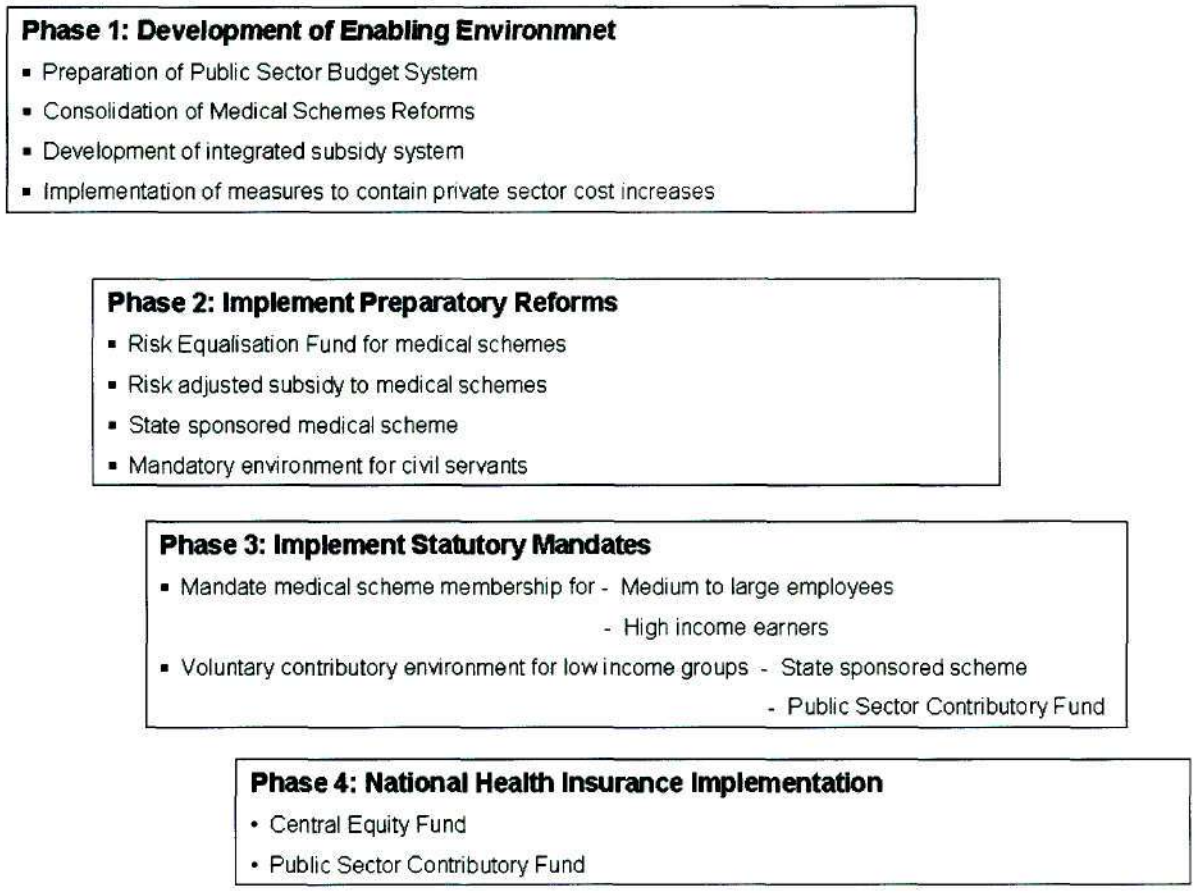

Figure 2.8 Reform Strategy and Approximate Timeline (adapted from SA Department of Health – Integrated strategy for Health System Reform. 2002)

Phase One and Phase Two have almost been completed, the biggest exception being the implementation of measures to contain private sector cost increases (Department of Health, 2002). To proceed with Phase Three it is essential that premiums to medical schemes are kept low. By revising the formularies and realising the cost savings of substituting generics medical schemes can reduce their payouts and pass on these savings to their members.

2.10 Conclusion

This chapter has given the researcher insight into studies and reports that have been conducted on many aspects of generics, brand-name drugs and the many ways they affect consumers' perceptions and behaviour. The literature

reviewed would indicate that there is the possibility of potential savings and that there are some key areas that need to be addressed and improved on. The theory of brand loyalty and strategy, including Porters Five Forces were discussed.

The next chapter discusses the methodology and how the research was conducted for this study.

CHAPTER 3 : METHODOLOGY

3.1 Introduction

This chapter details the research methodology used to enable the objectives to be addressed. Methodology is the procedures and techniques used to collect, store, analyse and present information. In this chapter the methodology employed is discussed and a detailed, step by step, explanation on how the data was obtained and analysed is included. The methods of data collection are discussed with an explanation of the decision taken with regard to the path this study followed.

This study consists of empirical quantitative data which is collected from various primary (books and government publications) and secondary sources (reports, published summaries and reviews) (see 3.4 Data Collection). Quantitative data is used. Quantitative research differs from qualitative research in the following ways:

- Data is usually gathered using more structured research instruments
- The results provide less detail on behaviour, attitudes and motivation
- The results are based on sample sizes that are representative of data required
- The research can usually be repeated, given its high reliability
- Quantitative data is used to make calculations and
- The analysis of the results is more objective (Saunders *et al.*, 2003: 378)

In quantitative research variables are identified, measured and a statistical model drawn up to evaluate the results of the manipulated data. It is a more efficient method of data collection as it uses formal instruments to collect data instead of the researcher themselves. The analysis is conducted using discrete

data and is in simple mathematical terms involving tables, charts and diagrams. (Saunders *et al.*, 2003: 328)

3.2 Concepts

3.2.1 Conceptual Definitions

According to the South African Concise Oxford Dictionary (2005:238) the meaning of the word concept is "an abstract idea". Concepts are not tangible and represent an object in an abstract form. According to Ghauri and Gronhaug (2002: 31), concepts are "the most critical element in any theory because they direct what is captured".

In the context of this study two concepts, 'savings' and 'use' are defined. The word savings as defined by the South African Concise Oxford Dictionary (2005:1040) is "preventing waste of a particular resource". In this study the concept of savings is utilised in reference to the cost of the drugs, the resource being money. The word 'use' in the context of 'one could use' as defined by the South African Concise Oxford Dictionary (2005:1295) is "one would like or benefit from". 'Use' in this study refers to the use of generics over and above brand-name drugs.

An operational definition follows on from the conceptual definitions described as it must indicate how the abstract concept will be measured.

3.2.2 Operational Definitions

An operational definition is "a set of procedures that describe the activities to be performed to establish empirically the existence or degree of existence of what is described by a concept" (Ghauri and Gronhaug, 2002).

The concept of "savings" is measured by establishing the cost differential between the lowest priced originator drug in a specific class to the lowest priced generic drug in the same class. The difference between the two will be the "savings". The concept of "use" is measured by whether there is a generic available for a particular class of drug and whether the consumer would benefit from it in terms of the savings.

3.3 Research Design

Research design is used to structure the research, and to provide answers to questions such as:

- What kind of sampling will be used?
- What techniques will be used to gather the data?
- How will time and cost constraints be dealt with?

The research process can be described by using the 'Research Process Onion'. Saunders *et. al.* (2003: 83) states that "the research process is like the layers of an onion that need to be peeled away before getting to the central issue of data collection". The first layer refers to the adopted research philosophy, the second looks at the research approach. The third layer examines the research strategy while the fourth layer refers to the time lines. The fifth and last layer is associated with data collection including sampling.

Figure 3.1 shows how the researcher conceptualised the research approach to be applied in this study in order to come up with the relevant data required to answer the research question as well as to arrive at the fulfillment of the research objectives.

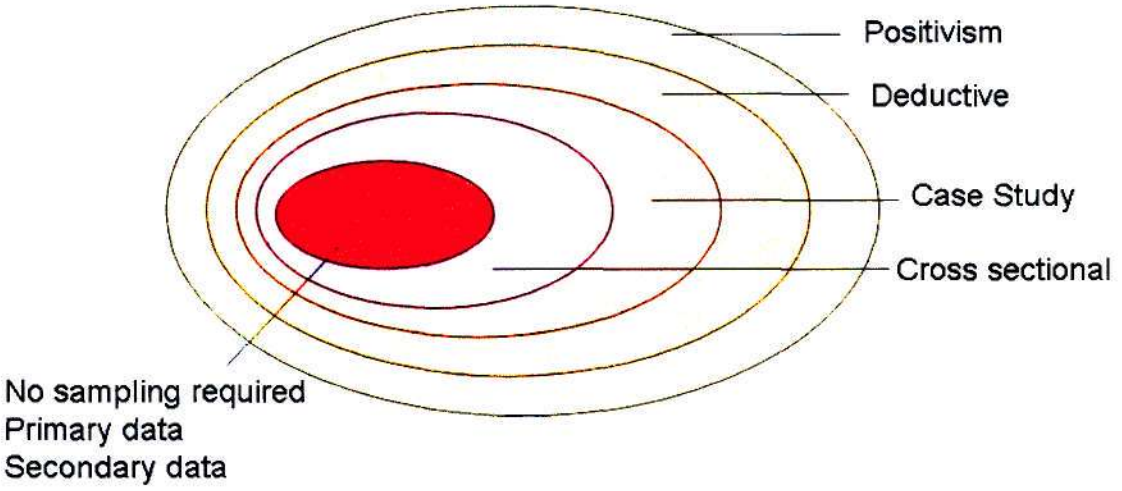

Figure 3.1 Research Process Onion. (Adapted from Saunders *et al* (2003))

This study aims to compare prices of medication required per month for chronic diseases by evaluating the cost per month of the daily defined dose in conjunction with the single exit price of the drugs. It is a cross-sectional study as it reveals a snapshot of this point in time.

3.4 Sampling

A census is conducted as data is collected from the entire population and no sampling is required (Saunders *et al.*, 2003: 150). The population consists of the 25 chronic diseases for which algorithms are available. It was decided to include all of the algorithms in the population as many of the drugs required are duplicated across diseases (e.g. bronchiectasis and chronic obstructive pulmonary disorder). In the case of four of the 25 chronic diseases, no generics could be identified, and these , therefore, did not require extensive analyses.

3.4.1 Inclusion Criteria

The Chronic Disease List (CDL) as per Government regulations was selected for analysis. Only the exact medicine, class of medicines or therapeutic groups mentioned in the algorithms are included in this study. Only data pertaining to

an adult was collected i.e. only adult dosages and routes of administration were recorded.

3.4.2 Exclusion Criteria

The two chronic diseases Bipolar Mood Disorder and HIVAids are excluded as no algorithms are as yet available. All paediatric drugs and / or dosages were also excluded as defined daily doses (DDDs) are determined for adults only.

Medicines are classified according to their anatomical, therapeutic and chemical characteristics (Bennett and Brown, 2003). A specific class of drug is one or more drugs which have the same pharmacological effect as each other. Within the class there may be sub-sets of classes which differ chemically. If a class of drug did not have a defined daily dose (DDD) it was excluded. Combination drugs (e.g. a combination of a oral blood glucose lowering drug, metformin and sulphonylurea) often, but not invariably, do not have a specified DDD and were excluded. An exception was the combination of levodopa and carbidopa. This combination has a DDD as levodopa cannot be administered on its own.

3.5 Data Collection

Generalised studies throughout the world have been conducted looking at potential savings of using generic drugs over brand-name drugs yet no study could be found that looked at chronic diseases only. Primary and secondary data were collected. Primary data was collected from the gazetted algorithms, the South African Medicines Formulary 7th Edition (SAMF, 2005) and the Monthly Index of Medical Specialities (MIMS) (May 2006). The online Pharmaceutical Blue Book and the World Health Organisation (WHO) Collaborating Centre for Drug Statistics Modelling (WHO, 2006) were also used for primary data collection. Secondary data was collected using various search engines (e.g. Google, PubMed, Elsevier), journals (e.g. Australian Prescriber,

British Medical Journal, Clinical Therapeutics) and the Medicines Review 2005 report and Global Health Watch 2005-2006.

3.5.1 Primary Data

Algorithms

The Council for Medical Schemes is a statutory body established by the Medical Schemes Act (1998) to provide regulatory supervision of private health financing through medical schemes. The minimum standards of diagnosis and treatment for all prescribed minimum benefit conditions have been published in the Government Gazette, and are known as treatment algorithms (benchmarks for treatment) (Appendix A). A medical scheme may decide what treatment it will pay for each chronic condition, but the treatment may not be below the standards published in the treatment protocols. The algorithm for each of the 25 chronic diseases analysed was looked at in order to record the basic medication required under government legislation. The steps in the algorithms for diagnosis and treatment were followed and the suggested class of medicines and / or general treatment were noted per condition (Department of Health, 1998A).

South African Medicines Formulary (SAMF)

The South African Medicines Formulary is researched and written by members of the Division of Clinical Pharmacology, Faculty of Health Sciences, University of Cape Town. The purpose of the formulary is to promote safe, rational and cost-effective use of medicines available in South Africa, to serve the various educational, information and drug regulatory programmes, and to support national health planning. It provides therapeutic information on most drugs registered in South Africa. The latest edition (2005 7th edition) was used for all collection of data. The treatments and class of drugs collected from the algorithms were reviewed in the SAMF(2005), and, where a class rather than a

specific medicine was stipulated, all available medicines for that condition were noted. The medicine's proprietary (trade) name, manufacturing company name and presentation e.g. tablets or nasal spray were recorded (SAMF, 2005).

Monthly Index Medical Specialties (MIMS)

The May 2006 MIMS was used to identify all generics and branded versions of the medicines identified in the algorithms and from the SAMF (2005). Constant double checking took place to ensure that no medicines were left out. It should be noted that the SAMF (2005) and MIMS (May 2006) do vary in one important manner. MIMS receives remuneration from the pharmaceutical manufacturing companies that advertise on its pages., while the SAMF does not accept advertising or industry support of this nature. The MIMS may not, therefore, include generic medicines produced by companies that choose not to advertise (MIMS, May 2006).

Daily Defined Dose

The daily defined dose (DDD) is the 'assumed average maintenance dose per day used for its main indication in adults.' The DDD is available online from the World Health Organisation Collaborating Centre for Statistical Modeling website (World Health Organisation, 2006). This is a unit of measurement and does not necessarily reflect the recommended or prescribed daily dose. However, by using the DDD for each specific medicine, a standardised figure is obtained which is independent of price and formulation enabling the researcher to perform comparisons between classes. The DDD was converted into a monthly defined dose by multiplying by 30 for the purpose of this study. The database of DDDs was last updated on 11-01-2006 (World Health Organisation, 2006).

The Pharmaceutical Blue Book

The Pharmaceutical Blue Book is published by Pharmaceutical Publishers, a wholly owned subsidiary of Alex White and Company and is available via subscription online (Pharmaceutical Blue Book, 2006). The Blue Book is renowned for supplying the pharmaceutical industry with independent and accurate price lists. Information available on the electronic database includes new or discontinued products; packet packaging or sizes; manufacturers; packing changes and presentation and prices. The single exit price (SEP) (excluding VAT) and corresponding quantity were recorded for this study. The price file is constantly updated and all effort has been made to collect the latest prices (Pharmaceutical Blue Book, 2006).

3.5.2 Secondary Data

A literature search was conducted accessing various databases. Searches in the Ebsco database were limited to Academic Search Premier, Business Source Premier, Newspaper Source, and MEDLINE. Searches in the PubMed databases as well as Science Direct and Elsevier were also used extensively. These databases contain numerous journal articles that are available for review and enable the researcher to determine whether peers have done research in the same field as the researcher. Key search words used to search the various databases were "generic drugs", "chronic disease and generics", "potential savings", "brand-name drugs", "brand loyalty and drugs", "me-too drugs", "generic substitution and perceptions" and "reference pricing".

Different internet websites of educational and government institutions were searched with reference to generic drugs, their savings and perceptions. This search was carried out utilising search engines Google and Alta Vista. Multiple source and time series based secondary data is collected from the book Global Health Watch 2005-2006 (Global Health Watch, 2005) and the report Mediscor

Medicines Review 2005 (Bester *et al.*, 2005) . This secondary resource material consists of statistics used to create some of the diagrams in Chapter 2.

3.6 Ethics

Ethics is not only limited to human subjects of research or to anyone affected by the study but also applies to the way the research is reported. As all data collected in this study is in the public domain and is easily accessible, ethics approval was easily obtained. However, the researcher has a moral responsibility to ensure that all data collected and analysed is valid and true (Ghauri and Gronhaug, 2002: 18). The strengths of the methods as well as the weaknesses must be honestly reported as this can affect the reliability of the results . Ethics approval has been received for this study (reference number HSS/06771A).

3.7 Limitations

A weakness of this study is that it does not allow for any comparison in the future for a price change and is a snap shot of the situation now. Another weakness is that it is open to human error i.e. syntax mistakes in entering data. All effort has been made to check and cross check data entered to ensure that it is accurate. Other limitations have already been described, together with the methods used to reduce the impact of those limitations on the quality of data collected.

3.8 Analysis of data

The Primary data collected was collated in an Excel spreadsheet, sorted and the monthly medicine acquisition cost - the monthly defined dosage cost - calculated using the defined daily dose, strength, quantity and single exit price (inclusive 14% VAT) (SEPV):

30 days = Taken as an average number of days in a month
SEPV = Single Exit Price inclusive of VAT (14%)
DDD / strength = Number of tablets/mls required for DDD
Quantity = Number of tablets or ml in presentation at the SEP

$$\text{Monthly defined dosage cost (R)} = \frac{(\text{SEPV}) \times 30 \text{ (days)} \times (\text{DDD/Strength}))}{(\text{Quantity})}$$

Preliminary data cleaning was done whereby the data was checked and corrected and any anomalies were reviewed and corrected where appropriate. Some of the chronic diseases have very similar treatment algorithms e.g. bronchiectasis and chronic obstructive pulmonary disease and are discussed as one. A percentage difference in the price between drugs in the same class was tabulated and reported.

In considering the potential costs savings in respect of each algorithm, the gazetted version for the private sector was also compared with the equivalent applicable in the public sector, using the 2003 Primary Health Care and the 1998 Hospital level national guidelines (Department of Health, 1998A).

3.9 Conclusion

The results from the calculated differences in price indicate that the objective to ascertain whether there will be potential savings using generic over brand-name drugs has been achieved. This leads to the next chapter where the data is analysed, tabulated and graphically represented and the results discussed.

CHAPTER 4 : RESULTS AND DISCUSSION

4.1 Introduction

In this chapter the results from Excel spreadsheets are analysed and discussed with reference to the problem statement and objectives. Data are the "facts, opinions and statistics that have been collected together and recorded for reference or for analysis." (Saunders *et al.*, 2003: 476). Analysis "is the ability to break down data and to clarify the nature of the component parts and the relationship between them" (Saunders *et al.*, 2003: 472).

The nature of the diseases listed by the Council for Medical Schemes', and the way in which each of the medicines is used in their management, is not described as these factors are irrelevant to the way in which data have been collected and presented.

4.2 Analysis of Tables

The tables address this study's objectives, which is to determine the number of generics available for the treatment of each chronic condition and to establish, by means of the single exit price (SEP) and the Defined Daily Dose (DDD) of each drug, whether there are price differentials between generic medicines themselves as well as between the generic and the brand name drug.

4.2.1 Addison's Disease

The CMS algorithm for Addison's disease (also known as adrenal insufficiency) is shown in Appendix A. Table 4.1 shows the listing of medicines included in the algorithm.

Table 4.1 Addison's Disease

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Corticosteroids									
Mineralocorticoids									
Fludrocortisone	1	0	Tablets 100mcg	0.1mg	55.37				
Corticosteroids									
Oral									
Methylprednisolone	1	0	Tablets 4mg	7.5mg	53.61				
Prednisone	1	3	Tablets 5mg	10mg	148.86	4.53	6.39	97.0	29.1
Prednisolone	0	2	Tablets 5mg	10mg		11.73	12.04		2.6
		2	Syrup 15mg/5ml	10mg		101.92	123.12		17.2
Budesonide	1	0	Capsules MR 3mg	9mg	766.85				
Hydrocortisone	1	0	Tablets 10mg	30mg	86.73				

Of the three possible medicines listed, two medicines (hydrocortisone and fludrocortisone) have no generic equivalents. The third, which could be interpreted as either oral prednisolone or prednisone, is available in two and three generic versions respectively (in the former case as either tablets or the oral liquid formulation). The cost differentials vary considerably, from 29.1% for prednisone tablets, to only 2.6% for the prednisolone variant.

The public sector STG uses the same medicines, except that it specifically lists only oral prednisone. In practice though, prednisone and prednisolone (the liver activated form) are considered therapeutically interchangeable.

4.2.2 Asthma

The CMS algorithm for asthma is complex, and is presented in Appendix A. It uses a 'stepwise approach' to treatment depending on the severity of the disease.

Table 4.2 Asthma

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Beta2 agonist -									
Short acting									
Inhalation									
Salbutamol	1	3	Inhaler 100mcg	0.8mg	39.30	20.15	22.67	48.7	11.1
Fenoterol HBr	1	0	Inhaler 100mcg	0.6mg	51.22				
Terbutaline	1	0	Inhaler 0.5mg	2mg	104.72				
Beta2 agonist -									
Long acting									
Formoterol	1	3	Inhaler 12mcg	24mcg	217.93	72.96	160.81	66.5	54.6
Salmeterol xinaforte	1	0	Inhaler 25mcg	0.1mg	230.02				
Corticosteroids									
Inhaled									
Beclomethasone	1	4	Inhaler 100mcg/200mcg/ 250mcg*	0.8mg	95.05	79.32	86.32	16.5	8.1
Budesonide	1	3	Inhaler 400mcg/200mcg*	0.8mg	87.17	67.65	74.66	22.4	9.4
Fluticasone	1	0	Inhaler 250mcg	0.6mg	186.12				
Corticosteroids									
Oral									
Methylprednisolone	1	0	Tablets 4mg	7.5mg	53.61				
Prednisone	1	3	Tablets 5mg	10mg	148.86	4.53	6.39	97.0	29.1
Prednisolone	0	2	Tablets 5mg	10mg		11.73	12.04		2.6
		2	Syrup 15mg/5ml	10mg		101.92	123.12		17.2
Budesonide	1	0	Capsules MR 3mg	9mg	766.85				
Hydrocortisone	1	0	Tablets 10mg	30mg	86.73				
Xanthines									
Theophylline	1	6	SR Tablets 250mg/300mg*	0.4g	85.48	20.14	28.82	76.4	30.1

* Please note that strengths differ for the originator and generic brands

Table 4.2 shows that Steps one and two (Mild Intermittent and Mild Persistent Asthma) require inhaled short-acting beta2 agonists and inhaled corticosteroids. Out of the six medicines available three (fenoterol, terbutaline and fluticasone) do not have any generic equivalents. For the remaining medicines the number of generic equivalents range from 3 (salbutamol and budesonide) to 4 (beclomethasone).

In steps three and four (Moderate and Severe Persistent Asthma), inhaled long-acting beta2 agonists or sustained release theophylline are mentioned. The number of generic equivalents for the two long-acting beta1 agonists are zero for salmeterol and three for formoterol. Theophylline has six generic

equivalents. Step five (Very severe persistent Asthma) includes oral corticosteroids in the treatment. Of the five medicines available three (methylprednisolone, budesonide and hydrocortisone) have no generic equivalent while prednisone and prednisolone have three and two respectively. However, prednisolone only has generic versions available. Budesonide offered the most expensive option at R766.85 for a month's supply at the DDD. Cost differentials between originator and generics range from 97% (prednisone) to 16.5% (beclomethasone). Cost differentials between generics only range from 54.6% (formoterol) to 2.6% (prednisone).

The public sector STGs for chronic persistent asthma mention the same classes of medicines in most cases. Only salbutamol and fenoterol are included as examples of the short-acting inhaled beta-agonists, and ipratropium as the inhaled anticholinergic. No anticholinergics are specifically mentioned in the CMS algorithm. As shown in the Table 4.2, there is one generic equivalent for this preparation. There is no mention, however, in the public sector STGs of the long-acting variants of the beta2-agonists, and only budesonide is listed as the inhaled steroid.

4.2.3 Bronchiectasis and Chronic Obstructive Pulmonary Disorder

The CMS algorithm is labeled as bronchiectasis, but needs to be read together with that for the management of chronic obstructive pulmonary disorder (COPD), as shown in Appendix A.

Table 4.3 Bronchiectasis and Chronic Obstructive Pulmonary Disorder

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Beta2 agonist -									
Short acting									
Inhalation									
Salbutamol	1	3	Inhaler 100mcg	0.8mg	39.30	20.15	22.67	48.7	11.1
Fenoterol HBr	1	0	Inhaler 100mcg	0.6mg	51.22				
Terbutaline	1	0	Inhaler 0.5mg	2mg	104.72				
Beta2 agonist -									
Long acting									
Formoterol	1	3	Inhaler 12mcg	24mcg	217.93	72.96	160.81	66.5	54.6
Salmeterol xinaforte	1	0	Inhaler 25mcg	0.1mg	230.02				
Corticosteroids									
Oral									
Prednisone	1	3	Tablets 5mg	10mg	148.86	4.53	6.39	97.0	29.1
Xanthines									
Theophylline	1	6	SR Tablets 250mg/ 300mg*	0.4g	85.48	20.14	28.82	76.4	30.1
Anticholinergics									
Ipratropium Bromide	1	1	Inhaler 40mcg	0.12mg	30.39	23.94		21.2	
Antibiotics									
Amoxycillin	1	14	Capsules 500mg	1g	350.39	17.09	17.10	95.1	0.1
	1	10	Suspension 125mg/5ml /250mg/5ml*	1g	490.70	37.55	40.36	92.3	7.0
Doxycycline**	0	3	Capsules 100mg	0.1g		9.99	10.78		7.3
	0	2	Tablets 100mg	0.1g		19.49	19.67		0.9

* Please note that strengths differ for the originator and generic brands

Table 4.3 indicates that Bronchiectasis treatment follows the algorithm for Chronic Obstructive Pulmonary Disease with the exception of the addition of antibiotics for the treatment of an infection (see Appendix A). Inhaled Beta2 agonists (short- and long-acting) consist of five medicines where three have no generic equivalents (fenoterol, terbutaline and salmeterol) and the remaining two have three generic equivalents each. The number of generic equivalents of the remaining five medicines range from 1 (ipratropium bromide) to 14 (amoxycillin). Amoxycillin has a large number of indications and is a commonly prescribed antibiotic (Carrie *et al.*, 2000). The originator for doxycycline (Vibraycin) is no longer manufactured. Cost differentials between originator and generics range from 97% (prednisone) to 21.2% (ipratropium bromide). Cost

differentials between generics only range from 54.6% (formoterol) to 0.1% (amoxicillin).

The public sector algorithm, in essence, mirrors that of the CMS for COPD. The same medicines are mentioned – salbutamol, fenoterol or ipratropium as inhaled agents, oral slow-release theophylline and oral prednisone. The appropriate antibiotics for treatment of infected cases is less well described.

4.2.4 Cardiac Failure

The CMS CDL algorithm is an example of a less prescriptive variant, in that six different pharmacological groups (see Appendix A) are mentioned, which include a total of 27 different medicines. Broadly, this mirrors the equivalent algorithm from the public sector STGs. There is, however, a major difference in meaning when each mentions a class or even an example within the class. In the case of the public sector, it is understood that the provinces will procure only one example from that class. In contrast, unless a medical scheme has an appropriately implemented formulary system, it will have to reimburse claims for any members of the class, regardless of the price.

Table 4.4 Cardiac Failure

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
ACE Inhibitors									
Captopril	1	7	Tablets 25mg/50mg*	50mg	153.38	7.04	16.00	95.4	56.0
Enalapril	1	6	Tablets 20mg	10mg	39.46	23.93	23.94	39.4	0.0
Benzapril	1	0	Tablets 20mg	7.5mg	72.07				
Cilazapril	1	0	Tablets 5mg	2.5mg	59.97				
Fosinopril	1	1	Tablets 20mg	15mg	133.14	86.53		35.0	
Moexipril	0	1	Tablets 15mg	15mg		127.67			
Perindopril	1	1	Tablets 10mg/4mg*	4mg	114.00	100.90		11.5	
Quinapril	1	1	Tablets 40mg/20mg*	15mg	126.88	84.47		33.4	
Ramipril	1	1	Tablets 2.5mg/1.25mg*	2.5mg	129.65	45.19	110.00	65.1	58.9
	1	5	Capsules 10mg	2.5mg	51.51	25.76	25.76	50.0	0.0
Trandolapril	1	0	Capsules 2mg	2mg	100.90				
Lisinopril	1	8	Tablets 20mg	10mg	35.02	22.70	27.93	35.2	18.7
Beta Blockers									
Atenolol	1	7	Tablets 100mg	75mg	153.05	17.83	18.60	88.4	4.1
Carvedilol	1	4	Tablets 25mg	37.5mg	149.74	87.60	103.46	41.5	15.3
Propranolol	1	4	Tablets 40mg	0.16g	324.93	11.65	15.05	96.4	22.6
Nadolol	1	0	Tablets 80mg	0.16g	376.68				
Sotalol	1	1	Tablets 160mg	0.16g	165.31	55.85		66.2	
Acebutolol	1	0	Tablets 400mg	0.4g	190.23				
	1	0	Capsules 200mg	0.4g	235.93				
Bisoprolol	1	2	Tablets 10mg	10mg	100.00	59.28	60.01	40.7	1.2
Metoprolol	1	0	Tablets 100mg	0.15g	286.00				
Nebivolol	1	0	Tablets 5mg	5mg	129.22				
Cardiac Glycosides									
Digoxin	1	1	Tablets 0.25mg	0.25mg	7.91	8.14		-2.9	
	1	0	Injection 0.5mg/2ml	0.25mg	197.57				
	1	0	Elixir 0.05mg/ml	0.25mg	149.15				
Thiazide diurectics									
Hydrochlorothiazide	0	2	Tablets 25mg	25mg		7.87	15.84		50.3
Loop diurectics									
Furosemide	1	7	Tablets 40mg	40mg	87.40	2.31	2.56	97.4	9.8
	1	5	Injection 10mg/ml / 20mg/2ml*	40mg	567.17	116.28	133.38	79.5	12.8
Torasemide	1	0	Tablets 10mg	15mg	174.66				
Butnetanide	1	0	Tablets 1mg	1mg	88.08				
Piretanide	1	0	Tablets 3mg	6mg	119.72				
Aldosterone Antagonists									
Spironolactone	1	2	Tablets 100mg/25mg*	75mg	139.44	68.40	68.40	50.9	0.0

* Please note that strengths differ for the originator and generic brands

Within the ACE Inhibitor group (see Table 4.4) the number of generic equivalents range from 1 (e.g. fosinopril) to 8 (lisinopril). Moexipril is itself a generic while three other medicines have no generic available. Cost differentials between the originator and generics within this group range from 95% (captopril) to 11.5% (perindopril).

Beta blockers include nine of the 27 medicines, five of which have generics available ranging from 1 (sotalol) to 7 (atenolol) and four with no generics. Cost differentials within this group range from 96% (propanolol) to 41% (bisoprolol).

Of the remaining medicines only one medicine in the Loop diurectic group has a significant number of generics available. Furosemide has seven generic equivalents for oral medication and five for parenteral route of administration. The cost differentials are 97% and 80% respectively. The remaining three medicines in this group have no generic equivalents available.

Cost differentials between generics range from 58.9% (ramipril) to 0% (spironolactone).

4.4.5 Cardiomyopathy

Table 4.5 shows that the CMS CDL algorithm for Cardiomyopathy (see Appendix A) follows closely to the CMS CDL algorithm for Cardiac Failure. If a patient is truly intolerant to ACE inhibitors, hydralazine and isorbide dinitrate combination therapy may be considered. Cardiomyopathy differs from Cardiac Failure by the inclusion of warfarin, nitrates, vasodilator and potassium supplement. The ACE inhibitors, beta blockers, digoxin, diuretics and spironolactone were discussed under Cardiac Failure above.

Table 4.5 Cardiomyopathy

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Vitamin K Antagonist									
Warfarin	1	0	Tablets 5mg	7.5mg	49.43				
ACE Inhibitors									
Captopril	1	7	Tablets 25mg/50mg*	50mg	153.38	7.04	16.00	95.4	56.0
Enalapril	1	6	Tablets 20mg	10mg	39.46	23.93	23.94	39.4	0.0
Benzapril	1	0	Tablets 20mg	7.5mg	72.07				
Cilazapril	1	0	Tablets 5mg	2.5mg	59.97				
Fosinopril	1	1	Tablets 20mg	15mg	133.14	86.53		35.0	
Moexipril	0	1	Tablets 15mg	15mg		127.67			
Perindopril	1	1	Tablets 10mg/4mg*	4mg	114.00	100.90		11.5	
Quinapril	1	1	Tablets 40mg/20mg*	15mg	126.88	84.47		33.4	
Ramipril	1	1	Tablets 2.5mg/1.25mg*	2.5mg	129.65	45.19	110.00	65.1	58.9
	1	5	Capsules 10mg	2.5mg	51.51	25.76	25.76	50.0	0.0
Trandolapril	1	0	Capsules 2mg	2mg	100.90				
Lisinopril	1	8	Tablets 20mg	10mg	35.02	22.70	27.93	35.2	18.7
Beta Blockers									
Atenolol	1	7	Tablets 100mg	75mg	153.05	17.83	18.60	88.4	4.1
Carvedilol	1	4	Tablets 25mg	37.5mg	149.74	87.60	103.46	41.5	15.3
Propranolol	1	4	Tablets 40mg	0.16g	324.93	11.65	15.05	96.4	22.6
Nadolol	1	0	Tablets 80mg	0.16g	376.68				
Sotalol	1	1	Tablets 160mg	0.16g	165.31	55.85		66.2	
Acebutolol	1	0	Tablets 400mg	0.4g	190.23				
	1	0	Capsules 200mg	0.4g	235.93				
Bisoprolol	1	2	Tablets 10mg	10mg	100.00	59.28	60.01	40.7	1.2
Metoprolol	1	0	Tablets 100mg	0.15g	286.00				
Nebivolol	1	0	Tablets 5mg	5mg	129.22				
Cardiac Glycosides									
Digoxin	1	1	Tablets 0.25mg	0.25mg	7.91	8.14		-2.9	
	1	0	Injection 0.5mg/2ml	0.25mg	197.57				
	1	0	Elixir 0.05mg/ml	0.25mg	149.15				
Thiazide diurectics									
Hydrochlorothiazide	0	2	Tablets 25mg	25mg		7.87	15.84		50.3
Loop diurectics									
Furosemide	1	7	Tablets 40mg	40mg	87.40	2.31	2.56	97.4	9.8
	1	5	Injection 10mg/ml / 20mg/2ml*	40mg	567.17	116.28	133.38	79.5	12.8
Torasemide	1	0	Tablets 10mg	15mg	174.66				
Butnetanide	1	0	Tablets 1mg	1mg	88.08				
Piretanide	1	0	Tablets 3mg	6mg	119.72				
Aldosterone Antagonists									
Spironolactone	1	2	Tablets 100mg/25mg*	75mg	139.44	68.40	68.40	50.9	0.0
Nitrates									
Isosorbide dinitrate	1	1	Sublingual 5mg	20mg	68.40	56.33		17.6	
	1	1	Tablets 10mg/30mg*	60mg	91.50	59.86		34.6	
	1	0	SR Tablets 40mg	60mg	153.42				
Potassium supplements									
Potassium chloride	1	2	Tablets 600mg	3g	121.78	105.45	105.54	13.4	0.1
Vasodilators									
Hydralazine	1	2	Tablets 25mg/50mg*	0.1g	277.29	29.53	32.31	89.4	8.6
								41.5	9.8

* Please note that strengths differ for the originator and generic brands

Warfarin does not have a generic. Isosorbide dinitrate has one generic each for sublingual tablets and tablets and no generic for the sustained release tablet. Potassium chloride and vasodilators both have two generics. The cost differentials between the originator and generics across the drugs discussed here range from 90% (hydralazine) to 13.4% (potassium chloride).

The public sector has no specific equivalent algorithm for cardiomyopathy, and this is subsumed under the heading of cardiac failure syndrome.

4.2.6 Chronic Renal Disease

Table 4.6 Chronic Renal Disease

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
ACE Inhibitors									
Captopril	1	7	Tablets 25mg / 50mg*	50mg	153.38	7.04	16.00	95.4	56.0
Enalapril	1	6	Tablets 20mg	10mg	39.46	23.93	23.94	39.4	0.0
Benzapril	1	0	Tablets 20mg	7.5mg	72.07				
Cilazapril	1	0	Tablets 5mg	2.5mg	59.97				
Fosinopril	1	1	Tablets 20mg	15mg	133.14	86.53		35.0	
Moexipril	0	1	Tablets 15mg	15mg		127.67			
Perindopril	1	1	Tablets 10mg / 4mg*	4mg	114.00	100.90		11.5	
Quinapril	1	1	Tablets 40mg / 20mg*	15mg	126.88	84.47		33.4	
Ramipril	1	1	Tablets 2.5mg / 1.25mg*	2.5mg	129.65	45.19	110.00	65.1	58.9
	1	5	Capsules 10mg	2.5mg	51.51	25.76	25.76	50.0	0.0
Trandolapril	1	0	Capsules 2mg	2mg	100.90				
Lisinopril	1	8	Tablets 20mg	10mg	35.02	22.70	27.93	35.2	18.7
Beta Blockers									
Atenolol	1	7	Tablets 100mg	75mg	153.05	17.83	18.60	88.4	4.1
Carvedilol	1	4	Tablets 25mg	37.5mg	149.74	87.60	103.46	41.5	15.3
Propranolol	1	4	Tablets 40mg	0.16g	324.93	11.65	15.05	96.4	22.6
Nadolol	1	0	Tablets 80mg	0.16g	376.68				
Sotalol	1	1	Tablets 160mg	0.16g	165.31	55.85		66.2	
Acebutolol	1	0	Tablets 400mg	0.4g	190.23				
	1	0	Capsules 200mg	0.4g	235.93				
Bisoprolol	1	2	Tablets 10mg	10mg	100.00	59.28	60.01	40.7	1.2
Metoprolol	1	0	Tablets 100mg	0.15g	286.00				
Nebivolol	1	0	Tablets 5mg	5mg	129.22				
Thiazide diurectics									
Hydrochlorothiazide	0	2	Tablets 25mg	25mg		7.87	15.84		50.3
Selective Calcium Channel blockers									
Nifedipine (ex. Adalat XL)	1	2	Tablets 20mg	30mg	281.20	25.61	26.16	90.9	2.1
(Adalat XL)	1	0	Tablets 60mg	30mg	120.76				
	1	0	Capsules 30mg	30mg	115.22				
Amlodipine	1	3	Tablets 10mg	5mg	72.29	54.22	56.43	25.0	3.9
Felodipine	1	1	Tablets 10mg	5mg	109.16	55.34		49.3	
Isradipine	1	0	Tablets 2.5mg	5mg	200.00				
Lercanidipine	0	1	Tablets 10mg	10mg		121.53			
Phosphate binder									
Calcium carbonate	0	1	Tablets 300mg	3g	544.12				

* Please note that strengths differ for the originator and generic brands

The CMS CDL algorithm mentions four therapeutic groups for the treatment of Chronic Renal Disease (see Appendix A). Table 4.6 shows that within the ACE Inhibitor group the number of generic equivalents range from 1 (e.g. fosinopril) to 8 (lisinopril). Moexipril only has a generic version available while three other medicines have no generic available. Cost differentials between the originator and generics within this group range from 95% (captopril) to 11.5% (perindopril).

Beta blockers include nine different drugs, five of which have generics available ranging from 1 (sotalol) to 7 (atenolol) and four with no generics. Cost differentials within this group range from 96% (propanolol) to 41% (bisoprolol).

Calcium channel blockers mentioned in the algorithm consist of five different drugs. The originator drug for lercanidipine is no longer available and isradipine does not have a generic. Cost differentials within this group range from 91% (nifedipine) to 25% amlodipine). Erythropoietin is mentioned in the algorithm but the DDD cannot be determined. The adult dose as indicated in the SAMF was used to calculate the amount required for a month. From this calculation an approximate cost per month can be determined.

In contrast, the public sector STGs focus more on acute renal insufficiency, mentioning the use of furosemide, the ACE Inhibitor (giving as an example, ramipril), the calcium channel blockers (listing verapamil as the example), as well as the alpha blocker (e.g. prazosin). The chronic renal failure STG also mentions a wide range of complications, such as hyperphosphataemia, anaemia (specifically mentioning the use of epoetin alfa {erythropoietin}, but stating that this should be prescribed by a specialist only, on a named patient basis), hyperparathyroidism, aluminum toxicity and acidosis. In contrast, the CMS binds every medical scheme to the provision of an expensive agent, stipulating that in cases of iron therapy failure, erythropoietin must be reimbursed if the patient's haemoglobin is below eight gm/dl.

4.2.7 Coronary Artery Disease

Hyperlipidaemia, Diabetes Mellitus and Hypertension occur frequently with Coronary Artery Disease and these chronic conditions must be managed as per the disease-specific algorithm (see Appendix A). Four therapeutic groups are mentioned in the algorithm with a total of 19 medicines between them.

Table 4.7 Coronary Artery Disease

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Beta Blockers									
Atenolol	1	7	Tablets 100mg	75mg	153.05	17.83	18.60	88.4	4.1
Carvedilol	1	4	Tablets 25mg	37.5mg	149.74	87.60	103.46	41.5	15.3
Propranolol	1	4	Tablets 40mg	0.16g	324.93	11.65	15.05	96.4	22.6
Nadolol	1	0	Tablets 80mg	0.16g	376.68				
Sotalol	1	1	Tablets 160mg	0.16g	165.31	55.85		66.2	
Acebutolol	1	0	Tablets 400mg	0.4g	190.23				
	1	0	Capsules 200mg	0.4g	235.93				
Bisoprolol	1	2	Tablets 10mg	10mg	100.00	59.28	60.01	40.7	1.2
Metoprolol	1	0	Tablets 100mg	0.15g	286.00				
Nebivolol	1	0	Tablets 5mg	5mg	129.22				
Nitrates									
Glyceyl Trinitrate	0	1	Tablets 0.5mg	5mg		183.59			
	0	1	Atomiser 0.4mg	2.5mg		1254.61			
	1	1	Inject 50mg/50ml	2.5mg	172.04	191.55		-11.3	
Isosorbide dinitrate	1	1	Sublingual 5mg	20mg	68.40	56.33		17.6	
	1	1	Tablets 10mg/30mg*	60mg	91.50	59.86		34.6	
	1	0	SR Tablets 40mg	60mg	153.42				
Isosorbide mononitrate	1	3	Tablets 20mg/60mg/ 20mg*	40mg	137.82	78.80	85.68	42.8	8.0
	1	0	Tablets LA 50mg	40mg	75.29				
Platelet Aggregation Inhibitors									
Aspirin	1	1	Tablets EC	1 tab	17.10	13.92		18.6	
	0	2	Tablets EC 100mg/125mg/81mg*	1 tab		1.83	18.24		90.0
Selective Ca+ Channel blockers									
Dihydropyridine derivatives									
Nifedipine (ex.Adalat XL)	1	2	Tablets 20mg	30mg	281.20	25.61	26.16	90.9	2.1
(Adalat XL)	1	0	Tablets 60mg	30mg	120.76				
	1	0	Capsules 30mg	30mg	115.22				
Amlodipine	1	3	Tablets 10mg	5mg	72.29	54.22	56.43	25.0	3.9
Felodipine	1	1	Tablets 10mg	5mg	109.16	55.34		49.3	
Isradipine	1	0	Tablets 2.5mg	5mg	200.00				
Lercanidipine	0	1	Tablets 10mg	10mg		121.53			

* Please note that strengths differ for the originator and generic brands

As can be seen in Table 4.7 Atenolol had the highest number of generics available i.e. seven while seven drugs have no generics available. The originator drugs for glyceryl trinitrate and lercanidipine are no longer manufactured. Within the nitrates group, glyceryl trinitrate's generic for the parenteral route of administration is more expensive than the originator by 11%. Cost differentials between all originator and generic drugs mentioned ranged from 97% (propanolol) to 18% (isosorbide dinitrate).

The public sector equivalent can be found under the heading of chronic stable angina pectoris, which lists the nitrates, beta blockers, calcium channel blockers and aspirin. In the case of the calcium channel blockers, the examples cited are the older, off-patent, cardiac selective types, verapamil and diltiazem. In contrast, the CMS algorithm calls for the long-acting dihydropyridine type. These are often more expensive, and generic equivalence is controversial. As the first of these, the long-acting formulations of nifedipine, are listed as non-substitutable by the Medicines Control Council (Medicines Control Council, 2006).

4.2.8 Crohn's Disease

The CMS CDL algorithm for Crohn's disease (see Appendix A) made mention of 13 medicines for the three stages of management: perianal disease, in remission and active disease.

Table 4.8 Crohn's Disease

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Disease modifying anti-rheumatic drugs									
Methotrexate	1	0	Tablets 2.5mg	2.5mg	30.52				
Immunosuppressive agents									
Azathioprine	1	3	Tablets 50mg	0.15g	929.79	153.90	409.43	83.4	62.4
Oral Corticosteroids									
Methylprednisolone	1	0	Tablets 4mg	7.5mg	53.61				
Prednisone	1	3	Tablets 5mg	10mg	148.86	4.53	6.39	97.0	29.1
Prednisolone	0	2	Tablets 5mg	10mg		11.73	12.04		2.6
		2	Syrup 15mg/5ml	10mg		101.92	123.12		17.2
Budesonide	1	0	Capsules MR 3mg	9mg	766.85				
Hydrocortisone	1	0	Tablets 10mg	30mg	86.73				
IV Corticosteroids									
Methylprednisolone	1	0	Injection 80mg/ml	20mg	428.70				
Intestinal anti-inflammatories									
Mesalazine	1	1	Tablets 400mg/500mg*	1.5g	406.91	297.14		27.0	
Olsalazine	1	0	Capsules 250mg	1g	311.25				
Sulfasalazine	1	0	Tablets 500mg	2g	281.94				
Fluroquinolone - Quinolone									
Ciprofloxacin	1	14	Tablets 500mg	1g	588.51	81.72	82.42	86.1	0.8
Agents agianst Amoebiasis									
Metronidazole	1	17	Tablets 200mg/400mg*	2g	397.51	12.41	13.66	96.9	9.2
	1	1	Suspension 200mg/5ml	2g	1165.37	641.25		45.0	
	1	2	Injection 500mg/100ml	1.5g	2534.22	1530.79	1530.79	39.6	0.0

* Please note that strengths differ for the originator and generic brands

Table 4.8 shows that only two medicines are listed for perianal disease and they have 14 (ciprofloxacin) and 17 (metronidazole) generic equivalents. One medicine only (prednisolone) has generic versions while seven do not have any generic equivalents at all. The number of generic equivalents for the remaining drugs ranged from 1 (mesalazine) to 3 (prednisone). Cost differentials between originator and generics ranged from 97% (prednisone and metronidazole) to 27% (mesalazine). The cost differential between the two generics of prednisolone is 17.2% for syrup and 2.6% for tablets.

The public sector STG lists an altogether narrower set of alternatives, ranging from the symptomatic (loperamide, codeine phosphate, vitamin and mineral supplementation, metronidazole), to simple disease modifying agents (sulfasalazine, prednisone – though including the prednisolone sodium phosphate retention enemas) and the older antineoplastics (azathioprine, methotrexate).

4.2.9 Diabetes Insipidus

Table 4.9 shows that there is only one drug (desmopressin) mentioned in the CMS CDL algorithm for diabetes insipidus (see Appendix A) and there is no generic equivalent. Cost savings cannot be attained. The same medicine is listed by the public sector.

Table 4.9 Diabetes Insipidus

					Price of DDD for 1 month (VAT inclusive) (R)				
	No. of originator	No. of generics	Presentation and Strength	DDD	Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Desmopressin	1	0	Tablets 0.2mg	0.4mg	797.75				
	1	0	Nasal spray 10mcg/0.1ml	25mcg	830.21				
	1	0	Injection 4mcg/ml	4mcg	1808.74				

4.2.10 Diabetes Type 1

This is a rapidly expanding area of medicine, with new forms of insulin reaching the market. These are often of marginal benefit but markedly more expensive. An algorithm that doesn't specify the type of insulin to be reimbursed therefore places the scheme at risk, unless effective managed care measures (such as a formulary) are in place.

Table 4.10 Diabetes Type 1

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Insulin									
Ultra fast acting	1	1	Injection 100units/mL	40IU	307.88	247.95		19.5	
	1	0	Injection 100units/mL	40IU	247.95				
Fast acting *	1	0	Injection 100units/mL	40IU	251.53				
	1	0	Injection 100units/mL	40IU	249.51				
Intermediate to long acting	1	0	Injection 100units/mL	40IU	249.51				
	1	0	Injection 100units/mL	40IU	251.53				
	1	0	Injection 100units/mL	40IU	30.536				
Long acting	1	0	Injection 100units/mL	40IU	415.27				
Biphasic	1	0	Injection 100units/mL	40IU	251.53				
	1	0	Injection 100units/mL	40IU	249.51				
	1	0	Injection 100units/mL	40IU	305.36				
	1	0	Injection 100units/mL	40IU	307.88				
	1	0	Injection 100units/mL	40IU	343.21				

All originators as they are not really interchangeable as 1 yeast based and the other bacteria based

Insulin is the only medicine mentioned for the treatment of diabetes type 1 in the CMS CDL algorithm (see Appendix A). Table 4.10 shows that there are five different types of insulin: ultra fast -, fast - , intermediate to long - , long acting and biphasic. Long acting only has one drug while the remaining insulins range from 2 (fast acting) to 5 different drugs (biphasic). However, only one drug for ultra fast acting insulin has a generic equivalent. The cost differential between the originator and generic is 20%.

The public sector STG uses the same format, but there, as with the ACE-inhibitors and beta-blockers, the expectation is of a province-wide, single selection made by a Pharmacy and Therapeutics Committee.

4.3.11 Diabetes Type 2

Four therapeutic treatments are mentioned in the CMS CDL algorithm for the treatment of diabetes type 2 (see Appendix A). Insulin is one of them and is discussed above under Diabetes Type 1.

Table 4.11 Diabetes Type 2

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Hypoglycaemic agent									
Biguanides									
Metformin	1	6	Tablets 500mg	2g	44.41	36.87	37.74	17.0	2.31
Sulphonamides, urea derivatives									
Glibenclamide	1	5	Tablets 5mg	10mg	205.43	9.9	10.76	95.2	7.99
Gliclazide	1	7	Tablets 80mg	0.16g	73.42	36.84	37.56	49.8	1.92
Glipizide	1	0	Tablets 5mg	10mg	117.14				
Glimepiride	1	3	Tablets 4mg	2mg	106.11	79.57	79.58	25.0	0.01
Thiazolidinediones									
Pioglitazone	1	0	Tablets 30mg	30mg	336.14				
Rosiglitazone	1	0	Tablets 4mg	6mg	283.78				
Insulin									
Ultra fast acting	1	1	Injection 100units/mL	40IU	307.88	247.95		19.5	
	1	0	Injection 100units/mL	40IU	247.95				
Fast acting *	1	0	Injection 100units/mL	40IU	251.53				
	1	0	Injection 100units/mL	40IU	249.51				
Intermediate to long actir	1	0	Injection 100units/mL	40IU	249.51				
	1	0	Injection 100units/mL	40IU	251.53				
	1	0	Injection 100units/mL	40IU	30.536				
Long acting	1	0	Injection 100units/mL	40IU	415.27				
Biphasic	1	0	Injection 100units/mL	40IU	251.53				
	1	0	Injection 100units/mL	40IU	249.51				
	1	0	Injection 100units/mL	40IU	305.36				
	1	0	Injection 100units/mL	40IU	307.88				
	1	0	Injection 100units/mL	40IU	343.21				

Insulin are all originators as they are not really interchangeable as 1 yeast based and the other bacteria based

In the other three therapeutic treatments (see Table 4.11), seven medicines are mentioned of which three are only available from the originator firm. The number of generic equivalents for the remaining four range from 3 (glimepiride)

to 7 (gliclazide). Cost differentials between originator and generic ranges from 95% (glibenclamide) and 17% (metformin).

The CMS algorithm is vague in the way it identifies the entire sulphonylurea class, rather than specific examples within that class. It also, unlike the public sector STGs, includes a newer class for which no generics exist. These are the thiazolidinediones.

4.2.12 Dysrrhythmias

The CMS algorithm in this regard is actually a set of three – covering Chronic Atrial Fibrillation, Chronic Atrial Flutter and Ventricular Tachycardia.

Table 4.12 Dysrrhythmias

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Vitamin K Antagonist									
Warfarin	1	0	Tablets 5mg	7.5mg	49.43				
Beta Blockers									
Atenolol	1	7	Tablets 100mg	75mg	153.05	17.83	18.6	88.4	4.1
Carvedilol	1	4	Tablets 25mg	37.5mg	149.74	87.6	103.46	41.5	15.3
Propranolol	1	4	Tablets 40mg	0.16g	324.93	11.65	15.05	96.4	22.6
Nadolol	1	0	Tablets 80mg	0.16g	376.68				
Sotalol	1	1	Tablets 160mg	0.16g	165.31	55.85		66.2	
Acebutolol	1	0	Tablets 400mg	0.4g	190.23				
	1	0	Capsules 200mg	0.4g	235.93				
Bisoprolol	1	2	Tablets 10mg	10mg	100.00	59.28	60.01	40.7	1.2
Metoprolol	1	0	Tablets 100mg	0.15g	286.00				
Nebivolol	1	0	Tablets 5mg	5mg	129.22				
Cardiac Glycosides									
Digoxin	1	1	Tablets 0.25mg	0.25mg	7.91	8.14		-2.9	
	1	0	Injection 0.5mg/2ml	0.25mg	197.57				
	1	0	Elixir 0.05mg/ml	0.25mg	149.15				
Calcium Channel Blockers with cardiac effects									
Phenylalkylamine derivatives									
Verapamil	1	2	Tablets 40mg	0.24g	110.15	50.82	53.6	53.9	5.2
	1	3	Tablets SR 240mg	0.24g	120	81.94	113.17	31.7	27.6
Antiarrythymics									
Class III									
Amiodarone	1	2	Tablets 200mg	0.2g	371.01	218.29	218.31	41.2	0.0
Platelet Aggregation Inhibitors									
Aspirin	1	1	Tablets EC	1 tab	17.1	13.92		18.6	
	0	2	Tablets EC 100mg/ 125mg/81mg*	1 tab		1.83	18.24		90.0

* Please note that strengths differ for the originator and generic brands

Table 4.12 shows that the generic of digoxin, one of the 14 drugs mentioned in the algorithm for dsyrrhythmias (see Appendix A), is more expensive than the originator by 3%. Of the remaining 13 drugs five have no generic equivalents and seven have generic equivalents ranging from 1 (digoxin) to 7 (atenolol). Cost differentials between originator and generics ranged from 97% (propanolol) to 19% (aspirin). Cost differentials between generics of the same drug ranged from 28% (verapamil) to 0% (amiodarone). The difference in price between the highest and lowest priced beta blocker originators is 66%.

Again, by not identifying specific medicines within a class, the CMS algorithm includes more and less expensive variants, whereas the public sector algorithm is more specific. It includes only propranolol and atenolol as the beta blockers, verapamil as the calcium channel blocker, digoxin, warfarin and amiodarone.

4.2.13 Epilepsy

Table 4.13 Epilepsy

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Hydantoin derivatives									
Phenytoin	1	0	Capsules 100mg	0.3g	130.61				
Benzodiazepine derivatives									
Clonazepam	1	0	Tablets 2mg	8mg	283.30				
Succinimide derivatives									
Ethosuximide	1	0	Capsules 250mg	1.25g	730.85				
Carboxamide derivatives									
Carbamazepine	1	3	Tablets 200mg	1g	341.49	83.51	96.97	75.5	13.9
	1	1	CR Tablets 400mg	1g	335.50	252.23		24.8	
Oxcarbazepine	1	0	Tablets 300mg	1g	352.24				
Other antiepileptics									
Lamotrigine	1	4	Tablets 200mg	0.3g	402.18	307.80	333.45	23.5	7.7
Topiramate	1	0	Tablets 200mg	0.3g	687.22				
Valproic acid									
Valproic acid	1	0	Tablets 500mg	1.5g	504.58				
Sodium valproate	1	0	Tablets 200mg	1.5g	392.40				
Barbiturates and derivatives									
Phenobarbital**	0	2	Tablets 30mg	1g		53.11	96.66		45.1

**Originator no longer manufacturered

The CMS CDL algorithm for epilepsy (see Appendix A) made mention of 10 medicines for the two stages of treatment: primary partial seizures and primary generalized seizures. Table 4.13 shows that 70% of the medicines have no generic equivalents available while one has no originator (phenobarbital). Carbamazepine and lamotrigine have three and four generic equivalents available respectively. The cost differentials between the originator and generics of these two drugs is 75.5% (carbamazepine) and 23.5% (lamotrigine). The cost differential between the two generics of phenobarbital is 45.1%.

Unlike other algorithms, the CMS algorithms for epilepsy is very specific about which medicines are to be reimbursed. That said, it does include a number of newer, more expensive agents that are not provided for in the public sector STGs, which only include phenytoin, carbamazepine, phenobarbitone, sodium valproate, ethosuximide and clonazepam. The additional agents are lamotrigine, topiramate and oxcarbazepine. As with all other CMS algorithms, no justification is given for this deviation from what are considered "essential medicines".

4.2.14 Glaucoma

Of the 12 medicines mentioned in the CMS CDL algorithm for Glaucoma and shown in Table 4.14, only two (timolol and acetazolamide) have a generic equivalent. The remaining 10 are all originator drugs. The cost differential between the originator and generics is 54.8% (acetazolamide) and 42.9% (timolol).

Table 4.14 Glaucoma

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Beta Blocker agents									
Non-selective									
Timolol	1	1	drops 0.25%/0.5%*	0.2ml	84.95	48.54		42.9	
Levobunolol	1	0	drops 0.5%	0.2ml	88.56				
Metipranolol	1	0	drops 0.3%	0.2ml	65.77				
Selective									
Betaxolol	1	0	drops 0.5%	0.2ml	133.33				
Alpha2-agonist									
Sympathomimetics in glaucoma									
Brimonidine	1	0	drops 2mg/mL	0.2ml	152.08				
Apracionidine	1	0	drops 5mg/mL	0.3ml	154.64				
Carbonic Anhydrase Inhibitor									
Acetazolamide	1	1	Tablets 250mg	0.75g	150.72	68.12		54.8	
Dorzolamide	1	0	drops 2%	0.3ml	195.86				
Brinzolamide	1	0	drops 10mg/mL	0.2ml	133.6				
Prostaglandin Analogues									
Latanoprost	1	0	drops 50mcg/mL	0.1ml	181.41				
Bimatoprost	1	0	drops 0.3mg/mL	0.1ml	183.83				
Travoprost	1	0	drops 40mcg/mL	0.1ml	177.27				

* Please note that strengths differ for the originator and generic brands

The greatest contrast between the CMS algorithm and the public sector STGs is again the use of broad classes, in this an example is the statement that topical alpha2-agonists, carbonic anhydrase inhibitors or prostaglandin analogues should be reimbursed. The public sector starts with the older, and potentially cheaper pilocarpine products (drops or gel), and then only includes a beta blocker (in this case, only timolol) and a carbonic anhydrase inhibitor (acetazolamide).

4.2.15 Haemophilia

For Haemophilia A there are three drugs (desmopressin, factor VIII and tranexamic acid) mentioned in the CMS CDL algorithm (see Appendix A) and for Haemophilia B only one drug (factor IX). Table 4.15 shows that there are no generic equivalents for any of these drugs. No public sector equivalent regimen exists.

Table 4.15 Haemophilia

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Haemophilia A									
Desmopressin	1	0	Tablets 0.2mg	0.4mg	797.75				
	1	0	Nasal spray 10mcg/0.1ml	25mcg	830.21				
	1	0	Injection 4mcg/ml	4mcg	1808.74				
Blood Coagulant Factors									
Factor VIII	1	0	Injection	500IU	27974.4				
Antifibrinolytics									
Tranexamic acid	1	0	Tablets 500mg	2g	512.73				
Haemophilia B									
Blood Coagulant Factors									
Factor IX	1	0	Injection 500IU	350IU	24217				

4.2.16 Hyperlipidaemia

Statins and fibrates are the only two therapies mentioned in the CMS CDL algorithm for hyperlipidaemia. There are seven medicines in total, three are only available from the originator firm and one (lovastatin) has no originator drug but one generic equivalent as shown in Table 2.16. The number of generic equivalents for the remaining three range from 1 (bezafibrate) to 8 (simvastatin). Cost differentials between the originator and generics range from 40.4% (pravastatin) to 32.7% (bezafibrate).

Table 4.16 Hyperlipidaemia

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Statins									
Simvastatin	1	8	Tablets 40mg	20mg	85.02	55.58	56.72	34.6	2.0
Atorvastatin	1	0	Tablets 20mg	10mg	124.50				
Fluvastatin	1	0	Capsules 40mg	40mg	156.50				
Lovastatin	0	1	Tablets 40mg	30mg		60.53			
Pravastatin	1	3	Tablets 40mg	20mg	126.14	75.20	75.24	40.4	0.1
Frbrates									
Bezafibrate	1	1	Tablets 200mg/400mg*	0.6g	304.88	205.18		32.7	
Gemfibrozil	1	0	Tablets 300mg	1.2g	233.47				

* Please note that strengths differ for the originator and generic brands

The equivalent public sector STG is labeled as dyslipidaemias, and is vague to the point of not mentioning anything other than that the "Principles of drug treatment" include "the rational use of hyperlipidaemic drugs – efficacy, proven effects, cost, side effects, additional benefits and comparisons" and that "classes of drugs to be used singly or in combination". According to the Department of Health (1998a), four million people in South Africa in 1998 had untreated hyperlipidaemia. Given the prevalence of this condition, considered an important contributory factor to deaths from coronary heart disease and strokes in the South African population, this is a remarkable omission (Department of Health, 1998A).

4.2.17 Hypertension

ACE Inhibitors, beta blockers and calcium channel blockers are discussed under Chronic Renal Disease section 4.2.6. Diuretics are discussed under Cardiac Failure in section 4.2.4.

Table 4.17 Hypertension

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Thiazide diurectics									
Hydrochlorothiazide	0	2	Tablets 25mg	25mg		7.87	15.84		50.3
Diurectics (ex. Thiazides)									
Indapamide	1	8	Tablets 2.5mg	2.5mg	95.32	6.18	6.24	93.5	1.0
Chlortalidone	1	0	Tablets 50mg	25mg	90.75				
Loop diurectics									
Furosemide	1	7	Tablets 40mg	40mg	87.40	2.31	2.56	97.4	9.8
	1	5	Injection 10mg/ml / 20mg/2ml*	40mg	567.17	116.28	133.38	79.5	12.8
Torasemide	1	0	Tablets 10mg	15mg	174.66				
Butnetanide	1	0	Tablets 1mg	1mg	88.08				
Piretanide	1	0	Tablets 3mg	6mg	119.72				
Aldosterone Antagonists									
Spironolactone	1	2	Tablets 100mg/25mg*	75mg	139.44	68.40	68.40	50.9	0.0
ACE Inhibitors									
Captopril	1	7	Tablets 25mg/50mg*	50mg	153.38	7.04	16.00	95.4	56.0
Enalapril	1	6	Tablets 20mg	10mg	39.46	23.93	23.94	39.4	0.0
Benzapril	1	0	Tablets 20mg	7.5mg	72.07				
Cilazapril	1	0	Tablets 5mg	2.5mg	59.97				
Fosinopril	1	1	Tablets 20mg	15mg	133.14	86.53		35.0	
Moexipril	0	1	Tablets 15mg	15mg		127.67			
Perindopril	1	1	Tablets 10mg/4mg*	4mg	114.00	100.90		11.5	
Quinapril	1	1	Tablets 40mg/20mg*	15mg	126.88	84.47		33.4	
Ramipril	1	1	Tablets 2.5mg/1.25mg*	2.5mg	129.65	45.19	110.00	65.1	58.9
	1	5	Capsules 10mg	2.5mg	51.51	25.76	25.76	50.0	0.0

Table 4.17 Hypertension continued.

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
ACE Inhibitors contd.									
Trandolapril	1	0	Capsules 2mg	2mg	100.90				
Lisinopril	1	8	Tablets 20mg	10mg	35.02	22.70	27.93	35.2	18.7
Alpha-adrenoreceptor antagonists									
Prazosin	1	0	Tablets 5mg	5mg	93.45				
Terazosin	1	0	Tablets 10mg	5mg	261.18				
Beta Blockers									
Atenolol	1	7	Tablets 100mg	75mg	153.05	17.83	18.60	88.4	4.1
Carvedilol	1	4	Tablets 25mg	37.5mg	149.74	87.60	103.46	41.5	15.3
Propranolol	1	4	Tablets 40mg	0.16g	324.93	11.65	15.05	96.4	22.6
Nadolol	1	0	Tablets 80mg	0.16g	376.68				
Sotalol	1	1	Tablets 160mg	0.16g	165.31	55.85		66.2	
Acebutolol	1	0	Tablets 400mg	0.4g	190.23				
	1	0	Capsules 200mg	0.4g	235.93				
Bisoprolol	1	2	Tablets 10mg	10mg	100.00	59.28	60.01	40.7	1.2
Metoprolol	1	0	Tablets 100mg	0.15g	286.00				
Nebivolol	1	0	Tablets 5mg	5mg	129.22				
Dihydropyridine derivatives									
Nifedipine (ex. Adalat	1	2	Tablets 20mg	30mg	281.20	25.61	26.16	90.9	2.1
(Adalat XL)	1	0	Tablets 60mg	30mg	120.76				
	0	1	Capsules 30mg	30mg	115.22				
Amlodipine	1	3	Tablets 10mg	5mg	72.29	54.22	56.43	25.0	3.9
Felodipine	1	1	Tablets 10mg	5mg	109.16	55.34		49.3	
Isradipine	1	0	Tablets 2.5mg	5mg	200.00				
Lercanidipine	0	1	Tablets 10mg	10mg	121.53				
Calcium Channel Blockers with cardiac effects									
Phenylalkylamine derivatives									
Verapamil	1	2	Tablets 40mg	0.24g	110.15	50.82	53.60	53.9	5.2
	1	3	Tablets SR 240mg	0.24g	120.00	81.94	113.17	31.7	27.6
Benzothiazepine derivatives									
Diltiazem	1	3	Tablets 60mg	0.25g	403.10	115.83	137.75	71.3	15.9
	1	1	Tablets CR 240mg	0.25g	211.32	154.01		27.1	
Angiotensin II Antagonists									
Losartan	1	0	Tablets 50mg	50mg	189.13				
Candesartan	1	0	Tablets 16mg	8mg	84.14				
Eprosartan	1	0	Tablets 600mg	0.6g	178.34				
Irbesartan	1	0	Tablets 300mg	0.15g	96.37				
Telmisartan	1	0	Tablets 80mg	40mg	93.1				
Valsartan	1	0	Tablets 160mg	80mg	91				

* Please note that strengths differ for the originator and generic brands

As shown in Table 4.17 there are six drugs within the angiotensin-receptor blockers group and two drugs in the alpha-blocker group mentioned in the algorithm for Hypertension (see Appendix A). None of these drugs have a generic. The cost differentials between the originators and generics of all therapeutic groups range from 97.4% (furosemide) to 11.5% (perindopril).

As with a number of other algorithms (notably for diabetes), the CMS algorithm only mentions classes, not specific medicines within those classes. The most notable difference between this and the equivalent public sector STG is the inclusion of the angiotensin-receptor blockers (ARBs), for which no generics are available. No motivation is given for the inclusion of the ARBs in the table (see Appendix A) of co-morbid conditions, where at times they appear as alternatives to ACE inhibitors and at times do not. ARBs are listed as alternatives to ACE inhibitors in patients with diabetes but not other co-morbid conditions.

4.2.18 Hypothyroidism

Table 4.18 shows that there is only one drug (levothyroxine sodium) mentioned in the CMS CDL algorithm for Hypothyroidism (see Appendix A) and there is no generic equivalent. The same medicine is prescribed in the public sector STG for this condition.

Table 4.18 Hypothyroidism

					Price of DDD for 1 month (VAT inclusive) (R)				
	No. of originator	No. of generics	Presentation and Strength	DDD	Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Levothyroxine sodium	1	0	Tablets 100mcg	0.15mcg	37.02				

4.2.19 Multiple Sclerosis

The CMS CDL algorithm for multiple sclerosis made mention of eight medicines for various stages of management (See Appendix A): symptomatic, acute relapse and frequent relapse.

Table 4.19 Multiple Sclerosis

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Muscle relaxants - centrally acting agents									
Baclofen	1	1	Tablets 25mg/10mg*	50mg	900.67	667.93		25.8	
IV Corticosteroids									
Methylprednisolone	1	0	Injection 80mg/ml	20mg	428.70				
Antidepressants									
Amitryptyline	1	2	Tablets 25mg	75mg	226.67	43.85	44.99	80.7	2.5
Imipramine	1	1	Tablets 25mg	0.1g	257.53	37.51		85.4	
Interferon Beta									
Interferon beta-1a	1	1	Injection 44mcg/0.5ml	4.3mcg	6477.94	1836.96		71.6	
Urinary Antispasmodics									
Oxybutynin	1	4	Tablets 5mg	15mg	320.36	87.77	88.18	72.6	0.5
Carboxamide derivatives									
Carbamazepine	1	3	Tablets 200mg	1g	341.49	83.51	96.97	75.5	13.9
Opiod Analgesic									
Morphine	1	1	Tablets 60mg	30mg	167.80	160.16		4.6	
	0	3	Injection 15mg/ml	30mg		119.15	170.32		30.0

* Please note that strengths differ for the originator and generic brands

Table 4.19 shows that of the six medicines listed for symptomatic management, all had a least one generic equivalent. The number of generic equivalents ranged from 1 (baclofen) to 4 (oxybutynin). In one case (morphine IV) only generic versions were available. Cost differentials between originator and generics ranged from 85% (imipramine) to 4.6% (morphine). However both single medicines listed for relapse were available from only the originator firm. Of these, beta interferon represented the most expensive option.

This condition is not included in the public sector STG/EDLs.

4.2.20 Parkinson's Disease

This CMS algorithm (see Appendix 2), unlike many others, is notable for not including a number of new treatments that are available for this distressing condition (such as entacapone and tolcapone). Instead, it broadly mirrors the public sector STG, which lists benzhexol, orphenadrine, levodopa/benserazide and levodopa/carbidopa.

Table 4.20 Parkinson's Disease

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Anticholinergic agents									
Trihexyphenidyl	1	0	Tablets 2mg	10mg	106.50				
Biperiden	1	0	Tablets 2mg	10mg	290.01				
	1	0	Injection 5mg.mL	10mg	1660.07				
Dopaminergic agents									
Adamantane derivatives									
Amantadine	1	1	Capsules 100mg	0.2g	474.25	219.02		53.8	
Dopamine Agonists									
Pramipexole	1	0	Tablets 1mg	2.5mg	770.70				
Ropinirole	1	0	Tablets 5mg	6mg	245.22				
Monamine oxidase type b inhibitors									
Selegiline	1	0	Tablets 5mg	5mg	323.81				
Dopa derivatives									
Carbidopa + Levodopa	1	1	Tablets (25mg/250mg)	0.6g	326.18	261.04		20.0	

* Please note that strengths differ for the originator and generic brands

Of the seven medicines mentioned in the CMS CDL algorithm for Parkinson's disease, only two (admantane and combination carbidopa and levodopa) have a generic equivalent as shown in Table 4.20. The remaining five are all originator drugs. The cost differential between the originator and generics is 53.8% (adamantine) and 20% (carbidopa / levodopa combination).

4.2.21 Rheumatoid Arthritis

Table 4.21 Rheumatoid Arthritis

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Disease modifying anti-rheumatic drugs									
Methotrexate	1	0	Tablets 2.5mg	2.5mg	30.52				
Sufasalazine	1	0	Tablets 500mg	2g	281.94				
Leflunomide	1	0	Tablets 20mg	20mg	573.83				
Other Disease modifying agents									
Immunosuppressive agents									
Azathioprine	1	3	Tablets 50mg	0.15g	929.79	153.90	409.43	83.4	62.41
Penicillamine									
Penicillamine	1	0	Tablets 300mg	0.5g	816.69				
Oral Corticosteroids									
Methylprednisolone	1	0	Tablets 4mg	7.5mg	53.61				
Prednisone	1	3	Tablets 5mg	10mg	148.86	4.53	6.39	97.0	29.1
Prednisolone	0	2	Tablets 5mg	10mg		11.73	12.04		2.6
		2	Syrup 15mg/5ml	10mg		101.92	123.12		17.2
Budesonide	1	0	Capsules MR 3mg	9mg	766.85				
Hydrocortisone	1	0	Tablets 10mg	30mg	86.73				
IV Corticosteroids									
Methylprednisolone	1	0	Injection 80mg/ml	20mg	428.70				
Non-steroidal anti-inflammatory drugs									
Acetic acid derivatives									
Diclofenac sodium	1	11	Tablets 25mg/50mg*	0.1g	92.37	7.03	7.91	92.4	11.1
	1	1	Suppositories 100mg	0.1g	253.56	129.65		48.9	
	1	9	Injection 75mg/3ml	0.1g	224.49	21.60	21.82	90.4	1.0
	0	2	Capsules SR 100mg/ 75mg**	0.1g		60.08	75.72		20.7
Indometacin	0	12	Capsules 25mg	0.1g		7.89	9.12		13.5
	1	1	Suppositories 100mg	0.1g	355.34	133.72			
	0	2	Capsules SR 75mg	0.1g		37.05	56.74		
Ketorolac	1	0	Tablets 10mg	30mg	472.86				
Sulindac	0	1	Tablets 200mg	0.4g	170.27				
Oxicams									
Lormoxicam	1	0	Tablets 8mg	12mg	158.67				
Meloxicam	1	7	Tablets 15mg/7.5mg*	15mg	209.89	41.84	53.58	80.1	21.9
Piroxicam***	0	5	Capsules 20mg	20mg		13.06	14.88		12.2
	0	1	Tablets 20mg	20mg		69.52			
	0	4	Dispersible Tablets 20mg	20mg		18.71	20.78		10.0
Tenoxicam	1	0	Tablets 20mg	20mg	294.44				
Propionic acid derivatives									
Ibuprofen	1	10	Tablets 400mg / 200mg*	1.2g	81.02	12.75	14.27	84.3	10.7
Naproxen	0	6	Tablets 250mg	0.5g		13.67	18.04		24.2
Ketoprofen	1	1	Capsules SR 200mg	0.15g	133.20	47.03			
Other Inflammatory agents									
Nabumetone	1	2	Tablets 500mg	1g	225.49	84.00	115.03	62.7	27.0

* Please note that strengths differ for the originator and generic brands

The CMS CDL algorithm for rheumatoid arthritis mentions three therapeutic groups for the treatment of this disease (see Appendix A): non-steroidal anti-inflammatory drugs (NSAID), corticosteroids and disease modifying anti-rheumatic drugs (DMARD). Table 4.21 shows that of the 12 medicines listed for NSAIDs, four have no originator drugs but only generic equivalents (e.g. piroxicam), three have no generic equivalents (e.g. ketorolac) and the remaining five have both originator and generic equivalents with the number of generics ranging from 1 (ketoprofen) to 11 (diclofenac sodium). Corticosteroids all have generic equivalents except for one (methylprednisolone) while one (prednisolone) does not have an originator but two generic equivalents. Within the DMARD group only one drug (azathioprine) has generic equivalents out of the five drugs mentioned in the algorithm. Of these five drugs, penicillamine offered the most expensive option. The cost differentials between the originator and generics for all groups ranged from 97% (prednisone) to 48.9% (diclofenac sodium).

The CMS algorithm includes only one of the newer agents in this field, leflunomide. Even this agent, which has no generic equivalent, is not included in the public sector STG. This only lists paracetamol (with or without codeine phosphate), indometacin or ibuprofen as the NSAID examples, and then chloroquine, sulfasalazine, azathioprine and methotrexate as the DMARDs. A range of steroids (e,g, prednisolone) are also provided for in this STG.

4.2.22 Schizophrenia

Table 4.22 Schizophrenia

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Antipsychotic drugs - Typical									
Phenoithiazines with alphatic side-chain									
Chloropromazine	1	2	Injection 50mg/2mL	0.3g	653.63	119.02	560.13	81.8	78.8
	1	0	Tablets 100mg	0.3g	290.42				
Phenothiazines with piperazine									
Fluphenazine	1	0	Injection 25mg/mL	1mg	15.20				
Prochlorperazine	1	2	Tablets 5mg	0.1g	1088.65	63.53	261.23	94.2	75.7
	1	0	Injection 12.5mg/mL	50mg	996.18				
Trifluoperazine	1	0	Tablets 1mg	20mg	248.31				
Butyrophenone									
Haloperidol	1	1	Tablets 5mg	6mg	125.33	38.92		68.9	
Thioxanthene derivatives									
Flupentixol	1	0	Tablets 1mg	6mg	1241.25				
	1	0	Injection depot 20mg/ml	4mg	269.76				
Zuclopenthixol	1	0	Tablets 10mg	30mg	166.09				
	1	0	Injection depot 20mg/ml	15mg	221.65				
Benzamides									
Sulpiride	1	2	Capsules 50mg	0.8g	917.11	485.31	485.48	47.1	0.0
	1	0	Tablets Forte 200mg	0.8g	700.85				
Amisulpiride	1	0	Tablets 200mg	0.4g	817.22				
Antipsychotic drugs - atypical									
Clozapine	1	2	Tablets 100mg	0.3g	700.31	505.31	505.31	27.8	0.0
Olanzapine	1	0	Tablets 10mg	10mg	1179.63				
Risperidone	1	0	Tablets 4mg	5mg	1322.57				
Quetiapine	1	0	Tablets 200mg	0.4g	1020.36				
Ziprasidone	1	0	Capsules 80mg	80mg	607.25				
Mood stablisers									
Lithoium carbonate	1	0	Tablets 400mg	1.8g	298.72				
	1	0	Tablets 450mg retard	1.8g	312.88				
Antidepressants									
Amitryptyline	1	2	Tablets 25mg	75mg	226.67	43.85	44.99	80.7	2.5
Imipramine	1	1	Tablets 25mg	0.1g	257.53	37.51		85.4	
Clomipramine	1	2	Tablets 25mg	0.1g	530.51	226.08	236.99	57.4	4.6
Dosulepin	1	2	Tablets 75mg	0.15g	281.56	156.66	156.76	44.4	0.1
	1	2	Capsules 25mg	0.15g	283.61	143.93	144.01	49.3	0.1
Lofepramine	1	0	Tablets 75mg	0.105g	109.53				
Trimipramine	1	1	Capsules 50mg	0.15g	555.75	237.35		57.3	

Of the 21 medicines mentioned in the CMS CDL algorithm for Schizophrenia, 10 are only available from the originator firm (see Table 4.22). The maximum number of generic equivalents available for the remaining medicines is two (e.g. clozapine). Cost differentials between the originator and generics ranged from 94.2% (prochlorperazine) to 27.8% (clozapine).

As with many others, the CMS algorithm for this condition makes use of very wide descriptors of medicine classes - typical antipsychotic or atypical antipsychotic, mood stabilizer and antidepressant. This places a medical scheme at increased risk of exposure to claims for newer, patented products which may not offer a clinical advantage.

In the public sector STG, in contrast, a very limited range of medicines is included: haloperidol, lorazepam, zuclopenthixol, chlorpromazine, fluphenazine, flupentixol decanoate, and, for the management of extrapyramidal side effects, biperiden.

4.2.23 Systemic Lupus Erythematosus

All of the drugs mentioned in the CMS CDL algorithm for systemic lupus erythematosus are also mentioned in the CMS CDL algorithm for rheumatoid arthritis (see Appendix A).

Table 4.23 Systemic Lupus Erythematosus

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
Non-steroidal anti-inflammatory drugs									
Propionic acid derivatives									
Ibuprofen	1	10	Tablets 400mg/200mg*	1.2g	81.02	12.75	14.27	84.3	10.7
Naproxen	0	6	Tablets 250mg	0.5g		13.67	18.04		24.2
Ketoprofen	1	1	Capsules SR 200mg	0.15g	133.20	47.03			
Acetic acid derivatives and related substances									
Diclofenac sodium	1	11	Tablets 25mg/50mg*	0.1g	92.37	7.03	7.91	92.4	11.1
	1	1	Suppositories 100mg	0.1g	253.56	129.65		48.9	
	1	9	Injection 75mg/3ml	0.1g	224.49	21.60	21.82	90.4	1.0
	0	2	Capsules SR 100mg/75mg**	0.1g		60.08	75.72		20.7
Indometacin	0	12	Capsules 25mg	0.1g		7.89	9.12		13.5
	1	1	Suppositories 100mg	0.1g	355.34	133.72			
	0	2	Capsules SR 75mg	0.1g		37.05	56.74		
Ketorolac	1	0	Tablets 10mg	30mg	472.86				
Sulindac	0	1	Tablets 200mg	0.4g	170.27				
Oxicams									
Lormoxicam	1	0	Tablets 8mg	12mg	158.67				
Meloxicam	1	7	Tablets 15mg/7.5mg*	15mg	209.89	41.84	53.58	80.1	21.9
Piroxicam***	0	5	Capsules 20mg	20mg		13.06	14.88		12.2
	0	1	Tablets 20mg	20mg		69.52			
	0	4	Dispersible Tablets 20mg	20mg		18.71	20.78		10.0
Tenoxicam	1	0	Tablets 20mg	20mg	294.44				
Oral Corticosteroids									
Methylprednisolone	1	0	Tablets 4mg	7.5mg	53.61				
Prednisone	1	3	Tablets 5mg	10mg	148.86	4.53	6.39	97.0	29.1
Prednisolone	0	2	Tablets 5mg	10mg		11.73	12.04		2.6
		2	Syrup 15mg/5ml	10mg		101.92	123.12		17.2
Budesonide	1	0	Capsules MR 3mg	9mg	766.85				
Hydrocortisone	1	0	Tablets 10mg	30mg	86.73				
IV Corticosteroids									
Methylprednisolone	1	0	Injection 80mg/ml	20mg	428.70				
Disease modifying amnt-rheumatic drugs									
Methotrexate	1	0	Tablets 2.5mg	2.5mg	30.52				
Salicyclic Acid									
Aspirin	1	3	Tablets 300mg	1 Tab	13.32	1.88	2.07	85.9	9.2

* Please note that strengths differ for the originator and generic brands

Table 4.23 shows that the cost differentials between the originator and generics for all groups ranged from 97% (prednisone) to 48.9% (diclofenac sodium).

The equivalent public sector algorithm is far more restrictive, mentioning only prednisone, azathioprine, cyclophosphamide and chloroquine.

4.2.24 Ulcerative Colitis

There are only three therapeutic groups of medicines mentioned in the ulcerative colitis CMS CDL algorithm for the treatment of the two stages of the disease: proctosigmoiditis and extensive colitis.

Table 4.24 Ulcerative Colitis

	No. of originator	No. of generics	Presentation and Strength	DDD	Price of DDD for 1 month (VAT inclusive) (R)				
					Originator Price (X)	Lowest generic price (Y)	Next lowest generic price (Z)	% diff between X and Y	% diff between Y and Z
5-aminosalicyclic acid agents (5-ASA)									
Intestinal anti-inflammatories									
Mesalazine	1	1	Tablets 400mg / 500mg*	1.5g	406.91	297.14		27.0	
	1	0	Suppositories 500mg	1.5g	958.54				
	1	0	Retention enema 2g/50mL	1.5g	2228.99				
Olsalazine	1	0	Capsules 250mg	1g	311.25				
Sulfasalazine	1	0	Tablets 500mg	2g	281.94				
Corticosteroid enemas									
Budesonide	1	0	Retention enema 2mg/100ml	1	1619.42				
Oral Corticosteroids									
Methylprednisolone	1	0	Tablets 4mg	7.5mg	53.61				
Prednisone	1	3	Tablets 5mg	10mg	148.86	4.53	6.39	97.0	29.1
Prednisolone	0	2	Tablets 5mg	10mg		11.73	12.04		2.6
		2	Syrup 15mg/5ml	10mg		101.92	123.12		17.2
Budesonide	1	0	Capsules MR 3mg	9mg	766.85				
Hydrocortisone	1	0	Tablets 10mg	30mg	86.73				
IV Corticosteroids									
Methylprednisolone	1	0	Injection 80mg/ml	20mg	428.70				
Immunosuppressive agents									
Azathioprine	1	3	Tablets 50mg	0.15g	929.79	153.90	409.43	83.4	62.4

* Please note that strengths differ for the originator and generic brands

Table 4.24 shows that the three therapeutic groups consist of 11 medicines of which seven have no generic equivalents. One drug (prednisolone) has no originator but two generic equivalents. The number of generic equivalents for the other three medicines range from 1 (mesalazine) to 3 (azathioprine). The cost differential between the originator and generics of prednisone is high at 97% while the lowest cost differential is 27% (mesalazine).

The public sector STG is presented as for Crohn's disease.

4.3 Discussion

The results presented above need to be placed in the context of the entire market. The relative contribution to beneficiaries payments of each of the chronic diseases provided for in the Prescribed Minimum Benefits is known from the annual report produced by the CMS (see Introduction), but more accurate figures on the numbers of patients receiving each medicine mentioned in the CMS CDL algorithms are, at this stage, not easily accessible. Modeling the possible impact of greater degrees of generic substitution is thus not easy.

Across all medicines supplied to medical scheme members, some indication of generic penetration of the market can be gleaned from individual medical scheme administrators' reports. For example, Mediscor has reported that, in 2005, the generic utilization rate increased to 43.7% (from 40.2% in 2004) in volume terms (Bester *et al.*, 2005). In 2000, generic medicines made up about 30% of the value of global sales of medicines. While in value terms generic penetration was noted in that report to be higher in some developing countries (e.g. 71% in Bangladesh, based on 2000 data), in volume terms South Africa would seem to be approaching a global maximum (World Health Organisation, 2004). Although the data are somewhat dated, it is notable that a generic utilisation rate, in volume terms, of just under 50% seems the most that can be achieved, across a range of health system designs (WHO, 2004). The WHO World Medicines Situation (2004) reported that, based on 1998 data, generic

utilisation by volume was 45% in the United States, 47% in the United Kingdom and 40% in Canada. That this was the result of deliberate policy stances and interventions was also clearly demonstrated by the rank outlier in this regard; in 1996 only 3% of prescription volume in France was for generic medicines (WHO, 2004).

4.3.1 Chronic Diseases with no generics available

It would seem that those conditions on the CMS CDL which account for a very low percentage of total CDL gross costs, suggesting a very low prevalence within the population, do not attract a large number of generic competitors. In such cases, no generic-friendly policy can result in cost saving by the patient. The diseases that fall within this category were:

(a) Diabetes Insipidus - this disease is ranked 26 (out of 27) according to the percentage of total Chronic Disease List Cost, Quarter 4 2005 while the percentage prevalence of diabetes insipidus is the second lowest with 0.003% of the population infected. There are no generics available and the gross cost per patient per month is an average of R370.

(b) Haemophilia - is ranked 23 out of 27 according to the percentage of total Chronic Disease List Cost, Quarter 4 2005 with the percentage prevalence the lowest with 0.0002% of the population infected. However, the gross cost per patient per month based on the DDD methodology is approximately R20 000, which is ten times the next highest cost for a disease (multiple sclerosis) on the CDL. This is an artefact of the DDD methodology, as the quantity used for utilisation research bears little resemblance to a clinically relevant dose for this indication as discussed in section 3.5.1.

(c) Hypothyroidism - although ranked 11 out of 27, the cost per patient per month (R37.02) is small while the prevalence is relatively high at 1.4% of

the population. There are no generics for the drug of choice, which is levothyroxine sodium.

Table 4.25 Chronic disease ranked according to the percentage of total CDL cost and their prevalence, Quarter 4 2005. (adapted from Mediscor Medicines Review 2005)

Chronic Disease	Rank	% Prevalence
Hypertension	1	6.4
Hyperlipideamia	2	3.3
Diabetes Type II	3	1.5
Asthma	4	1.0
Diabetes Type I	5	0.3
HIV/AIDS	6	0.4
Coronary artery disease	7	1.3
Epilepsy	8	0.4
Chronic renal failure	9	0.04
Cardiac failure	10	04
Hypothyroidism	11	1.4
Glaucoma	12	0.3
Parkinson's disease	13	0.1
Cardiomyopathy	14	0.2
Rheumatoid arthritis	15	0.2
COPD	16	0.1
Dysrrhythmias	17	0.2
Multiple sclerosis	18	0.01
Schizophrenia	19	0.04
Ulcerative colitis	20	0.04
Bipolar mood disorder	21	0.04
Crohn's disease	22	0.02
Haemophilia	23	0.0002
Systemic lupus erythematosus	24	0.01
Bronchiectasis	25	0.01
Diabetes Insipidus	26	0.003
Addison's disease	27	0.01

A mean cannot be weighted against prevalence as no strong reliable data exists. The data from Mediscor Medicines Review (Bester *et al.*, 2005) is obtained by analyzing claims processed by the Mediscor Pharmaceutical Benefit Management (see Table 4.25) . The data supplied in the latest Council of Medical Schemes Health Report (2006) should be used with caution. The Report states "There were other concerns with this data. For instances, during 2005 certain schemes reported as much as half the cases seen in 2004; in some cases this was due to a change in definitional criteria for chronic diseases. This data should therefore be interpreted with great caution" (Council for Medical Schemes, 2006). In light of this the median of cost differentials was used to produce graphs for the discussion.

4.3.2 Cost differential median between originator drugs and generic equivalents per chronic disease

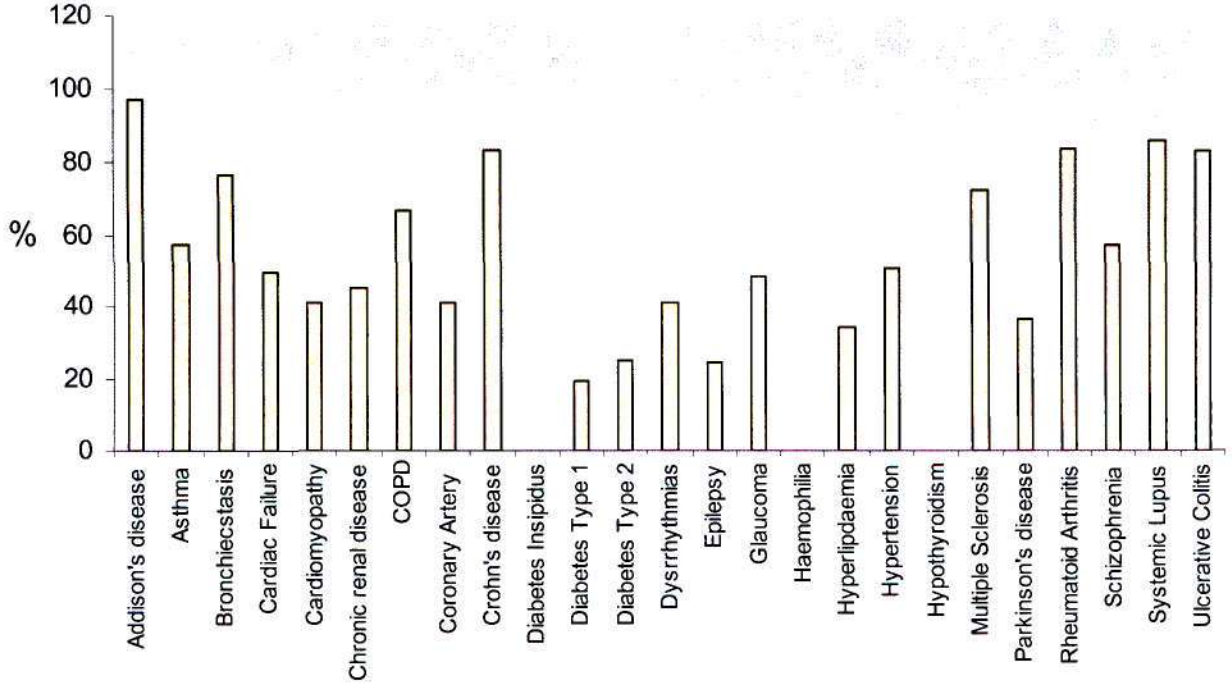

Figure 4.1 Cost differential median between originator and generic equivalents per chronic disease.

The median of the cost differentials between originator and generic equivalents was calculated for each disease and is shown in Figure 4.1. Three of the diseases stipulated did not have any medicines with generic equivalents to compare (see 4.3.1). The median cost differential of the remaining 22 chronic conditions ranges from 19.5% for Type 1 diabetes mellitus to 97% for Addison's disease although only one generic equivalent was available for each. Taking the cost differentials throughout the whole range of chronic diseases the overall cost differential median is 49.9% (22 diseases, 80 drugs with generic equivalents). This could be interpreted as meaning that, by using generics, the patient has the potential to save up to 49.9% on the cost of medicines (inter quartile range 32 to 78.5%). Such an interpretation ignores the prevalence of each condition. Accordingly, it does not correspond to that reported by Djolov (2003), who used an arithmetical view and sales value of the top 200 selling drugs to determine potential saving. A previous study by Karim *et al.* (1996) showed a savings of only 6.8% by substituting generics for prescribed drugs. In addition to the consideration of the differences in methods employed, interpretation of these results must take into account the contribution of a variety of factors, including:

- patent expiries and new generic entrants in recent years
- changes in the policy environment, especially since 2003, when an offer of generic substitution became mandatory
- changes in medicine pricing practices since the single exit price became applicable in 2004.

Karim *et al.* (1996) felt that restrictive prescribing and dispensing practices resulted in the low cost differential. However, this study, by using the SEP of the drug per chronic condition shows potential savings ranging from 0% to as much as 97% before it moves along the distribution chain.

4.3.3 Cost differential median between generic equivalents per chronic disease

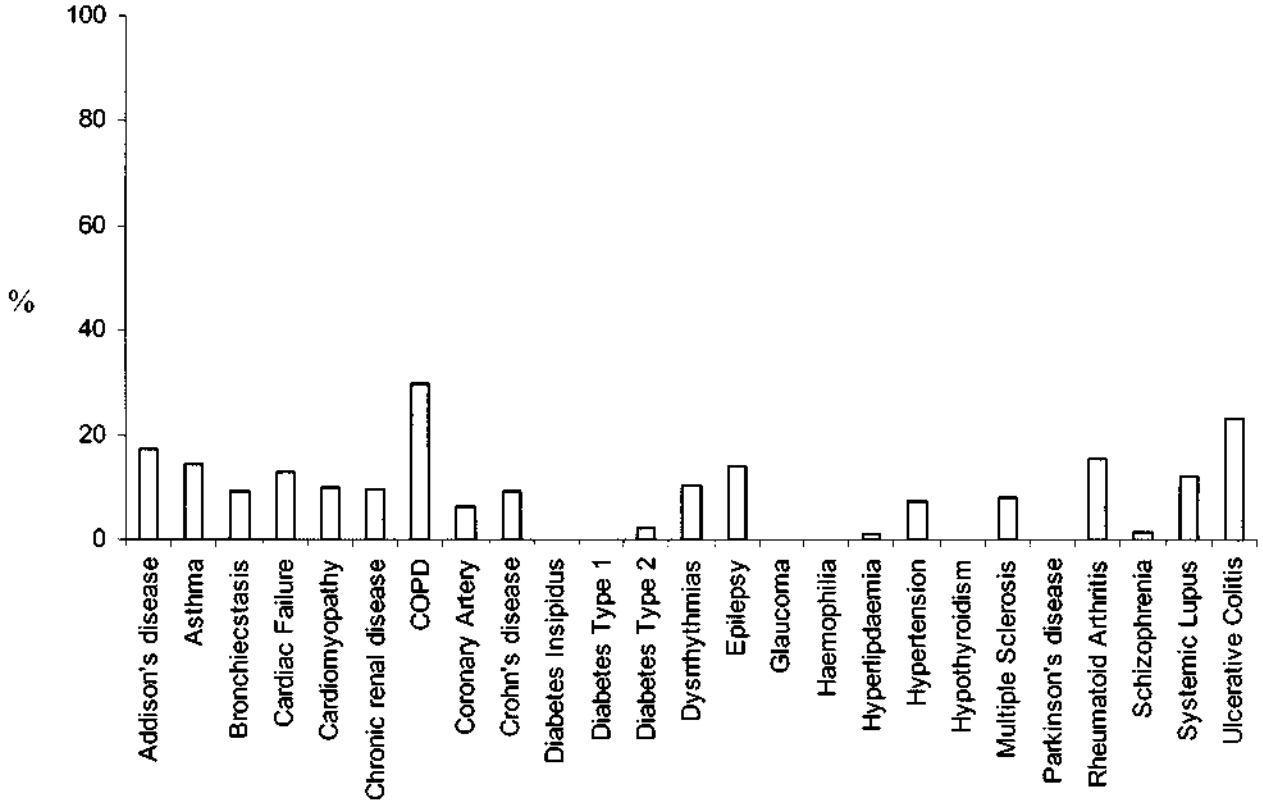

Figure 4.2 Median of the cost differential between generic equivalents per chronic disease.

The median cost differential of only the generic equivalents per chronic disease was calculated. Six of the chronic diseases did not have more than one generic to compare. Figure 4.2 shows that the cost differentials median of the remaining 19 diseases range from 0% (see Table 4.26) to 90% (aspirin – Coronary Artery Disease). Taking the cost differentials of only generics throughout the whole range of chronic diseases gives an overall cost differential median of 9.2% (19 diseases, 74 drugs with more than one generic equivalent) (inter quartile range from 1.38 to 21.6%).

4.3.4 Cost differentials – brands and generics

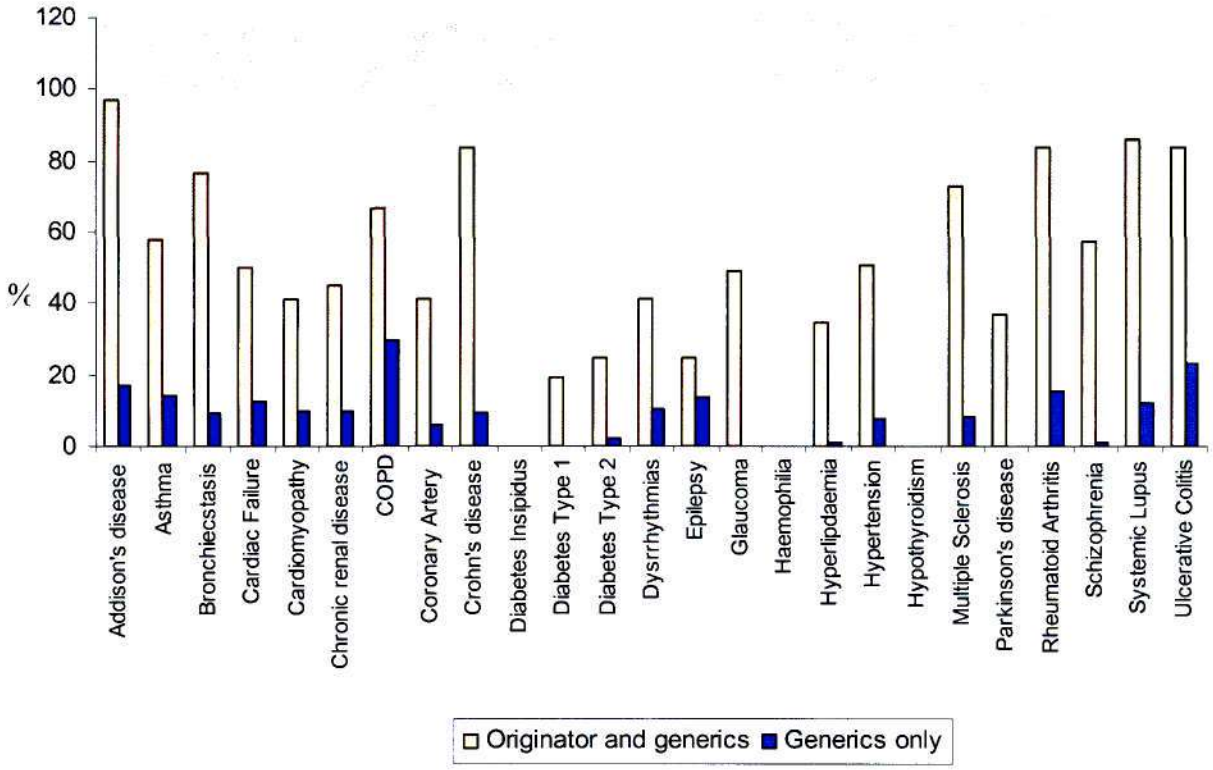

Figure 4.3 Median of the cost differential between originator and generic equivalents vs. median of the cost differential between generics only.

Figure 4.3 shows that the median cost differentials between originators and generics are greater than the median cost differential between generics only. To some extent, this may be explained if one accepts the argument made by industry-friendly analysts (DiMasi *et al.*, 2003). According to this approach, the higher cost of innovator medicines is explained by the cost of research and development and the need to recoup this expense. Even if this argument is accepted, it is difficult to understand that such amortization has not occurred by the time the patent expires and generic competitors reach the market. A continued price differential after patent expiry to some extent reflects the residual brand loyalty attached to a product, and thus the premium consumers are willing to pay for that particular brand (Pearce, 2006) . To some extent it also reflects continued costs of marketing such a brand aggressively. That a smaller cost differential exists between generic competitors is easier to explain,

as these are differentiated in the market largely on the basis of cost. Input costs in this segment of the market are also expected to be more similar, and competition would result in margins that are closer to one another. This may, on the other hand, point to anti-competitive behaviour in this market. There are cases throughout the 25 chronic diseases where the cost differential of the generic equivalent for a particular drug is between 0 and 1% (see Table 4.26). This points to the possibility of price collusion between generic producing companies.

Table 4.26 Cost differential of between 0 and 1% of generic equivalents.

Drug	Cost differential between generics (%)
Amoxicillin capsules 500mg	0.1
Doxycycline Tablets 100mg	0.9
Enalapril Tablets 20mg	0
Ramipril Capsules 10mg	0
Ciprofloxacin Tablets 500mg	0.9
Metronidazole 500mg/100ml	0
Glimepiride Tablets 4mg	0
Amiodarone Tablets 200mg	0
Pravastatin Tablets 40mg	0.1
Indapamide Tablets 2.5mg	1
Spironolactone Tablets 25mg	0
Oxybutynin Tablets 5mg	0.5
Sulpiride Capsules 50mg	0
Clozapine Tablets 100mg	0
Clomipramine Tablets 25mg	0.1
Dosulepin Tablets 75mg	0.1

The Department of Health (DOH) is planning to introduce an international benchmarking exercise in 2007. Innovator products will be compared with their exact equivalents in four comparator markets (Canada, Australia, New Zealand,

Spain). South African prices will not be allowed to exceed the lowest price available in this basket of countries. Thereafter, generic prices will be compared, and will be required to be at least 40% less than the innovator price. This may have the adverse effect of setting a price floor, rather than a ceiling, as competitors set prices that meet, but do not necessarily exceed, the benchmark.

Competition theory would seem to support a contention that the cost differential between the innovator and the lowest priced generic would be related to the number of generic equivalents in the market. It is received wisdom in this field that the maximal cost differentials are only achieved when at least nine products are in the market (Gray, A. pers. comm.). In order to test this contention, within the narrow sample of medicines used in the management of chronic conditions, the cost differentials were plotted against the corresponding number of generic equivalents.

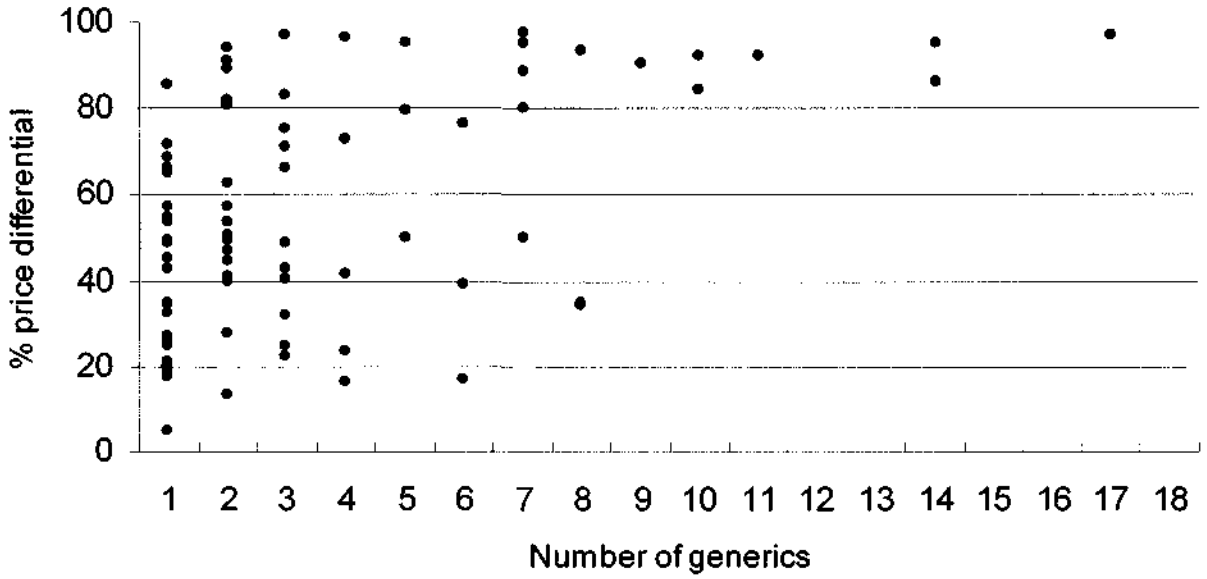

Figure 4.4 Percentage cost differentials vs. number of generic equivalents available.

Figure 4.4 shows that there are many originators with one or two generic equivalents with price differentials below 60%. It does seem, at least visually, that the greater the number of generic equivalents, the higher the cost differential. The correlation coefficient is, however, not entirely convincing, at only 0.49. There are examples of high cost differentials in highly competitive areas of this market – for example, metronidazole has 17 generic equivalents with a cost differential of 96.9% (see Table 4.27). There are exceptions. Drugs with a small number of generics may occasionally display high cost differentials (imipramine has one generic equivalent with a cost differential of 85.4% - see Table 4.19).

Table 4.27 Breakdown of percentage cost differentials by number of generic equivalents.

			Mean cost differentials %					
Number of generics	Total Number of drugs	Median % cost differential	<=20%	>20% <=40%	>40% <=60%	>60% <=80%	>80% <=100%	Total %
1	25	35.0	20	32	28	16	4	100
2	17	50.9	6	12	47	6	29	100
3	12	45.8	0	33	25	25	17	100
4	5	41.5	20	20	20	20	20	100
5	3	79.5	0	0	33.3	33.3	33.4	100
6	3	39.4	33.3	33.3	0	33.4	0	100
7	5	88.4	0	0	20	0	80	100
8	3	35.2	0	66.7	0	0	33.3	100
9	1	90.4	0	0	0	0	100	100
10	2	88.3	0	0	0	0	100	100
11	1	92.4	0	0	0	0	100	100
14	2	90.6	0	0	0	0	100	100
17	1	96.9	0	0	0	0	100	100

Table 4.27 shows that the median cost differential for the total number of drugs with generic equivalents is 49.9% (inter quartile ranges from 34.1 to 81) and the mean is 55.4%. Sixty-seven percent of all cost differentials between originator

and generics are greater than the Department of Health's proposed 40% benchmark. The setting of this low benchmark may lead to an increase in the price of generics as manufacturers may use the 40% as the highest and not lowest cost differential allowed.

4.4 Conclusion

This chapter analysed and presented the information of the data gathered by means of tables and graphs. The results show that there are large cost differentials between originator drugs and their generic equivalents and smaller cost differentials between generics themselves. The results and analysis of the above will aid in making recommendations in the next chapter on how to improve potential cost savings in chronic diseases.

CHAPTER 5 : RECOMMENDATION AND CONCLUSION

5.1 Introduction

This study assesses the potential savings of substituting generics for brand name (originator) drugs within the chronic disease algorithms as set out by the Council for Medical Schemes. The study begins with the research idea which generated a problem statement. Chapter One outlines the framework of the study and objectives were set. The main objective critical to this study was to determine whether there was the potential for cost savings by looking at the number of generics available for the treatment of each chronic condition and to establish, by means of the single exit price (SEP) and the Defined Daily Dose (DDD) of each drug, whether there are price differentials between the generic and the brand name drug as well as between generic medicines themselves.

Chapter Two discusses the current literature with reference to other research that has been conducted pertaining to the study. An insight into how other people have approached their research was also discussed. A look at the current situation in South Africa today with regard to generic substitution and cost savings was included. Chapter Three looks at the research methodology used to meet the objective and the reasoning behind the use of specific data. Chapter Four is the presentation and analyses in tabular and graphical form of the data obtained from the Pharmaceutical Blue Book, the SAMF, the MIMS, the DDDs and the Algorithms. From these chapters recommendations to promote cost savings are proposed.

5.2 Strategies to lower the cost of medicines

It has been argued that the pricing section of the National Drug Policy was not well developed in 1996 (Gray and Matsebula, 2000). The aim of the policy was clear enough – "To promote the availability of safe and effective drugs at the

lowest possible cost". How this was to be achieved was less clear. The policy document was less developed in respect of how prices would be controlled or, at least, how downward pressure on prices would be exerted apart from the introduction of "transparency". Some sort of reference pricing was envisaged, if not spelled out in detail. In fact, the State was committed to an intervention which has not been realised:

- "Where the State deems that the retail prices of certain pharmaceuticals are unacceptable and that these pharmaceuticals are essential to the well being of any sector of the population, the State will make them available to the private sector at acquisition cost plus the transaction costs involved." (Department of Health, 1996).

The generic policy was more simply stated:

- "The availability of generic, essential drugs will be encouraged through the implementation of incentives that favour generic drugs and their production in the country."

- "The policy will aim at achieving generic prescribing in both the public and private sectors. Until this aim is achieved, generic substitution will be allowed, through legislation, in the public and the private sector. It will be incumbent on the pharmacist, prior to dispensing a prescription, to inform the patient on the benefits of generic substitution and to ensure that substitution takes place with the patient's full understanding and consent."

- "Patients have the right to make informed decisions concerning their own health, including a choice for generic drugs."

- "A regularly updated list of products that cannot be substituted will be prepared and disseminated by the MCC."

(Department of Health, 1996)

Although no specific industrial policies have emerged, the concept of mandatory offer of generic substitution has been enshrined in South African law, and patients' rights to an informed choice have been preserved in this system. The Medicines Control Council has produced two versions of the non-substitutable list, but is at present reconsidering this issue.

However, the aims of the NDP have not been fulfilled and much more can be done by Government to promote the availability of cheaper generics by implementing price controls, encouraging the production of generics and reviewing their policies.

5.2.1 Price Controls

While it is true that the cost of a medicine increases the further it moves along the distribution chain, all links in that chain need to be addressed if any price intervention is to be effective. The situation in South Africa is, at the present time, somewhat confusing. Virtually all links in this chain, from wholesalers to managed care drug distributors and pharmacies, are profiting before the generic medicines reach the patients. It may well be that consumers only receive a fraction of the cost differential found in this study for a particular medicine. The South African Government has, over the past three years, attempted to introduce a complex set of dispensing fees. Even at this late stage, there are statements that the livelihoods of pharmacies are in question, as they cannot make enough profit from the dispensing fee stipulated and that, therefore, many will face closure (Minister of Health and Another v New Clicks South Africa (Pty) Ltd and Others, 2005). It is stated that this is especially problematic in rural areas where easy access to medicines will be compromised.

Less controversial, but particularly effective, has been government's intervention in relation to the ex-manufacturer cost of medicines, the single exit price. When initially introduced in 2004, the pricing regulations required manufacturers to set their single exit prices at the weighted mean of all private

sector prices in 2003, taking into account all discounts and rebates offered at that time. Comment has recently been invited in the next step in the process. Draft Regulations were published on 1 December 2006, providing for a "Methodology for International Benchmarking of the Prices of Medicines and Scheduled Substances in South Africa". It is proposed that innovator products be compared, product by product, with their exact equivalents sold in Australia, New Zealand, Canada and Spain. The South African price will not be allowed to exceed the lowest price from that basket of countries. The relevant section of the proposed methodology for generic medicines reads as follows:

"The benchmarking will be done one month after the SEP has been published for the originator medicines. The South African ex-manufacturer price shall be used as a basis for benchmarking. The benchmark price (ex-manufacturer) for generic medicines shall be at least 40% lower than the ex-manufacturer of the originator medicine. The benchmark price will become the new maximum manufacturer price." (Medicines and Related Substances Act, 2006).

There is the risk that, in the absence of strong competition in a particular therapeutic area, the cost differential will be set by this process at 40%, and will not exceed that level. Preserving competition will depend on having more than one generic equivalent to every innovator, where possible in terms of patent law.

5.2.2 Barriers to entry and drug importation

In economics and especially in the theory of competition, barriers to entry are obstacles in the path of a firm which wants to enter a given market. In particular, in the pharmaceutical industry, barriers to entry include Government regulations, patents, customer loyalty, advertising and research and development. The patent system creates a monopoly-like power which results in very high prices.

A number of provisions exist that can weaken this stranglehold. The Medicines Act has already been amended to allow for parallel importation of medicines, based on the principle of international exhaustion of patent rights. Parallel importation would allow the importation of a drug, cheaper in another country, to be resold in South Africa, without authorization of the original seller. This would allow Government to search for the lowest world price.

The Patents Act (Patents Act of South Africa, 1978) also makes provision for compulsory licensing. The Government could issue a license to a local company for a patented drug manufactured by a large pharmaceutical company. This local company would then manufacture the drug for sale in South Africa under a generic name and it would pay a reasonable royalty to the patent holder.

Interestingly, neither of these provisions has been put into effect in South Africa. No parallel traded medicines have been marketed in the three years since section 15C of the 1997 amended Medicines and Related Substances Control Act 1965 (Medicines and Related Substances Act, 1965) became operable. This could be due to the bureaucratic barriers provided for in that section and the accompanying regulations, or it could be due to an inability to secure large enough volume suppliers of lower cost patented medicines in countries with acceptable medicines regulatory standards. Bolar provisions (whereby manufacturers of generic pharmaceuticals use the technology of a patented drug to perform work that would assist in the marketing or regulatory approval of the generic product, while the patent is in force) have been created in local patent law, and do, to some extent, aid generic entry.

The greatest barriers to new generic entrants would, however, seem to be in the more traditional areas that are specific to the pharmaceutical industry. Long delays in obtaining marketing authorisation, high costs of imported technology and a lack of incentives from government would seem to be the dominant factors at play. Despite the NDP promise to "support the development of the

local pharmaceutical industry and the local production of essential drugs", little has been done in this area.

5.2.3 Review of Algorithms

As has been shown in this study, the current CMS CDL algorithms in some cases seem to be following a similar track to the public sector STG/EDLs, but in other cases vary considerably. In some cases, these additions or variations include expensive medicines for which few or no less expensive generic equivalents exist. The process whereby these algorithms have been developed is not transparent, nor are any reasons for additions or deletions provided. By contrast, the National Essential Drugs List (Department of Health, 1998A) committee is made up of Ministerial appointees. In terms of the National Health Act (Act 61 of 2003), (National Health Act, 2004) the Minister will be making regulations on "the development of an essential drugs list and medical and other assistive devices list" (section 90(1)(d)).

In order to improve the quality of the system, and also increase the degree of convergence between the public and private sectors, it is recommended that the National Essential Drugs List selection structures prescribed by these envisaged regulations also take on the task of determining the algorithms applicable to the ambulatory care PMBs, the CMS CDL. This is also in line with the intentions of the 1996 National Drug Policy. While the initial intention of the EDL was directed at public sector services ("The national list of essential drugs will be used as a foundation for: the basic health care package of the National Health System for Universal Primary Care; procurement and use of drugs; standard treatment guidelines and training in rational prescribing; drug information to health care providers, including a national formulary; support to the national pharmaceutical industry; drug donations"), the policy went on to state: "The list may also be used as a model for medical aid schemes" . (Department of Health, 1996)

In particular, a more direct and prescriptive approach could reduce costs - for example, where the algorithm specifies a therapeutic class of drugs. In the algorithm for cardiac failure, ACE inhibitors are a recommended line of treatment. There are 11 'Me-Too' originator drugs within the class of ACE inhibitors, with a total number of 31 generic equivalents. The cost differentials between the originator drugs themselves is 77% (between captopril and lisinopril) while the lowest cost differential between originator and their generic equivalent is 35% (fosinopril). The onus of cost saving is transferred to medical schemes, which may specify in their formularies which medicines in the class they will cover fully. This problem can be addressed either by more specific algorithms, or by the use of therapeutic reference pricing. It would, however, demand a far more rigorous approach to documenting the decision-making process and a commitment to an evidence-based approach. Even in countries where this has been attempted, there have been attacks on the structures responsible. In the United Kingdom, the National Institute for Health and Clinical Excellence has been criticized, and in Germany, the equivalent structure, the Institute for Quality and Economic Efficiency in Health Care has been accused of a lack of transparency (Tufts, 2006).

5.3 Specific recommendations

The CMS CDL algorithms should follow the public sector STG/EDLs more closely. This can be achieved by utilising the National Essential Drugs List selection structures to determine the algorithms for use as by medical schemes. The algorithms need to be more specific especially in the area where there are many drugs available in one therapeutic group.

In relation to the pricing section of the National Drug Policy, Government needs to define more clearly how they are going to control prices. Regulating prices by stipulating what dispensing fees may be charged does not take into consideration all the other costs along the distribution chain. Government's intervention in relation to the single exit price can be seen as a step towards rectifying this problem. However, in Figure 4.4 the proposed figure of generics

being 40% lower than the SEP of the originator drug has been shown, in this study, to be too low. As stated previously (section 4.3.4) 67.5% of all generics for chronic diseases have cost differentials greater than 40%. Government needs to reassess this figure. Greater competition must also be encouraged by reducing barriers to entry.

The provisions that exist to weaken barriers to entry must be taken up by the Government. More effort must be made to implement parallel imports as this can be an important source of price competition for medicines and would be a tool to lower prices for consumers.

Compulsory licensing would not only lower prices to consumers by creating competition in the market for the patented good but would boost the economy by encouraging investment into the manufacturing of these medicines. However, Government would also need to look at offering incentives to these companies by means of reduced tariffs on imported technology and changing legislation which will reduce the amount of time it takes to obtain marketing authorization.

The impact on prices would be similar to the introduction of generic competition at the end of a drug's patent term i.e. prices would decrease significantly.

The majority of drug information or advertising is usually released by the actual manufacturing companies. As Government and universities can play an important role in educating undergraduate and postgraduate doctors on generic substitution, a change in the quality of drug information available to students should be considered. Consumers should be made more aware of their rights with regard to generic substitution and prescribing.

The mechanisms to implement the majority of these recommendations are already in place within South Africa. However, only when Government is able to realise the aims specified in the National Drug Policy (1996) will consumers benefit from lower drug prices.

5.3 Conclusion

This study has shown that there is potential for cost savings by comparing the single exit price of originator drugs and their generic equivalents. This has been done within a South African context concentrating on the chronic disease list.

All of the objectives as stated in chapter one have been covered and the data collected and analyses conducted in chapter four have allowed these objectives to be achieved. Subsequently, the information taken from the various analyses has provided the basis for the recommendations.

It is recommended that further research be undertaken, especially in the area of addressing price controls as a more realistic benchmark percentage to be set by Government needs to be investigated.

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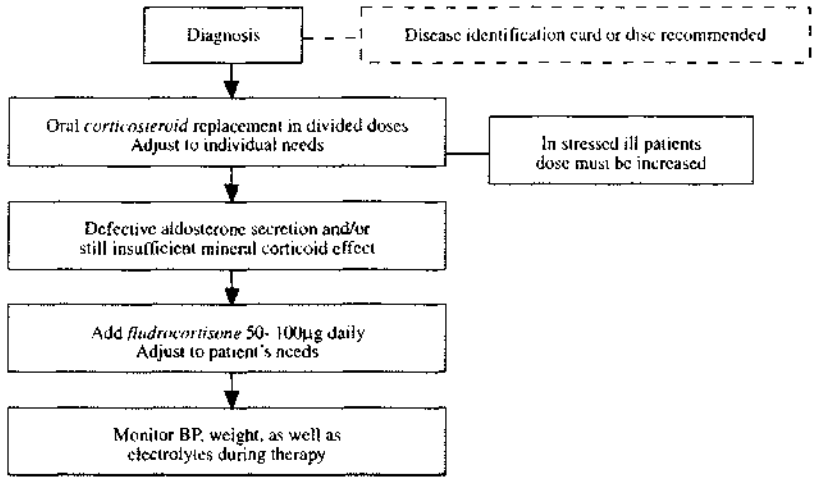
APPENDIX A

ALGORITHMS

ADDISON'S DISEASE



Note:

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ASTHMA

Diagnosis

Made on symptoms and signs
Objective measurement:
FEV1 improvement possible ≥ 15%
[& 200ml increase after short acting *β2 agonist* (400µg MDI and spacer)]

Aims of Management:
Control symptoms and prevent exacerbations
Achieve best possible peak flow
Minimise adverse effects

Stepwise Approach:

Start treatment at step most appropriate to initial severity
Achieve early control
Maintain stepping up or stepping down therapy

CLASSIFICATION OF SEVERITY

Management of Chronic Asthma in Adults

Classify Severity at Presentation

	Intermittent	**Persistent**		
		Mild	**Moderate**	**Severe**
Category	**I**	**II**	**III**	**IV**
Daytime symptoms	≤ 2/week	2-4/week	> 4/week	Continuous
Night-time symptoms	≤1/month	2-4/month	> 4/week	Frequent
PEF (predicted)	≥ 80%	≥ 80%	60-80%	< 60%

START TREATMENT AT MOST APPROPRIATE STEP

Step 1: Mild Intermittent Asthma
Inhaled *short acting β2 agonist* as required

Step 2: Mild Persistent Asthma

Reliever: *β2 agonist* as required;
Preventer: Add inhaled *corticosteroid* 400-800µg/day
(Equivalent to *beclomethasone* MDI & spacer)

Step Down

Step Up

ASTMA

Step 3: Moderate Persistent Asthma

1. *Short-acting β2 agonist* as required
2. Increase dose of inhaled *cortisosteroid* to 1200 µg/day (*beclomethasone* or equivalent)

If not controlled

3. Add inhaled *long-acting β2 agonist* (*LAβA*) to 1200 µg/day inhaled *corticosteroid* (*beclomethasone* or equivalent)
4. Reassess control:
   - If adequate: continue *LAβA*
   - If no response: stop *LAβA*; consider *SR theophylline*

Step Down

Step Up

Step 4: Severe Persistent Asthma

1. *Short-acting β2 agonist* as required
2. Increase inhaled *steroid* to 2000 µg/day (*beclomethasone* or equivalent); plus *LAβA* or *SR theophylline*

Step 5: Very Severe Persistent Asthma

1. Therapy as in Step 4
2. Review for oral *steroids*

Glossary:

- FEV1 – Forced expiratory volume in 1 second

- *β2* – Beta-2 receptor
- MDI – Metered dosage inhaler
- PEF – Peak expiratory flow
- *LAβA* – Long acting beta-2 receptor agonist
- SR – Slow release

Applicable ICD 10 Coding:

- J45 Asthma
  - J45.0 Predominantly allergic asthma
  - J45.1 Nonallergic asthma
  - J45.8 Mixed asthma
  - J45.9 Asthma, unspecified
- J46 Status asthmaticus

Note:

1. Medical management reasonably necessary for the delivery of treatment described in this algorithm is included within this benefit, subject to the application of managed health care interventions by the relevant medical scheme.
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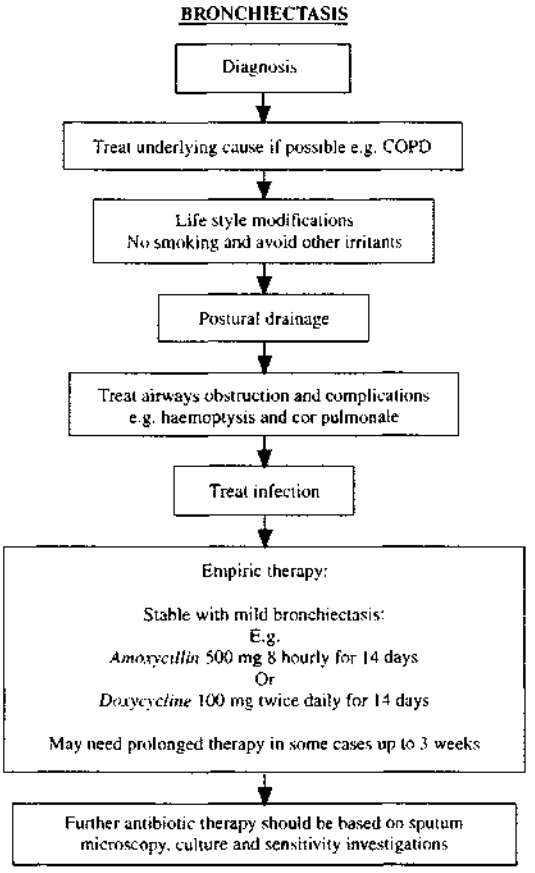

Glossary:

- COPD – Chronic obstructive pulmonary disease

Applicable ICD 10 Coding:

- J47 Bronchiectasis
- Q33.4 Congenital bronchiectasis

Note:

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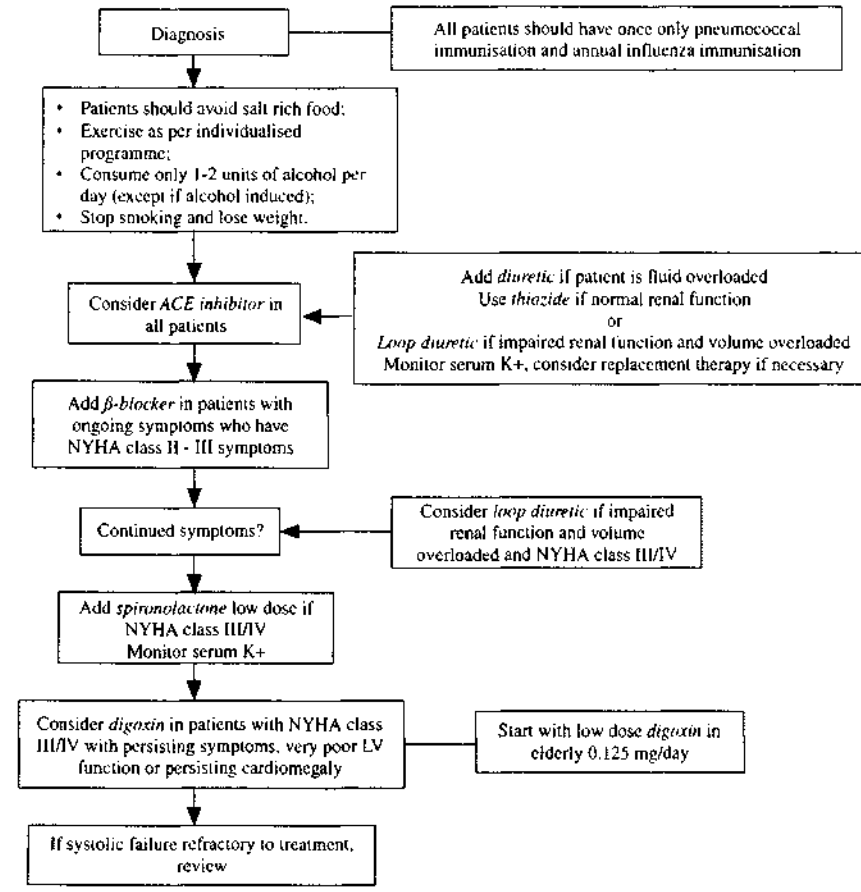
CARDIAC FAILURE



NOTE: If patient truly intolerant to *ACE inhibitor*, consider *hydralazine & isosorbide dinitrate* combination therapy

Glossary:

- *ACE inhibitor* – Angiotensin converting enzyme inhibitor
- Serum K+ – Serum potassium
- *β-blocker* – Beta-receptor blocker
- NYHA – New York Heart Association
- LV – Left ventricular

Applicable ICD 10 Coding:

- I50 Heartfailure
  - I50.0 Congestive heart failure
  - I50.1 Left ventricular failure
  - I50.9 Heart failure, unspecified
- I11.0 Hypertensive heart disease with (congestive) heart failure
- I13.0 Hypertensive heart and renal disease with (congestive) heart failure
- I13.2 Hypertensive heart and renal disease with both (congestive) heart failure and renal failure

Note:

1. Medical management reasonably necessary for the delivery of treatment described in this algorithm is included within this benefit, subject to the application of managed health care interventions by the relevant medical scheme.
2. To the extent that a medical scheme applies managed health care interventions in respect of this benefit, for example clinical protocols for diagnostic procedures or

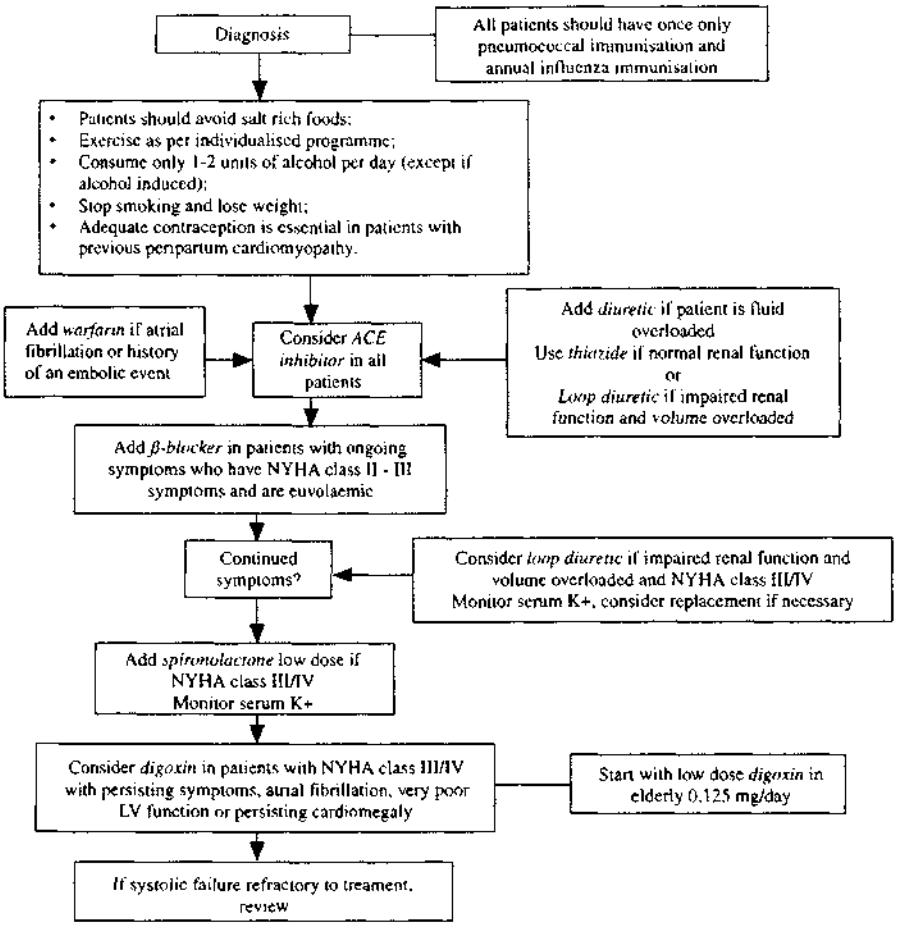
medical management, such interventions must—

a. not be inconsistent with this algorithm;

b. be developed on the basis of evidence-based medicine, taking into account considerations of cost-effectiveness and affordability; and

c. comply with all other applicable regulations made in terms of the Medical Schemes Act, 131 of 1998.

3. This algorithm may not necessarily always be clinically appropriate for the treatment of children. If this is the case, alternative paediatric clinical management is included within this benefit if it is supported by evidence-based medicine, taking into account considerations of cost-effectiveness and affordability.



NOTE: If patient truly intolerant to *ACE inhibitor*, consider *hydralazine & isosorbide dinitrate* combination therapy

Glossary:

- *ACE inhibitor* – Angiotensin converting enzyme inhibitor
- Serum K+ – Serum potassium
- *β-blocker* – Beta-receptor blocker
- NYHA – New York Heart Association
- LV – Left ventricular

Applicable ICD 10 Coding:

- I42 Cardiomyopathy
  - I42.0 Dilated cardiomyopathy
  - I42.1 Obstructive hypertrophic cardiomyopathy

- I42.2 Other hypertrophic cardiomyopathy
- I42.3 Endomyocardial (eosinophilic) disease
- I42.4 Endocardial fibroelastosis
- I42.5 Other restrictive cardiomyopathy
- I42.6 Alcoholic cardiomyopathy
- I42.7 Cardiomyopathy due to drugs and other external agents
- I42.8 Other cardiomyopathies
- I42.9 Cardiomyopathy, unspecified

• I25.5 Ischaemic cardiomyopathy

Note:

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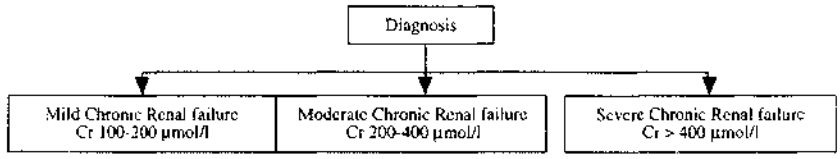
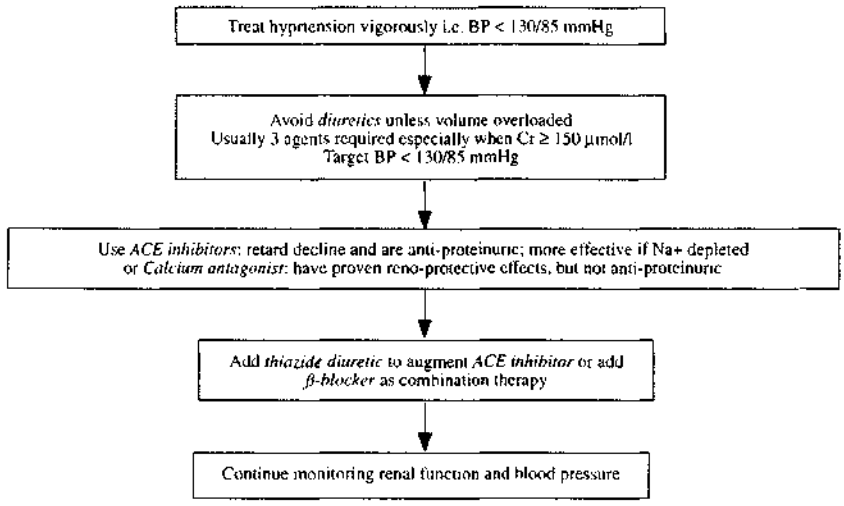
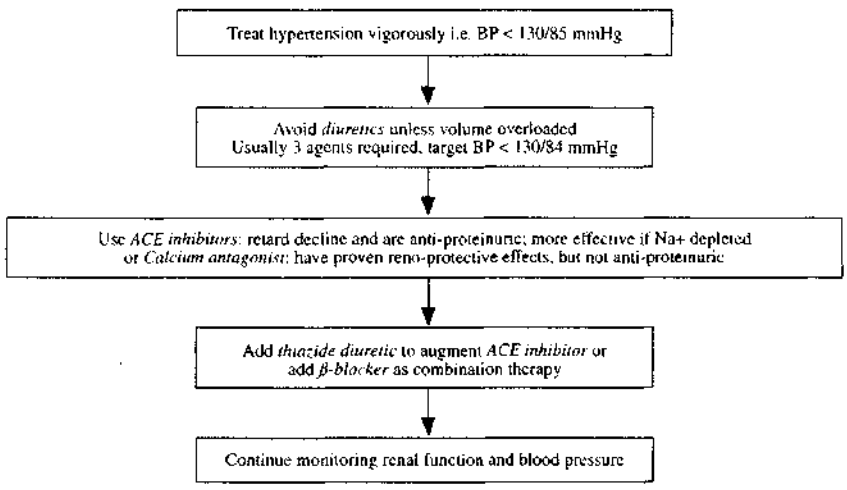
CHRONIC RENAL DISEASE

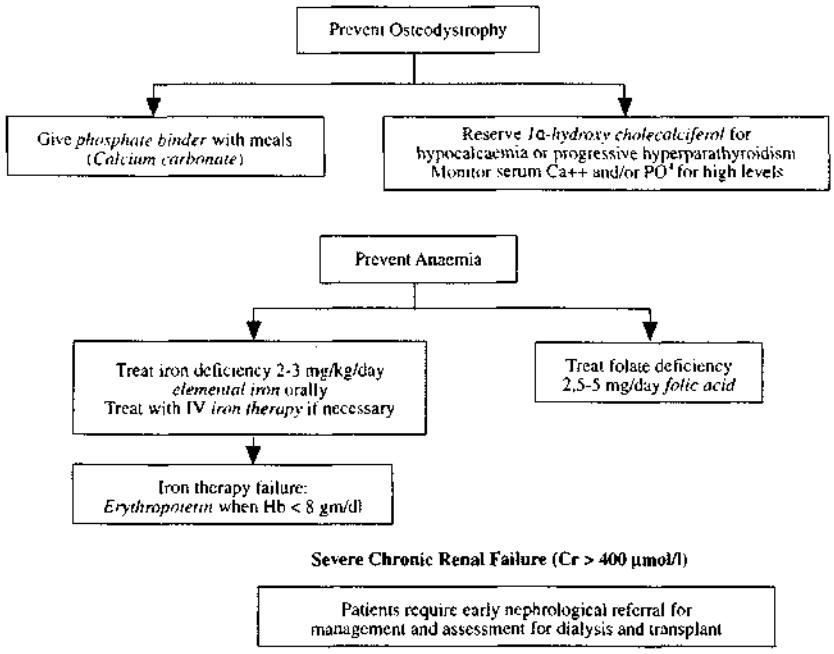


Mild Chronic Renal Failure (Cr 100-200 µmol/l)



Moderate Chronic Renal Failure (Cr 200-400 µmol/l)





Glossary:

- *ACE inhibitor* – Angiotensin converting enzyme inhibitor
- Serum Na+ – Serum sodium
- *β-blocker* – Beta-receptor blocker
- BP – Blood pressure
- Hb – Haemoglobin
- Cr/Serum Cr – Serum creatinine
- Serum Ca++ – Serum calcium
- *1α-hydroxy* – 1-alpha-hydroxy
- PO^4 – Phosphate

Applicable ICD 10 Coding:

- N03 Chronic nephritic syndrome
  - N03.0 Chronic nephritic syndrome, minor glomerular abnormality
  - N03.1 Chronic nephritic syndrome, focal and segmental glomerular lesions
  - N03.2 Chronic nephritic syndrome, diffuse membranous glomerulonephritis
  - N03.3 Chronic nephritic syndrome, diffuse mesangial proliferative glomerulonephritis
  - N03.4 Chronic nephritic syndrome, diffuse endocapillary proliferative glomerulonephritis
  - N03.5 Chronic nephritic syndrome, diffuse mesangiocapillary glomerulonephritis
  - N03.6 Chronic nephritic syndrome, dense deposit disease
  - N03.7 Chronic nephritic syndrome, diffuse crescentic glomerulonephritis
  - N03.8 Chronic nephritic syndrome, other
  - N03.9 Chronic nephritic syndrome, unspecified

- N11 Chronic tubulo-interstitial nephritis
  - N11.0 Nonobstructive reflux-associated chronic pyelonephritis
  - N11.1 Chronic obstructive pyelonephritis
  - N11.8 Other chronic tubulo-interstitial nephritis

- N11.9 Chronic tubulo-interstitial nephritis, unspecified
- N18 Chronic renal failure
  - N18.0 End-stage renal disease
  - N18.8 Other chronic renal failure
  - N18.9 Chronic renal failure, unspecified
- I12.0 Hypertensive renal disease with renal failure
- I13.2 Hypertensive heart and renal disease with both (congestive) heart failure and renal failure
- O10.2 Pre-existing hypertensive renal disease complicating pregnancy, childbirth and the puerperium
- O10.3 Pre-existing hypertensive heart and renal disease complicating pregnancy, childbirth and the puerperium

Note:

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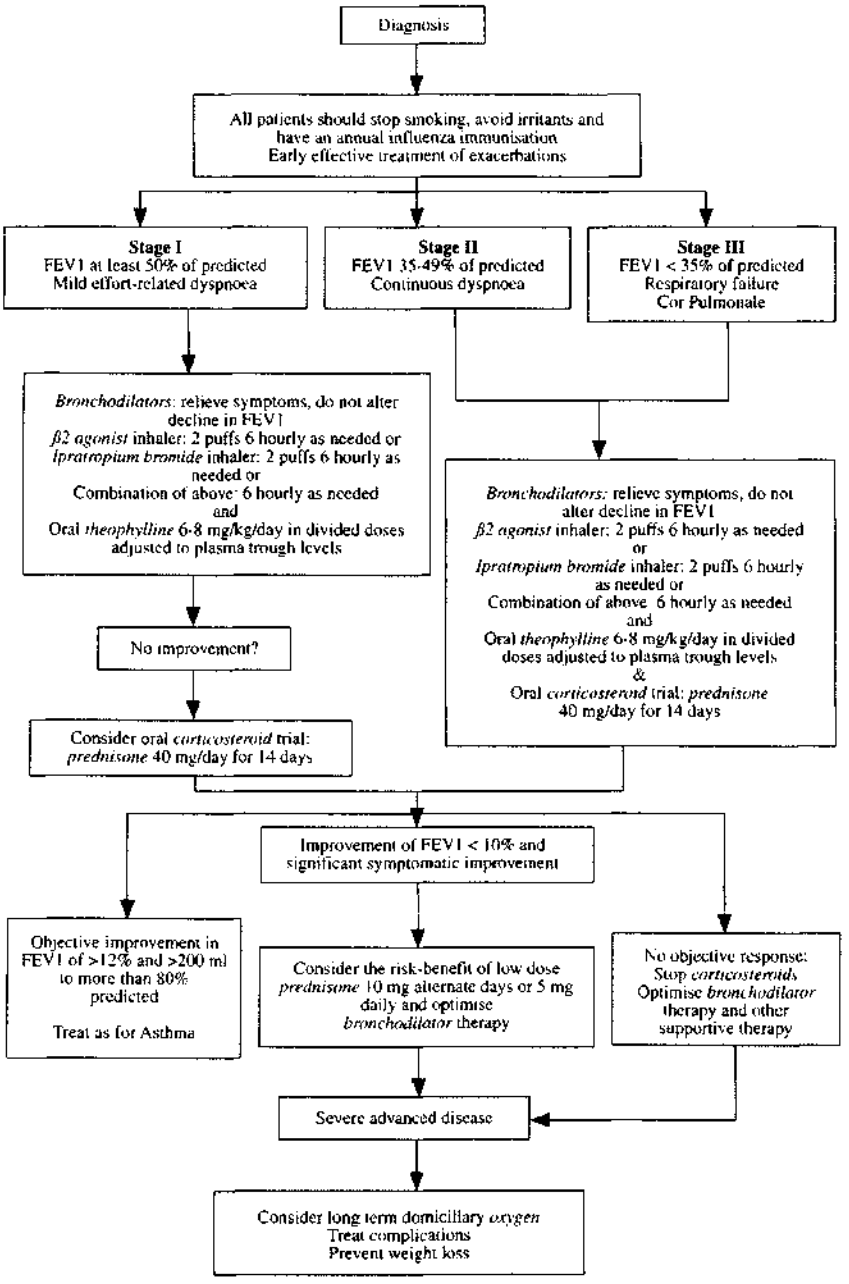
3. This algorithm may not necessarily always be clinically appropriate for the treatment of children. If this is the case, alternative paediatric clinical management is included within this benefit if it is supported by evidence-based medicine, taking into account considerations of cost-effectiveness and affordability.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE



Glossary:

- FEV1 – Forced expiratory volume in 1 second
- *β-blocker* – Beta-2 receptor

Applicable ICD 10 Coding:

- J43 Emphysema
  - J43.0 MacLeod's syndrome
  - J43.1 Panlobular emphysema
  - J43.2 Centrilobular emphysema
  - J43 8 Other emphysema
  - J43.9 Emphysema, unspecified
- J44 Other chronic obstructive pulmonary disease
  - J44.0 Chronic obstructive pulmonary disease with acute lower respiratory infection
  - J44.1 Chronic obstructive pulmonary disease with acute exacerbation,

unspecified

- J44.8 Other specified chronic obstructive pulmonary disease
- J44.9 Chronic obstructive pulmonary disease, unspecified

Note:

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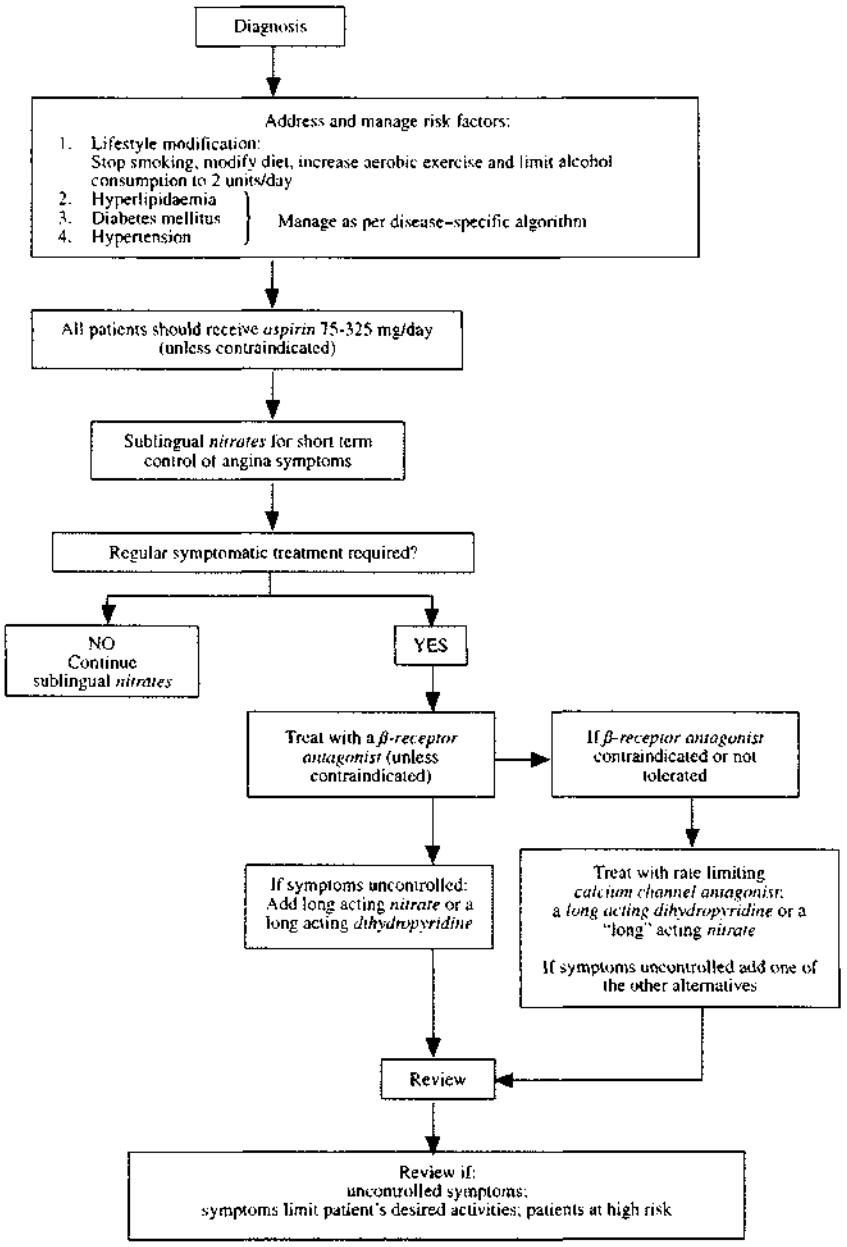
CORONARY ARTERY DISEASE



Glossary:

- *β-receptor antagonist* – Beta-receptor antagonist

Applicable ICD 10 Coding:

- I20 Angina pectoris
  - I20.0 Unstable angina
  - I20.1 Angina pectoris with documented spasm
  - I20.8 Other forms of angina pectoris
  - I20.9 Angina pectoris, unspecified
- I25 Chronic ischaemic heart disease
  - I25.0 Atherosclerotic cardiovascular disease, so described
  - I25.1 Atherosclerotic heart disease
  - I25.2 Old myocardial infarction
  - I25.3 Aneurysm of heart
  - I25.4 Coronary artery aneurysm

- I25.5 Ischaemic cardiomyopathy
- I25.6 Silent myocardial ischaemia
- I25.8 Other forms of chronic ischaemic heart disease
- I25.9 Chronic ischaemic heart disease, unspecified

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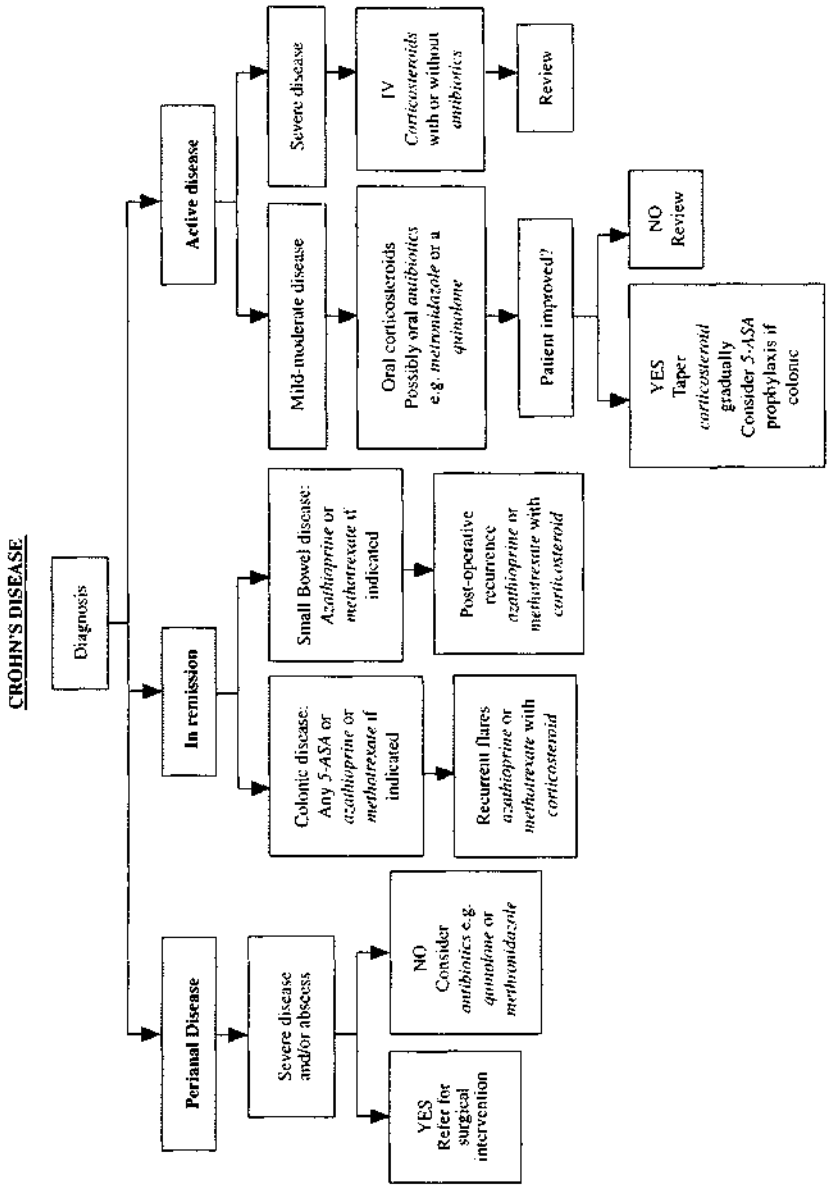
3. This algorithm may not necessarily always be clinically appropriate for the treatment of children. If this is the case, alternative paediatric clinical management is included within this benefit if it is supported by evidence-based medicine, taking into account considerations of cost-effectiveness and affordability.



Glossary:

- *5-ASA* – 5-Aminosalicylic acid
- IV – Intravenous

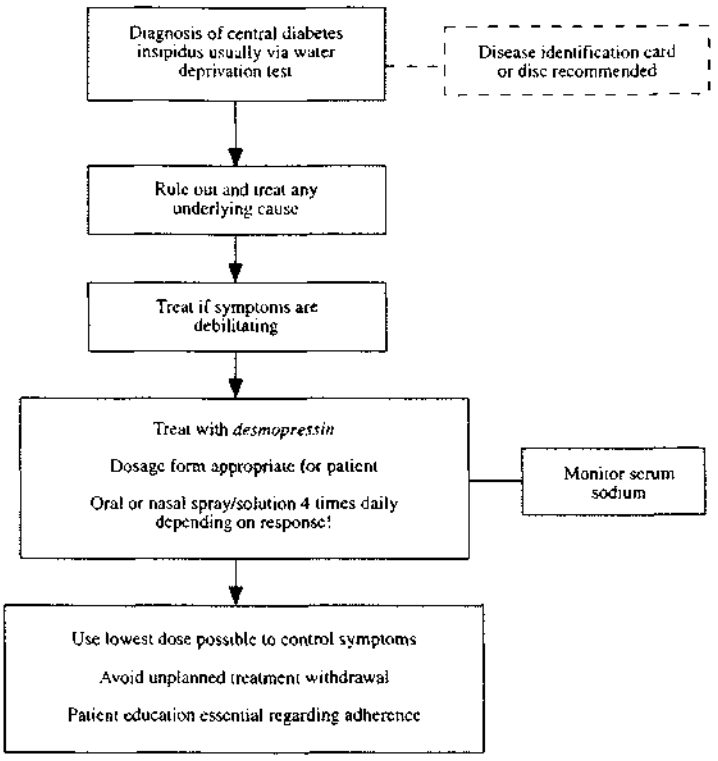
Applicable ICD 10 Coding:

- K50 Crohn's disease [regional enteritis]
  - K50.0 Crohn's disease of small intestine
  - K50.1 Crohn's disease of large intestine
  - K50.8 Other Crohn's disease
  - K50.9 Crohn's disease, unspecified

Note:

1. Medical management reasonably necessary for the delivery of treatment described in this algorithm is included within this benefit, subject to the application of managed health care interventions by the relevant medical scheme.
2. To the extent that a medical scheme applies managed health care interventions in respect of this benefit, for example clinical protocols for diagnostic procedures or medical management, such interventions must—
   a. not be inconsistent with this algorithm;

DIABETES INSIPIDUS



Applicable ICD 10 Coding:

- E23.2 Diabetes insipidus

Note:

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b. be developed on the basis of evidence-based medicine, taking into account considerations of cost-effectiveness and affordability; and

c. comply with all other applicable regulations made in terms of the Medical Schemes Act, 131 of 1998.

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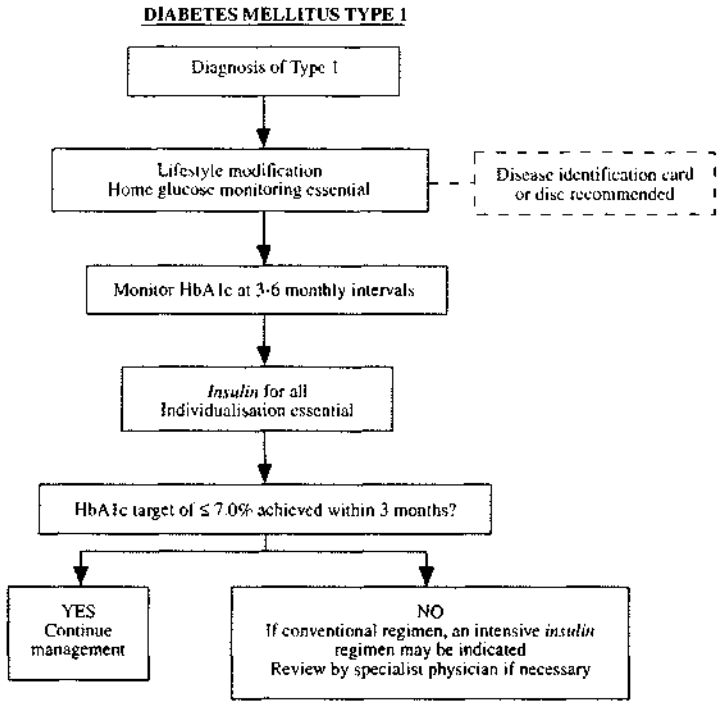

Glossary:

- HbAlc – Glycosylated haemoglobin

Applicable ICD 10 Coding:

- E10 Insulin-dependent diabetes mellitus
  - E10.0 Insulin-dependent diabetes mellitus with coma
  - E10.1 Insulin-dependent diabetes mellitus with ketoacidosis
  - E10.2 Insulin-dependent diabetes mellitus with renal complications
  - E10.3 Insulin-dependent diabetes mellitus with ophthalmic complications
  - E10.4 Insulin-dependent diabetes mellitus with neurological complications
  - E10.5 Insulin-dependent diabetes mellitus with peripheral circulatory complications
  - E10.6 Insulin-dependent diabetes mellitus with other specified complications
  - E10.7 Insulin-dependent diabetes mellitus with multiple complications
  - E10.8 Insulin-dependent diabetes mellitus with unspecified complications
  - E10.9 Insulin-dependent diabetes mellitus without complications
- E12 Malnutrition-related diabetes mellitus
  - E12.0 Malnutrition-related diabetes mellitus with coma
  - E12.1 Malnutrition-related diabetes mellitus with ketoacidosis
  - E12.2 Malnutrition-related diabetes mellitus with renal complications
  - E12.3 Malnutrition-related diabetes mellitus with ophthalmic complications
  - E12.4 Malnutrition-related diabetes mellitus with neurological complications
  - E12.5 Malnutrition-related diabetes mellitus with peripheral circulatory complications
  - E12.6 Malnutrition-related diabetes mellitus with other specified complications
  - E12.7 Malnutrition-related diabetes mellitus with multiple complications
  - E12.8 Malnutrition-related diabetes mellitus with unspecified complications
  - E12.9 Malnutrition-related diabetes mellitus without complications

- 024 Diabetes mellitus in pregnancy
  - 024.0 Pre-existing diabetes mellitus, insulin-dependent
  - 024.2 Pre-existing malnutrition-related diabetes mellitus
  - 024.3 Pre-existing diabetes mellitus, unspecified

Note:

1. Medical management reasonably necessary for the delivery of treatment described in this algorithm is included within this benefit, subject to the application of managed health care interventions by the relevant medical scheme.
2. To the extent that a medical scheme applies managed health care interventions in respect of this benefit, for example clinical protocols for diagnostic procedures or medical management, such interventions must—
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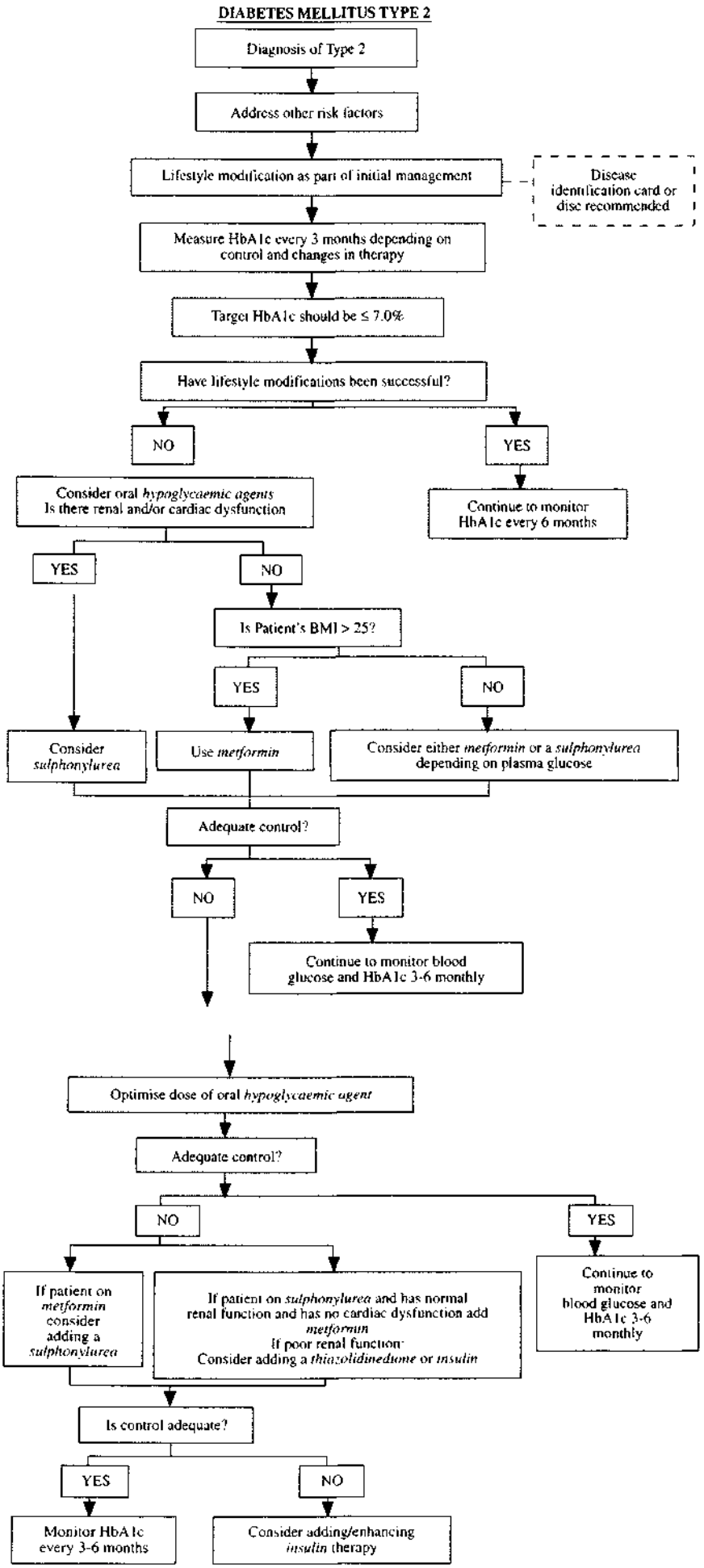
DIABETES MELLITUS TYPE 2
Diagnosis of Type 2
Address other risk factors
Lifestyle modification as part of initial management
Disease identification card or dise recommended
Measure HbA1c every 3 months depending on control and changes in therapy
Target HbA1c should be ≤ 7.0%
Have lifestyle modifications been successful?
NO
YES
Consider oral hypoglycaemic agents Is there renal and/or cardiac dysfunction
Continue to monitor HbA1c every 6 months
YES
NO
Is Patient's BMI > 25?
YES
NO
Consider sulphonylurea
Use metformin
Consider either metformin or a sulphonylurea depending on plasma glucose
Adequate control?
NO
YES
Continue to monitor blood glucose and HbA1c 3-6 monthly
Optimise dose of oral hypoglycaemic agent
Adequate control?
NO
YES
If patient on metformin consider adding a sulphonylurea
If patient on sulphonylurea and has normal renal function and has no cardiac dysfunction add metformin
If poor renal function: Consider adding a thiazolidinedione or insulin
Continue to monitor blood glucose and HbA1c 3-6 monthly
Is control adequate?
YES
NO
Monitor HbA1c every 3-6 months
Consider adding/enhancing insulin therapy

Glossary:

- HbAlc – Glycosylated haemoglobin
- BMI – Body mass index

Applicable ICD 10 Coding:

- El I Non-insulin-dependent diabetes mellitus
  - E11.0 Non-insulin-dependent diabetes mellitus with coma
  - E11.1 Non-insulin-dependent diabetes mellitus with ketoacidosis
  - E11.2 Non-insulin-dependent diabetes mellitus with renal complications
  - E11.3 Non-insulin-dependent diabetes mellitus with ophthalmic complications
  - E11.4 Non-insulin-dependent diabetes mellitus with neurological complications
  - E11.5 Non-insulin-dependent diabetes mellitus with peripheral circulatory complications
  - E11.6 Non-insulin-dependent diabetes mellitus with other specified complications
  - E11.7 Non-insulin-dependent diabetes mellitus with multiple complications
  - E11.8 Non-insulin-dependent diabetes mellitus with unspecified complications
  - E11.9 Non-insulin-dependent diabetes mellitus without complications
- E12 Malnutrition-related diabetes mellitus
  - E12.0 Malnutrition-related diabetes mellitus with coma
  - E12.1 Malnutrition-related diabetes mellitus with ketoacidosis
  - E12.2 Malnutrition-related diabetes mellitus with renal complications
  - E12.3 Malnutrition-related diabetes mellitus with ophthalmic complications
  - E12.4 Malnutrition-related diabetes mellitus with neurological complications
  - E12.5 Malnutrition-related diabetes mellitus with peripheral circulatory complications
  - E12.6 Malnutrition-related diabetes mellitus with other specified complications
  - E12.7 Malnutrition-related diabetes mellitus with multiple complications
  - E12.8 Malnutrition-related diabetes mellitus with unspecified complications
  - E12.9 Malnutrition-related diabetes mellitus without complications
- 024 Diabetes mellitus in pregnancy
  - 024.1 Pre-existing diabetes mellitus, non-insulin-dependent
  - 024.2 Pre-existing malnutrition-related diabetes mellitus
  - 024.3 Pre-existing diabetes metlitus, unspecified

Note:

1. Medical management reasonably necessary for the delivery of treatment described in this algorithm is included within this benefit, subject to the application of managed health care interventions by the relevant medical scheme.
2. To the extent that a medical scheme applies managed health care interventions in respect of this benefit, for example clinical protocols for diagnostic procedures or medical management, such interventions must—
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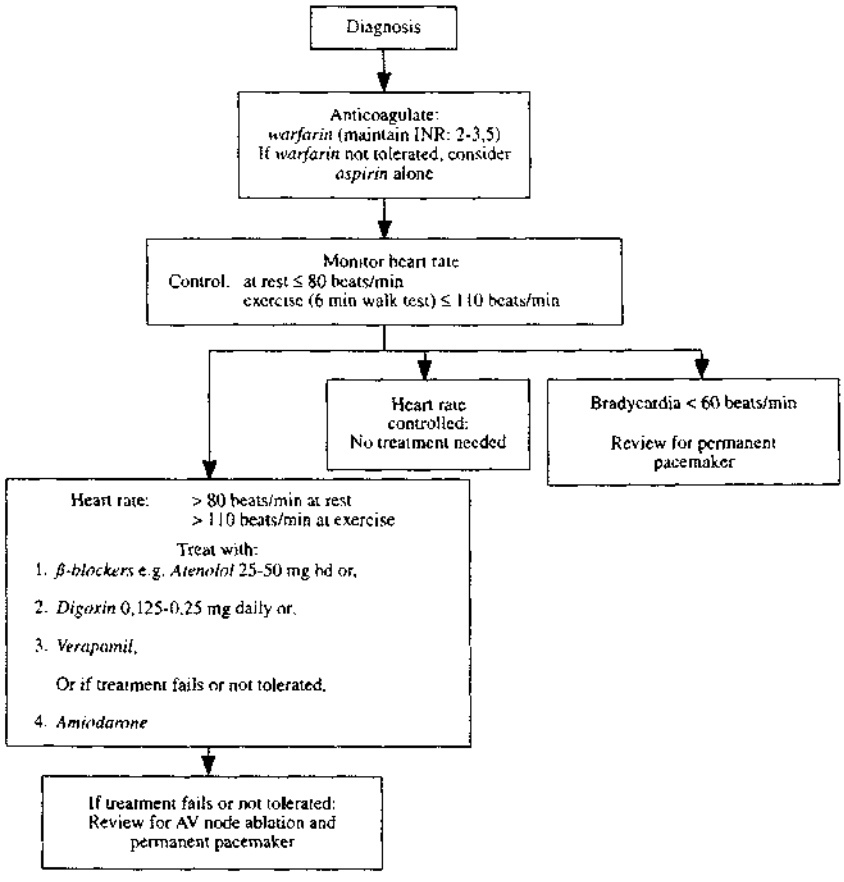
considerations of cost-effectiveness and affordability; and

c. comply with all other applicable regulations made in terms of the Medical Schemes Act, 131 of 1998.

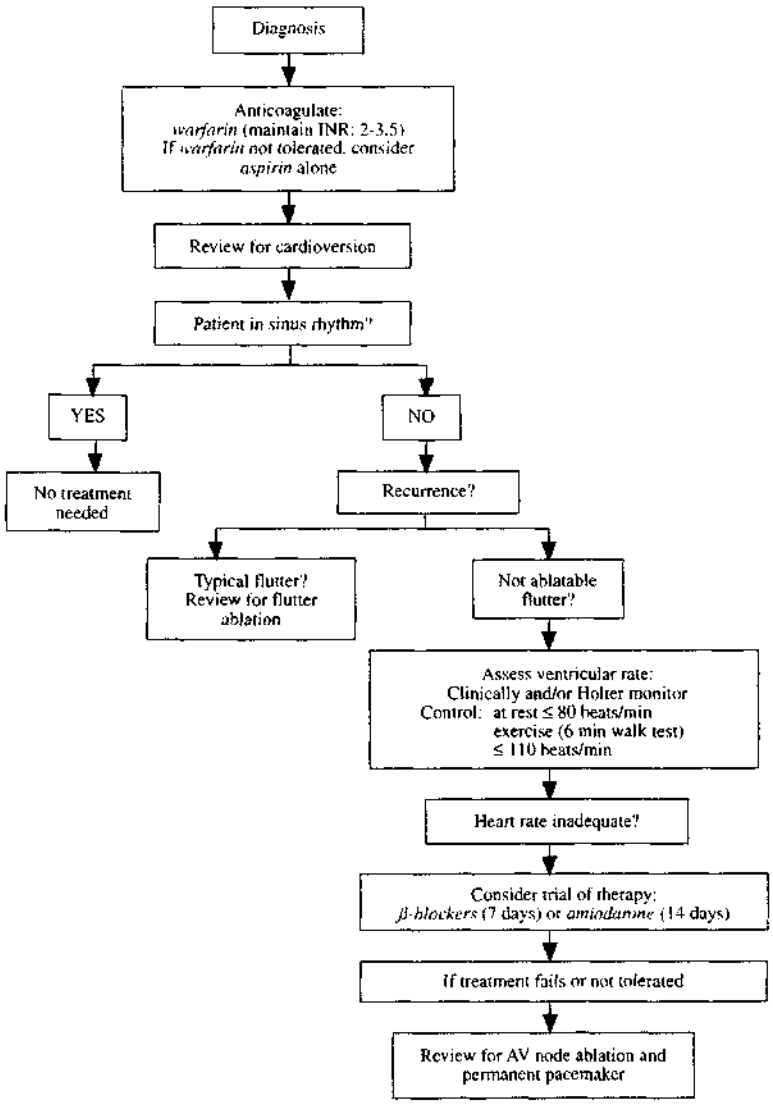
3. This algorithm may not necessarily always be clinically appropriate for the treatment of children. If this is the case, alternative paediatric clinical management is included within this benefit if it is supported by evidence-based medicine, taking into account considerations of cost-effectiveness and affordability.

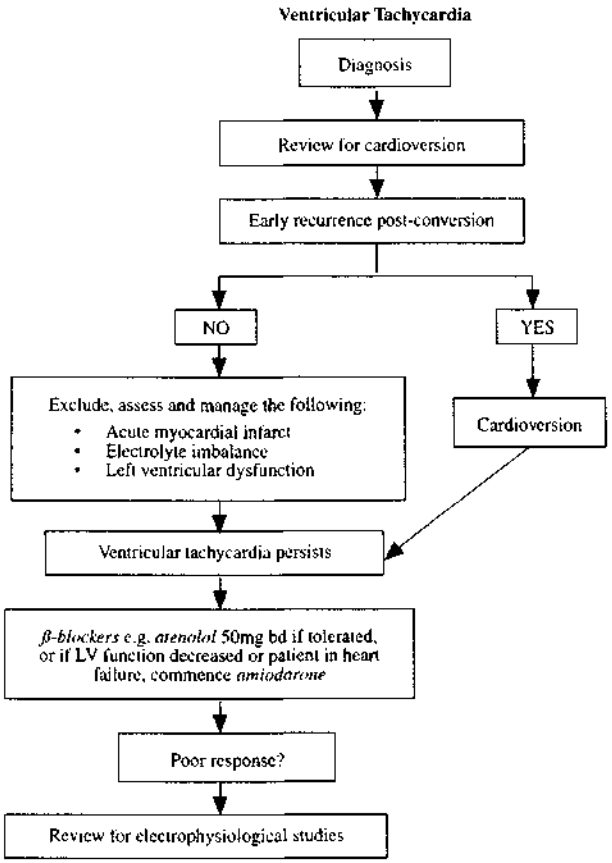
DYSRHYTHMIAS

Chronic Atrial Fibrillation



Chronic Atrial Flutter





Glossary:

- INR – International normalized ratio
- *ß-blocker* – Beta-receptor blocker
- AV node – Atrioventricular node
- LV – Left ventricular

Applicable ICD 10 Coding:

- I47.2 Ventricular tachycardia
- I48 Atrial fibrillation and flutter

Note:

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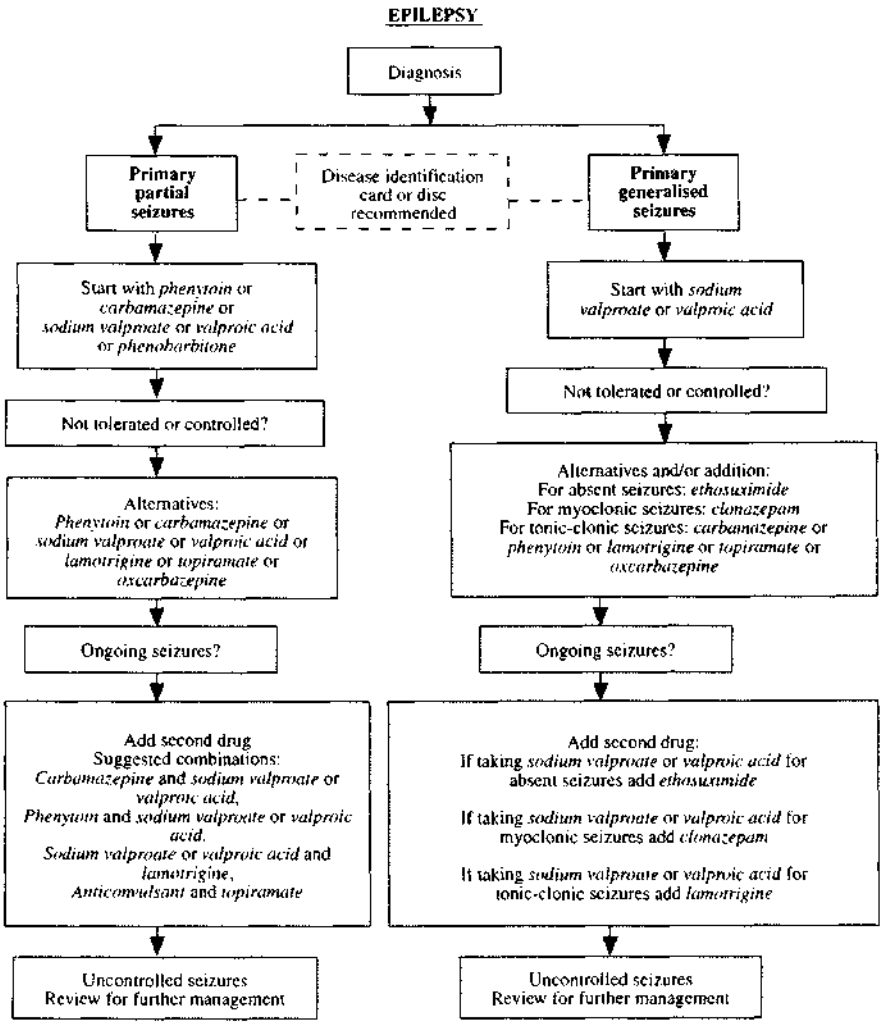

Applicable ICD 10 Coding:

- G40 Epilepsy
  - G40.0 Localization-related (focal)(partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset
  - G40.1 Localization-related (focal)(partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures
  - G40.2 Localization-related (focal)(partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures
  - G40.3 Generalized idiopathic epilepsy and epileptic syndromes
  - G40.4 Other generalized epilepsy and epileptic syndromes
  - G40.5 Special epileptic syndromes
  - G40.6 Grand mal seizures, unspecified (with or without petit mal)
  - G40.7 Petit mal, unspecified, without grand mal seizures
  - G40.8 Other epilepsy
  - G40.9 Epilepsy, unspecified
- G41 Status epilepticus
  - G41.0 Grand mal status epilepticus
  - G41.1 Petit mal status epilepticus
  - G41.2 Complex partial status epilepticus
  - G41.8 Other status epilepticus
  - G41.9 Status epilepticus, unspecified

Note:

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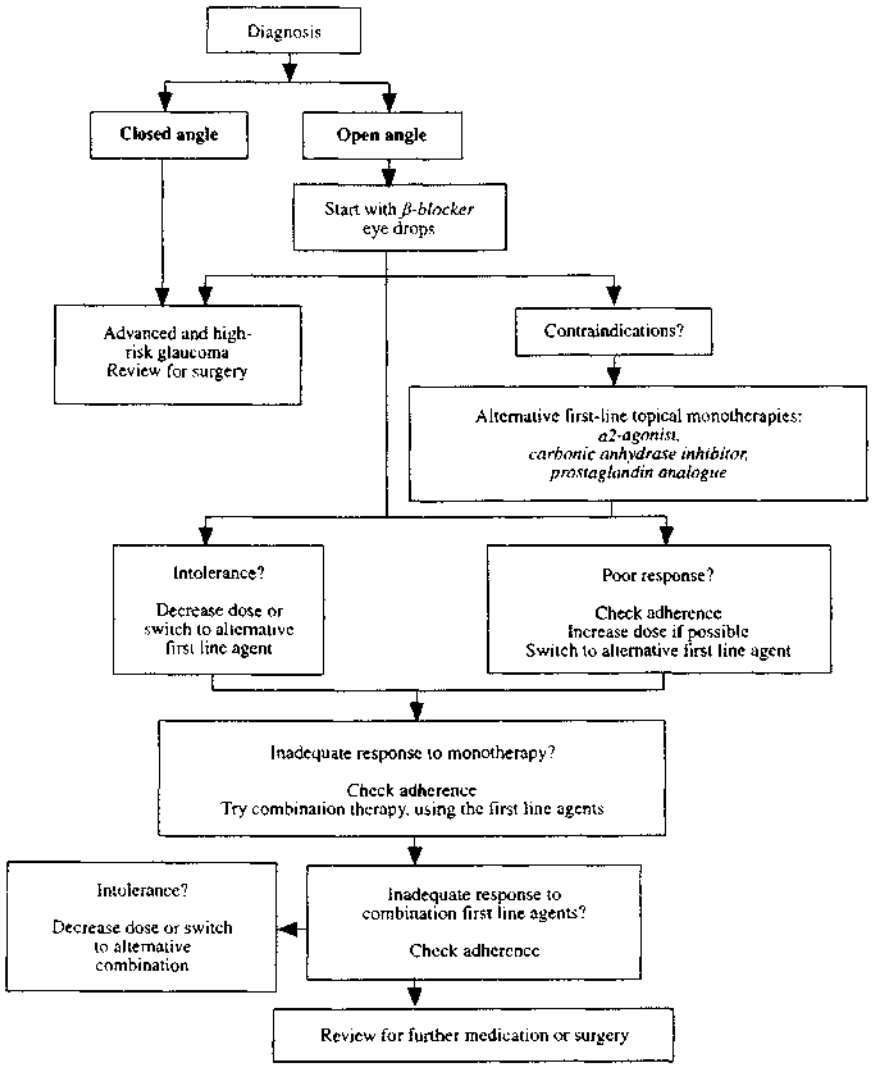
GLAUCOMA



Glossary:

- *β-blocker* – Beta-receptor blocker

- *a2-agonist* – Alpha-2 receptor agonist

Applicable ICD 10 Coding:

- H40 Glaucoma
  - H40.0 Glaucoma suspect
  - H40.1 Primary open-angle glaucoma
  - H40.2 Primary angle-closure glaucoma
  - H40.3 Glaucoma secondary to eye trauma
  - H40.4 Glaucoma secondary to eye inflammation
  - H40.5 Glaucoma secondary to other eye disorders
  - H40.6 Glaucoma secondary to drugs
  - H40.8 Other glaucoma
  - H40.9 Glaucoma, unspecified
- Q15.0 Congenital glaucoma

Note:

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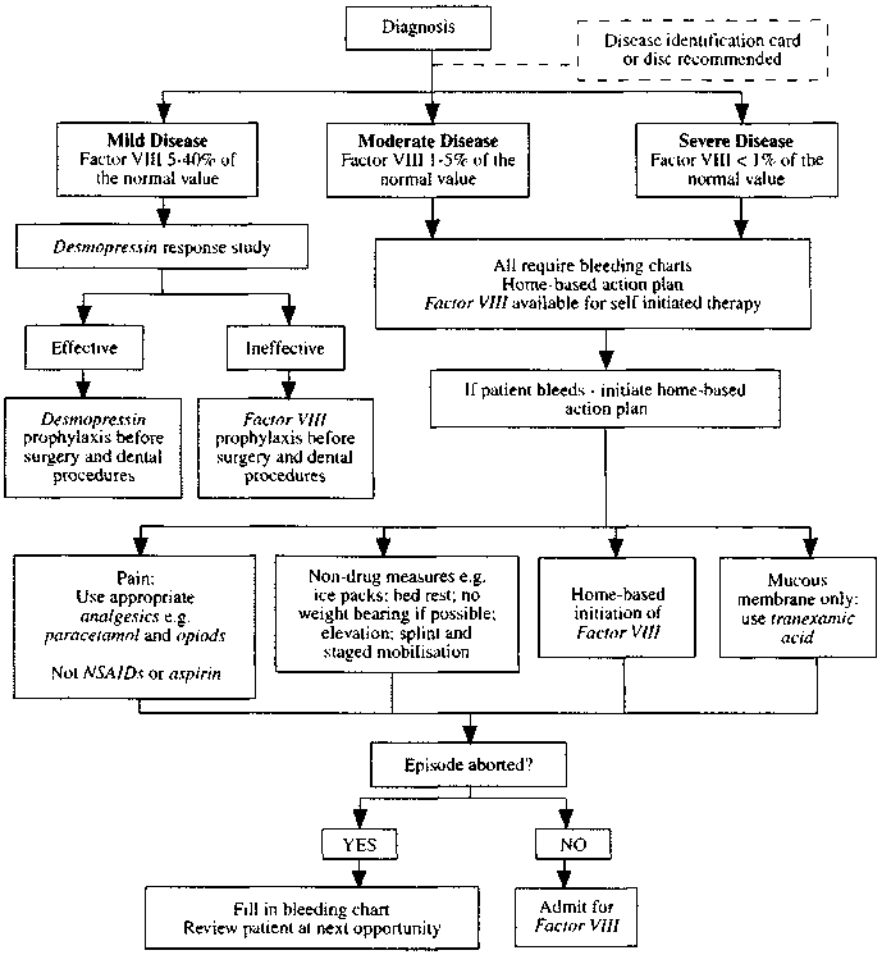
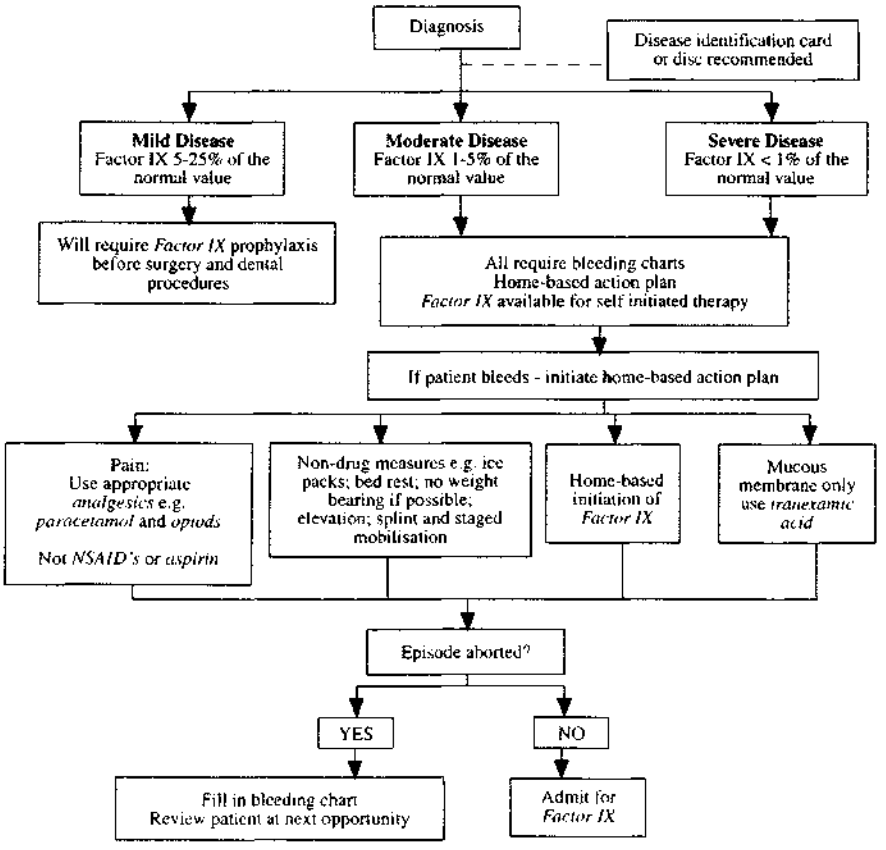
HAEMOPHILIA

Haemophilia A



Haemophilia B



Glossary:

- *Factor VIII* – Factor eight
- *Factor IX* – Factor nine
- *NSAIDs* Non-steroidal anti-inflammatory agents

Applicable ICD 10 Coding:

- D66 Hereditary factor VIII deficiency
- D67 Hereditary factor IX deficiency

Note:

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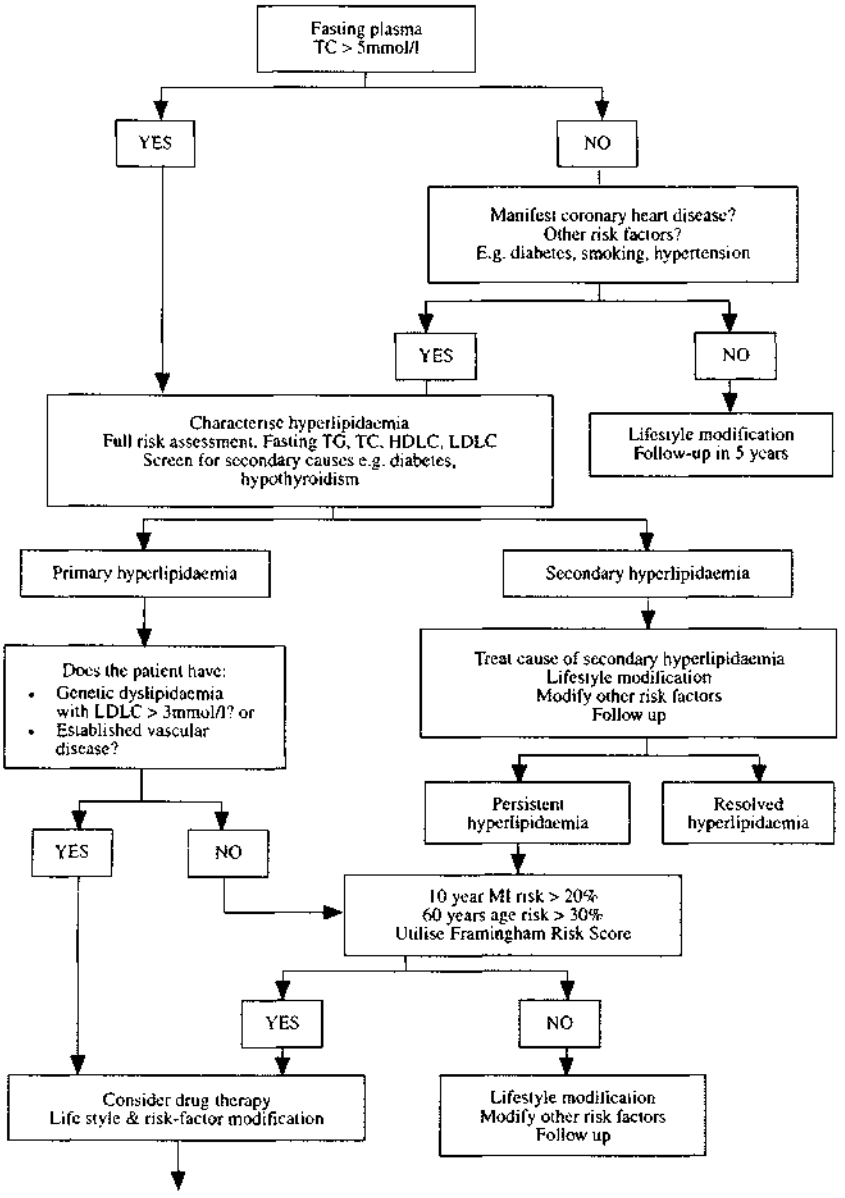
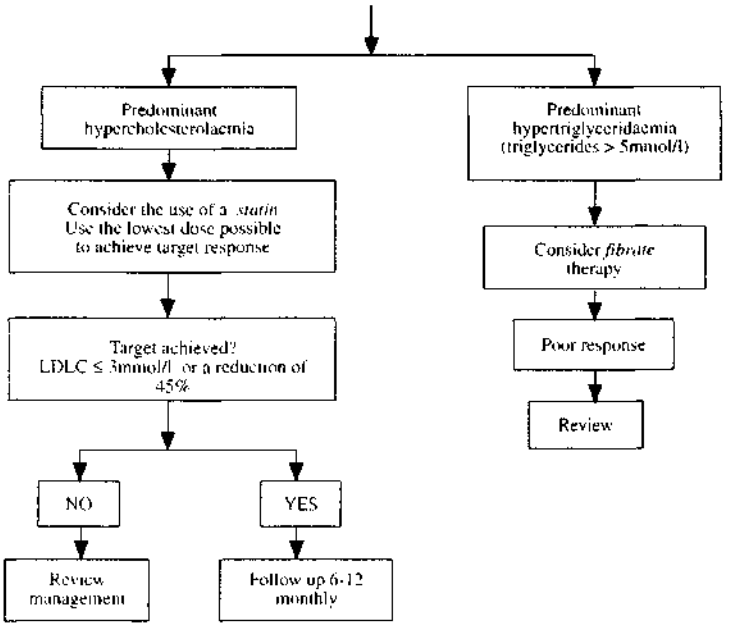
HYPERLIPIDAEMIA



HYPERLIPIDAEMIA



Glossary:

- TC – Total cholesterol
- TG – Triglycerides
- HDLC – High density lipoproteins cholesterol
- LDLC – Low density lipoproteins cholesterol
- M1 – Myocardial infarct

Applicable ICD 10 Coding:

- E78.0 Pure hypercholesterolaemia
- E78.1 Pure hyperglyceridaemia
- E78.2 Mixed hyperlipidaemia
- E78.3 Hyperchylomicronaemia
- E78.4 Other hyperlipidaemia
- E78.5 Hyperlipidaemia, unspecified

Note:

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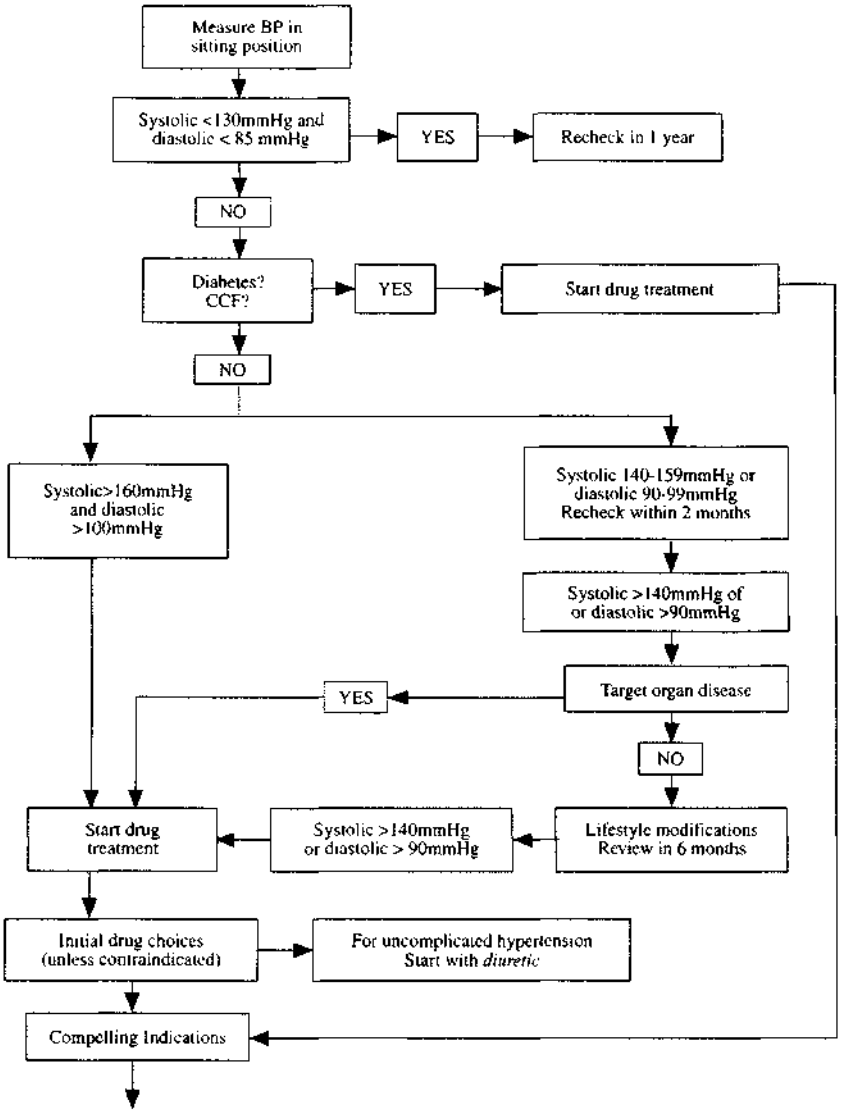
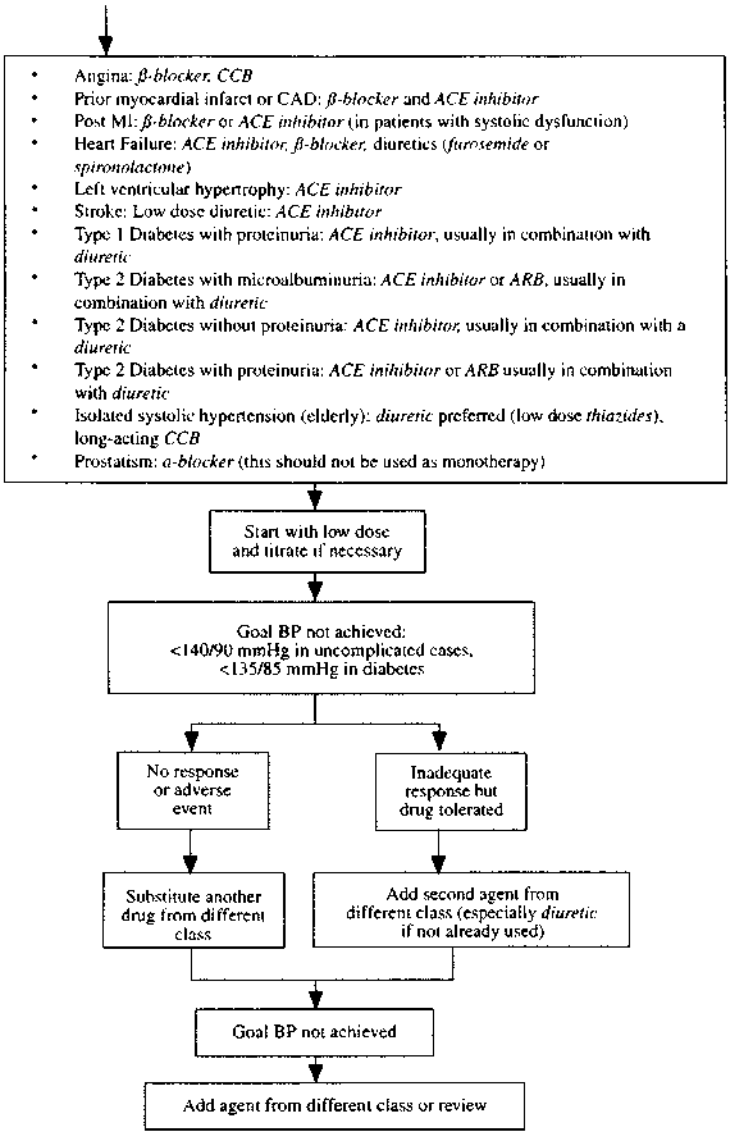
HYPERTENSION





Glossary:

- *α-blocker* – Alpha-receptor blocker
- *ACE inhibitor* – Angiotensin converting enzyme inhibitor
- *ARB* – Angiotensin receptor blocker
- BP – Blood pressure
- *β-blocker* – Beta-receptor blocker
- *CCB* – Calcium channel blocker
- CCF – Chronic / Congestive cardiac failure
- CAD – Coronary artery disease
- LV – Left ventricular
- MI – Myocardial infarct

Applicable ICD 10 Coding:

- I10 Essential (primary) hypertension
- I11 Hypertensive heart disease
  - I11.0 Hypertensive heart disease with (congestive) heart failure
  - I11.9 Hypertensive heart disease without (congestive) heart failure
- I12 Hypertensive renal disease
  - I12.0 Hypertensive renal disease with renal failure

- I12.9 Hypertensive renal disease without renal failure
- I13 Hypertensive heart and renal disease
  - I13.0 Hypertensive heart and renal disease with (congestive) heart failure
  - I13.1 Hypertensive heart and renal disease with renal failure
  - I13.2 Hypertensive heart and renal disease with both (congestive) heart failure and renal failure
  - I13.9 Hypertensive heart and renal disease, unspecified
- I15 Secondary hypertension
  - I15.0 Renovascular hypertension
  - I15.1 Hypertension secondary to other renal disorders
  - I15.2 Hypertension secondary to endocrine disorders
  - I15.8 Other secondary hypertension
  - I15.9 Secondary hypertension, unspecified
- O10 Pre-existing hypertension complicating pregnancy, childbirth and the puerperium
  - O10.0 Pre-existing essential hypertension complicating pregnancy, childbirth and the puerperium
  - O10.1 Pre-existing hypertensive heart disease complicating pregnancy, childbirth and the puerperium
  - O10.2 Pre-existing hypertensive renal disease complicating pregnancy, childbirth and the puerperium
  - O10.3 Pre-existing hypertensive heart and renal disease complicating pregnancy, childbirth and the puerperium
  - O10.4 Pre-existing secondary hypertension complicating pregnancy, childbirth and the puerperium
  - O10.9 Unspecified pre-existing hypertension complicating pregnancy, childbirth and the puerperium
- O1-1 Pre-existing hypertensive disorder with superimposed proteinuria

Note:

1. Medical management reasonably necessary for the delivery of treatment described in this algorithm is included within this benefit, subject to the application of managed health care interventions by the relevant medical scheme.
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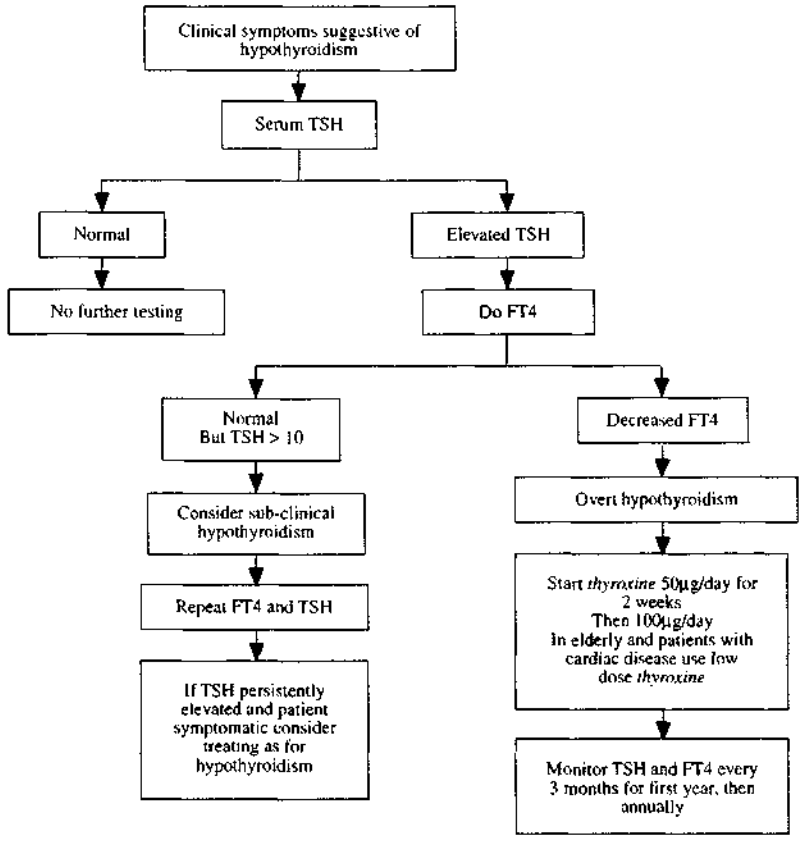
   c. comply with all other applicable regulations made in terms of the Medical Schemes Act, 131 of 1998.
3. This algorithm may not necessarily always be clinically appropriate for the treatment of children. If this is the case, alternative paediatric clinical management is included within this benefit if it is supported by evidence-based medicine, taking into account considerations of cost-effectiveness and affordability.

HYPOTHYROIDISM



Glossary:

- *TSH* – Thyroid stimulating hormone
- *FT4* – Free thyroxine

Applicable ICD 10 Coding:

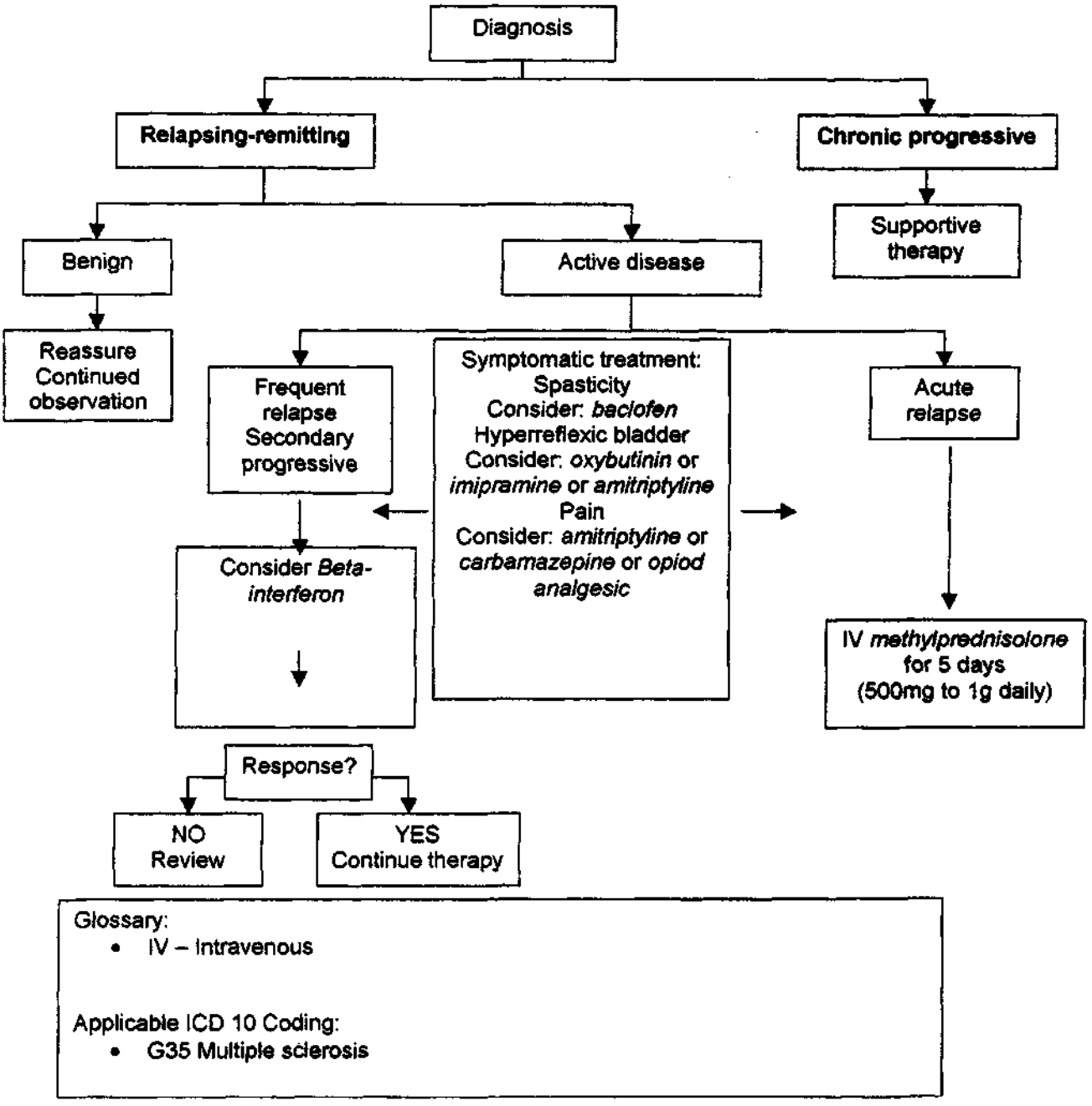
- E01.8 Other iodine-deficiency-related thyroid disorders and allied conditions
- E02 Subclinical iodine-deficiency hypothyroidism
- E03 Other hypothyroidism
  - E03.0 Congenital hypothyroidism with diffuse goitre
  - E03.1 Congenital hypothyroidism without goitre
  - E03.2 Hypothyroidism due to medicaments and other exogenous substances
  - E03.3 Postinfectious hypothyroidism
  - E03.4 Atrophy of thyroid (acquired)
  - E03.5 Myxoedema coma
  - E03.8 Other specified hypothyroidism
  - E03.9 Hypothyroidism, unspecified
- E89.0 Postprocedural hypothyroidism

Note:

1. Medical management reasonably necessary for the delivery of treatment described in this algorithm is included within this benefit, subject to the application of managed health care interventions by the relevant medical scheme.
2. To the extent that a medical scheme applies managed health care interventions in respect of this benefit, for example clinical protocols for diagnostic procedures or

This algorithm was amended on 11th February 2005

MULTIPLE SCLEROSIS



Glossary:

- IV – Intravenous

Applicable ICD 10 Coding:

- G35 Multiple sclerosis

Note:

1. **Medical management reasonably necessary for the delivery of treatment described in this algorithm is included within this benefit, subject to the application of managed health care interventions by the relevant medical scheme.**

2. **To the extent that a medical scheme applies managed health care interventions in respect of this benefit, for example clinical protocols for diagnostic procedures or medical management, such interventions must –**
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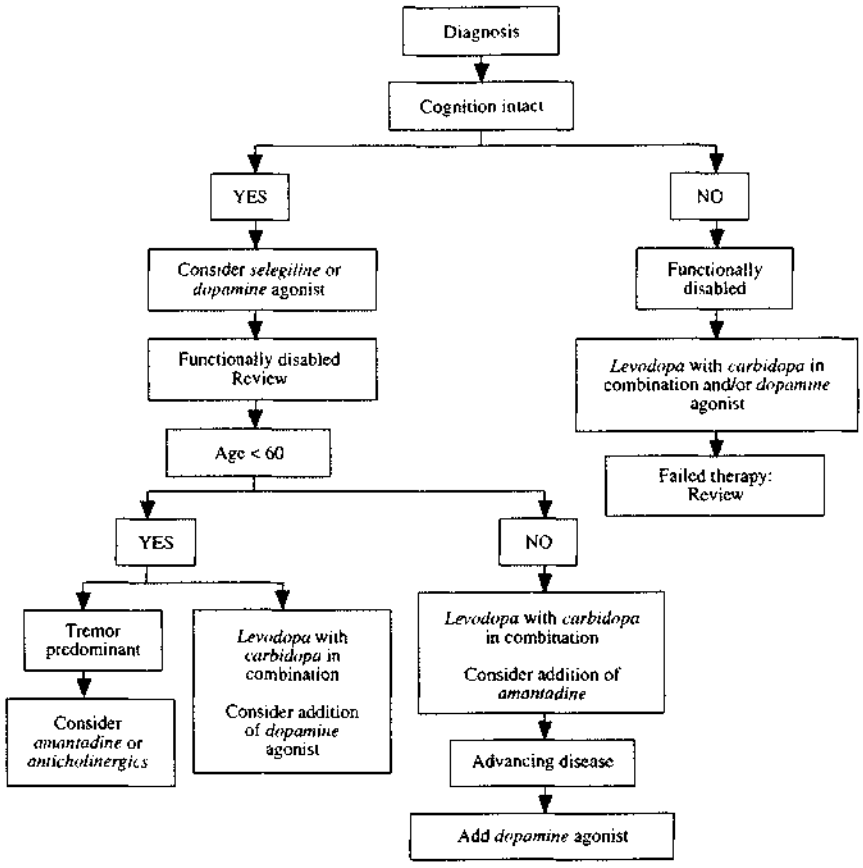
3. **This algorithm may not necessarily always be clinically appropriate for the treatment of children. If this is the case, alternative paediatric clinical management is included within this benefit if it is supported by evidence-based medicine, taking into account considerations of cost-effectiveness and affordability.**

ME TSHABALALA-MSIMANG
MINISTER OF HEALTH

PARKINSON'S DISEASE



Applicable ICD 10 Coding:

- G20 Parkinson's disease
- G21 Secondary parkinsonism
  - G21.0 Malignant neuroleptic syndrome
  - G21.1 Other drug-induced secondary parkinsonism
  - G21.2 Secondary parkinsonism due to other external agents
  - G21.3 Postencephalitic parkinsonism
  - G21.8 Other secondary parkinsonism
  - G21.9 Secondary parkinsonism, unspecified

Note:

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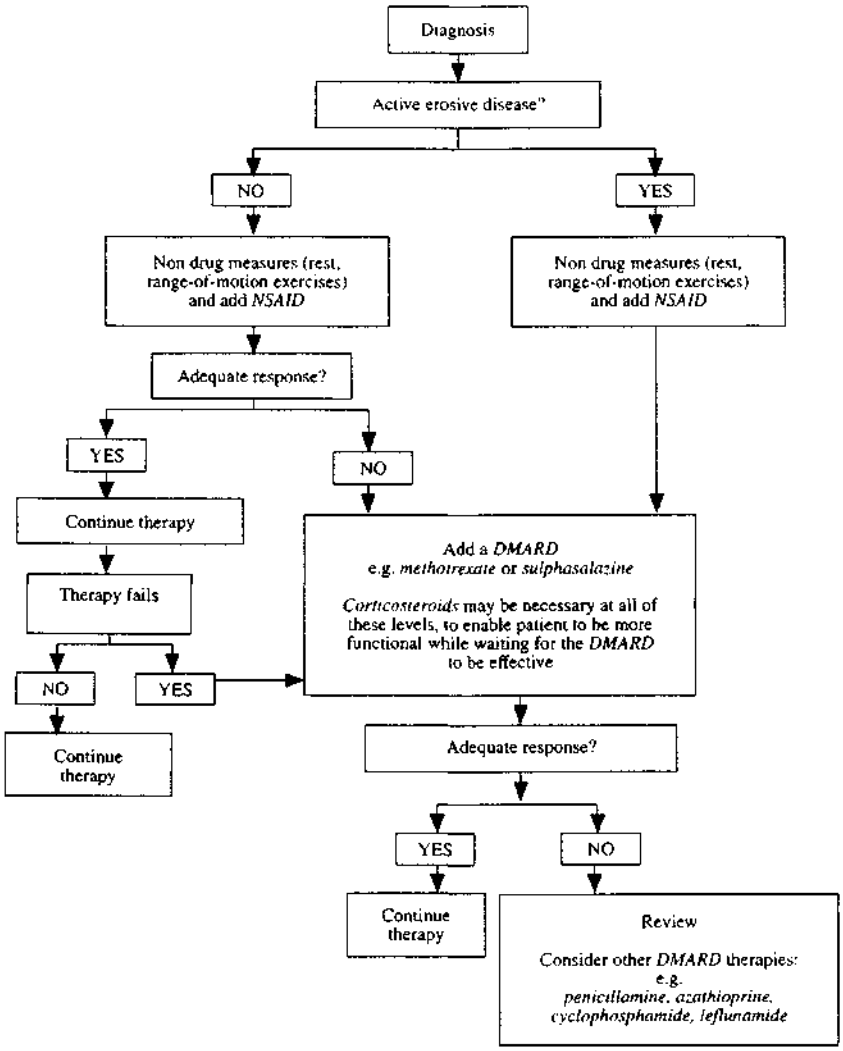
   c. comply with all other applicable regulations made in terms of the Medical Schemes Act, 131 of 1998.
3. This algorithm may not necessarily always be clinically appropriate for the treatment of children. If this is the case, alternative paediatric clinical management is included within this benefit if it is supported by evidence-based medicine, taking into account considerations of cost-effectiveness and affordability.

RHEUMATOID ARTHRITIS



Glossary:

- *DMARD* – Disease modifying antirheumatic drugs
- *NSAID* – Non-steroidal anti-inflammatory agents

Applicable ICD 10 Coding:

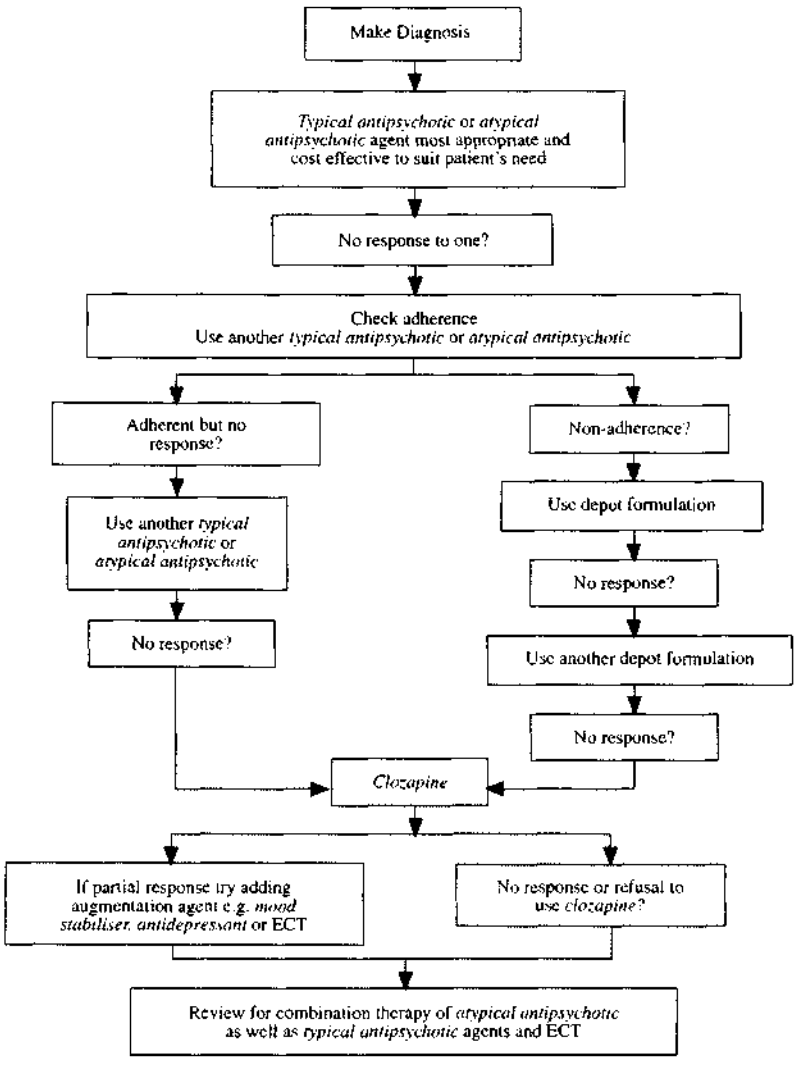
- M05 Seropositive rheumatoid arthritis
  - M05.0 Felty's syndrome
  - M05.1 Rheumatoid lung disease (J99-0*)
  - M05.2 Rheumatoid vasculitis
  - M05.3 Rheumatoid arthritis with involvement of other organs and systems
  - M05.8 Other seropositive rheumatoid arthritis
  - M05.9 Seropositive rheumatoid arthritis, unspecified

- M06 Other rheumatoid arthritis
  - M06.0 Seronegative rheumatoid arthritis
  - M06.1 Adult-onset Still's disease
  - M06.2 Rheumatoid bursitis
  - M06.3 Rheumatoid nodule
  - M06.4 Inflammatory polyarthropathy
  - M06.8 Other specified rheumatoid arthritis
  - M06.9 Rheumatoid arthritis, unspecified
- M08.0 Juvenile rheumatoid arthritis

Note:

1. Medical management reasonably necessary for the delivery of treatment described in this algorithm is included within this benefit, subject to the application of managed health care interventions by the relevant medical scheme.
2. To the extent that a medical scheme applies managed health care interventions in respect of this benefit, for example clinical protocols for diagnostic procedures or medical management, such interventions must—
   a. not be inconsistent with this algorithm;
   b. be developed on the basis of evidence-based medicine, taking into account considerations of cost-effectiveness and affordability; and
   c. comply with all other applicable regulations made in terms of the Medical Schemes Act, 131 of 1998.
3. This algorithm may not necessarily always be clinically appropriate for the treatment of children. If this is the case, alternative paediatric clinical management is included within this benefit if it is supported by evidence-based medicine, taking into account considerations of cost-effectiveness and affordability.

SCHIZOPHRENIA



Glossary:

- ECT – Electroconvulsive therapy

Applicable ICD 10 Coding:

- F20 Schizophrenia
  - F20.0 Paranoid schizophrenia
  - F20.1 Hebephrenic schizophrenia
  - F20.2 Catatonic schizophrenia
  - F20.3 Undifferentiated schizophrenia
  - F20.4 Post-schizophrenic depression
  - F20.5 Residual schizophrenia
  - F20.6 Simple schizophrenia
  - F20.8 Other schizophrenia
  - F20.9 Schizophrenia, unspecified

Note:

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respect of this benefit, for example clinical protocols for diagnostic procedures or medical management, such interventions must—

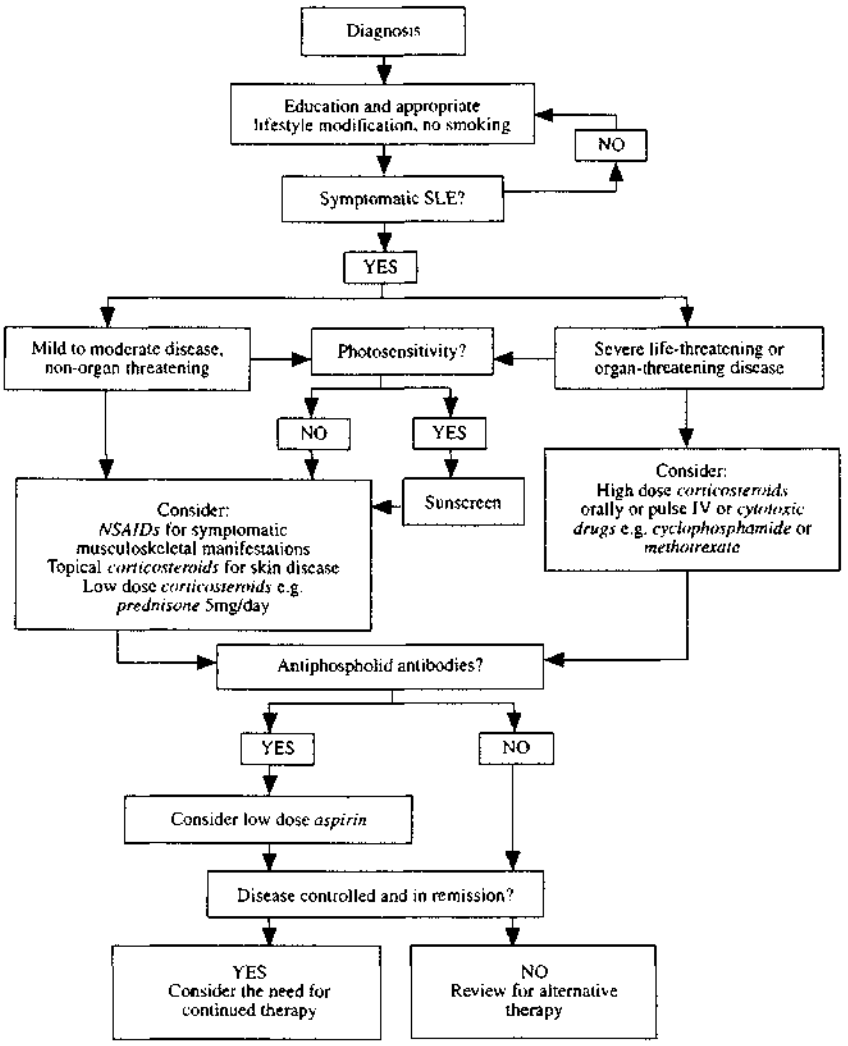
a. not be inconsistent with this algorithm;

b. be developed on the basis of evidence-based medicine, taking into account considerations of cost-effectiveness and affordability; and

c. comply with all other applicable regulations made in terms of the Medical Schemes Act, 131 of 1998.

3. This algorithm may not necessarily always be clinically appropriate for the treatment of children. If this is the case, alternative paediatric clinical management is included within this benefit if it is supported by evidence-based medicine, taking into account considerations of cost-effectiveness and affordability.

SYSTEMIC LUPUS ERYTHEMATOSUS



Glossary:

- IV – Intravenous
- NSAIDs – Non-steroidal anti-inflammatory agents
- SLE – Systemic lupus erythematosus

Applicable ICD 10 Coding:

- M32 Systemic lupus erythematosus
  - M32.0 Drug-induced systemic lupus erythematosus

- M32.1 Systemic lupus erythematosus with organ or system involvement
- M32.8 Other forms of systemic lupus erythematosus
- M32.9 Systemic lupus erythematosus, unspecified

• L93 Lupus erythematosus

- L93.0 Discoid lupus erythematosus
- L93.1 Subacute cutaneous lupus erythematosus
- L93.2 Other local lupus erythematosus

Note:

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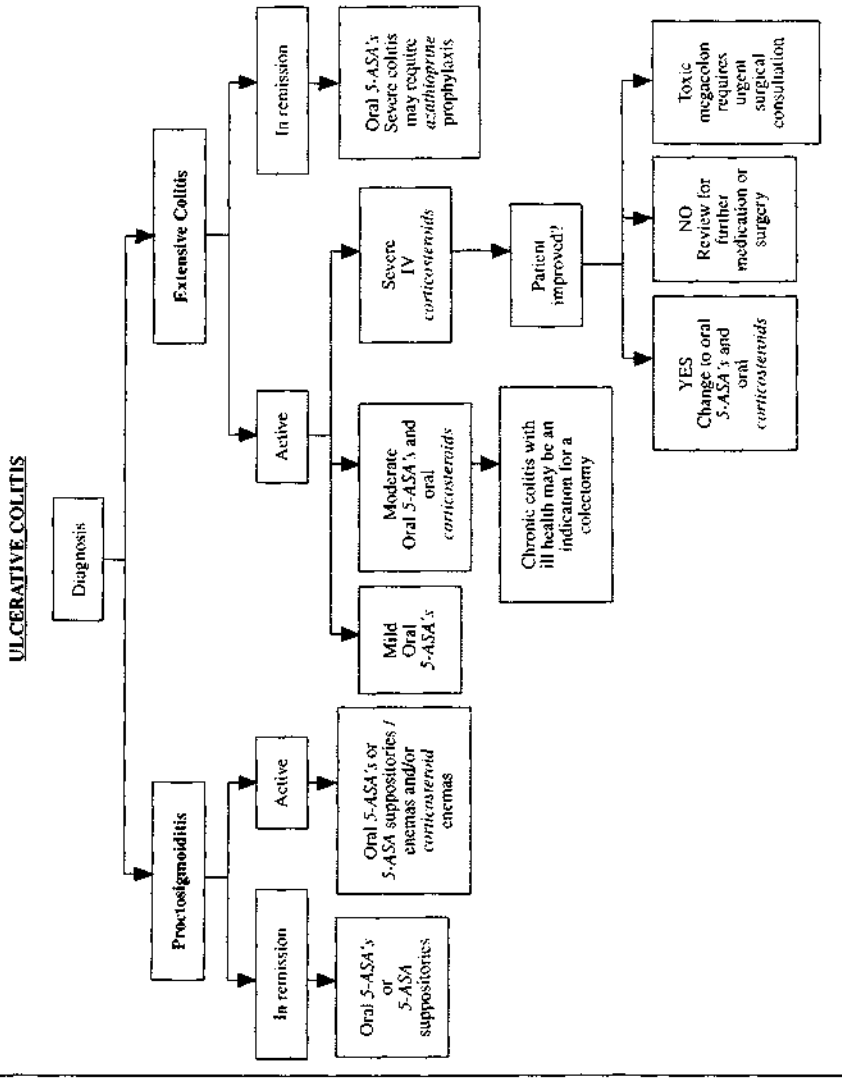

Glossary:

- 5-ASA – 5-Aminosalicylic acid
- IV – Intravenous

Applicable ICD 10 Coding:

- K51 Ulcerative colitis
  - K51.0 Ulcerative (chronic) enterocolitis
  - K51.1 Ulcerative (chronic) ileocolitis
  - K51.2 Ulcerative (chronic) proctitis
  - K51.3 Ulcerative (chronic) rectosigmoiditis
  - K51.4 Pseudopolyposis of colon
  - K51.5 Mucosal proctocolitis
  - K51.8 Other ulcerative colitis
  - K51.9 Ulcerative colitis, unspecified

Note:

1. Medical management reasonably necessary for the delivery of treatment described in this algorithm is included within this benefit, subject to the application of managed health care interventions by the relevant medical scheme.
2. To the extent that a medical scheme applies managed health care interventions in respect of this benefit, for example clinical protocols for diagnostic procedures or

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UNIVERSITY OF
KWAZULU-NATAL

27 NOVEMBER 2006

MRS. E NICOLOSI (202526385)
GRADUATE SCHOOL OF BUSINESS

Dear Mrs. Nicolosi

ETHICAL CLEARANCE APPROVAL NUMBER: HSS/06771A

I wish to confirm that ethical clearance has been granted for the following project:

"The potential for cost saving by extensively using generics for chronic conditions in South Africa"

Yours faithfully

.....
MS. PHUMELELE XIMBA
RESEARCH OFFICE

cc. Faculty Office (Christell Haddon)
cc. Supervisor (Ms. G Manion, Mr. A Gray)