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COST SAVING FROM THE USE OF GENERIC MEDICINES FOR THE TREATMENT OF THE MOST COMMON NON-COMMUNICABLE DISEASES IN ADULTS IN SOUTH AFRICA

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DECLARATION

I, Dhirendra Gyanasivan Redhi, declare that

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DEDICATION

This dissertation is dedicated to my parents, for their endless love, support and encouragement.

ABSTRACT

Access to quality and affordable healthcare is a worldwide problem. Making healthcare affordable to the ordinary South African is a priority of the national government and therefore the use of generic medicine is encouraged. Generic medicines are manufactured by pharmaceutical companies without a licence from the innovator company, and are expected to work physiologically in the same manner as the innovator, based on their bioequivalence. These medicines normally cost less than innovator medicines. One method of reducing the costs of healthcare is by the introduction of generic medicine for the treatment of non-communicable diseases. This cross-sectional retrospective study investigated the potential savings from the use of generic medicine for the treatment of the most common non-communicable diseases of adults in South Africa.

Five of the most common non-communicable chronic diseases in South Africa were extracted from the Council for Medical Schemes chronic disease list. The innovator drug, along with available generic drugs, was selected and an algorithm was designed to compare the single exit price differences for a treatment period of 30 days. To assess the price changes over a period of time, the innovator and generic medicine prices were compared in 2006 and 2014.

This study has shown that there was a major saving potential from the use of generic medicines over innovator medicines for the treatment of the most common non-communicable diseases in adults in South Africa. This has been proven by comparing the single exit price of innovator medicines against that of generic alternatives. However, these

findings confirm that medicine prices between innovator and generic brands vary extensively. A major saving of 97.14% for furosemide, 97.11% for prednisone and 95.70% for glibenclamide existed when generic medicines were used. Minor savings of 8.06% for budesonide and 12.68% for metformin existed when generic medicines were used instead of the innovator product. Secondly, this study has shown that over a period of eight years, most generic drug prices have increased in line with the South Africa's nominal inflation rate, except for the methotrexate which increased by 75.70%, while simvastatin 10mg and 20mg generics decreased by 69.95% and 72.32% respectively. These results confirm the recommendations that generic medicine can be utilised effectively to ensure accessibility and affordable quality healthcare to all. However, constant monitoring of price changes is needed to ensure that above inflation increases do not erode affordability of quality healthcare achieved with the use of generic medicines.

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ABBREVIATIONS

ACE	-	Angiotensin-Converting Enzyme
AIDS	-	Acquired Immunodeficiency Syndrome
AUC	-	Area Under the Curve
CMS	-	Council for medical schemes
DDD	-	Defined Daily Dose
FDA	-	Food and Drug Administration
HIV	-	Human Immunodeficiency Virus
MCC	-	Medicines Control Council
MDDD	-	Monthly Defined Daily Dosage
NCD	-	Non-communicable Disease
NHI	-	National Health Insurance
NHP	-	National Health Plan
PHC	-	Primary Healthcare
RDP	-	Reconstruction Development Programme
SAMF	-	South African Medicines Formulary
SEP	-	Single Exit Price
UK	-	United Kingdom
US	-	United States
VAT	-	Value Added Tax
WHO	-	World Health Organisation

PUBLICATION

The results for this mini-dissertation are in preparation for publication into the, The African Journal of Primary Health Care and Family Medicine.

CHAPTER 1: INTRODUCTION

The South African Constitution states that "everyone has the right to have access to healthcare (Act 108 of 1996)." As a result, making healthcare affordable and accessible to ordinary people is a major priority for the national government in South Africa (Gordhan, 2014). Therefore, to make quality healthcare accessible, the Department of Health (DoH) has encouraged the use of generic medicines to ensure affordability. Generic medicines offer a solution to the healthcare network, allowing access to quality medicines at a cost affordable to many people.

The World Health Organisation (WHO) defines a generic medicine as follows:

> "*A pharmaceutical product, usually intended to be interchangeable with an innovator product that is manufactured without a licence from the innovator company and marketed after the expiry date of the patent or other exclusive rights. Generic drugs are marketed under a non-proprietary or approved name rather than a proprietary or brand name. Generic drugs are frequently as effective as, but much cheaper than, brand-name drugs. Because of their low price, generic drugs are often the only medicines that the poorest can access. A brand name is a name given to a drug by the manufacturer. The use of the name is reserved exclusively for its owner (WHO, 2014)*."

As described by the WHO, Colligan in 2009 stated that, generics are made of the same active ingredients, and are expected to work the same way in the body, they also have the same risks and benefits as their innovator counterparts (Colligan, 2009). These medicines are expected to be less expensive because manufacturers don't have the investment costs of developing a new drug. As a result, each year generic medicines save consumers and the healthcare systems tens of billions of US dollars (Colligan, 2009). Nearly 69 per cent of all

prescriptions in the United States (US) are filled with generic medicines, with roughly 16 cents of every dollar spent on prescriptions, are being spent on generic medicines (Colligan, 2009). However, generic medicines should be comparable to the innovator drug based on bioequivalence to achieve the same therapeutic effect (de Lira *et al*., 2014).

The US Food and Drug Administration (FDA) defined bioequivalence as:

> *"The rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of action. For drug products that are not intended to be absorbed into the bloodstream, bioavailability may be assessed by measurements intended to reflect the rate and extent to which the active ingredient or active moiety becomes available at the site of action* (US Food and Drug Administration, 2011)."

The US has approved the Hatch-Waxman Act in 1984, which allowed the FDA to accept the use of generic medicines based on bioequivalence. The purpose of this law was to increase affordability and accessibility of medication to the consumer, by allowing generic manufacturers not to subject their products for clinical trials and tests, resulting in cheaper production costs (Lichanda *et al*., 2013). Many high income countries (e.g. the US, the United Kingdom (UK), Switzerland), allowed generic medicines into their health systems and imposed generic substitution of innovator or branded medication wherever possible, to save costs (Lichanda *et al*., 2013). These medicines generally cost between 20%-90% less than an innovator medicine (Dunne *et al.,* 2013). In the US, generic medicines account for two thirds of all prescriptions and 20% of the spending on pharmaceuticals (Lichanda *et al*., 2013).

Other countries all over the world also encourage the use of generic medicines to enable access to quality healthcare. For example, in Canada, regulators have set minimum standards for the acceptance of generic drugs onto the local market, these standards include 90% confidence intervals for the maximum peak concentration and total drug exposure over time, with an area under the curve limit of 0.80 to 1.25 (McCormack & Chmelicek, 2014). This translates into a bioequivalence difference of no more than 5% to 7% when compared to the innovator (McCormack & Chmelicek, 2014).

In a study conducted by Olszynski *et al.* (2014) in Canada, the dissolution rates of innovator and generic forms of alendronate and risedronate were compared. The results were unexpected, as the two generic versions of the alendronates disintegrated faster than the innovator. This posed as a risk, as the drug may cause an interaction with the esophageal mucosa and enhance the possibility of side effects (Olszynski *et al.,* 2014).

A pilot study, which was conducted in Penang, in Malaysia, measured the extent to which generic substitution practices took place at community pharmacy level (Ping *et al*., 2008). This study reported that 47% of pharmacists had promoted generic substitution to their customers, and most of the prescribers when contacted by pharmacists accepted the suggestion of generic substitution. Eighty (80%) percent of consumers accepted a pharmacist's recommendation to substitute their prescribed treatment with generic medicines (Ping *et al*., 2008).

The prescribing patterns of doctors are influenced by many dynamics. However, the most influential factor is the visit from a pharmaceutical sales representative (Fugh-Berman &

Ahari, 2007). It is projected that some 20 million visits are made by sales representatives to doctors and hospitals in Germany annually (Lieb & Scheurich, 2014). Fifty three percent (53%) of prescribers believed that the prescribing habits were influenced by incentives received from a sales representative be it drugs samples, stationary or dinner invitations (Lieb & Scheurich, 2014).

In Brazil, generic drugs were introduced in 1999. Since then, the prices of medication in general have fallen between 40% and 62% (de Lira *et al*., 2014). However, the sales of generic medicines account for only 27.1% of the total pharmaceutical market spend analysis (de Lira *et al*., 2014), while family expenditure on medication accounts for approximately 48.6% of total healthcare expenses. Therefore the introduction of generic medicine in Brazil became a good alternative for large segments of the population (de Lira *et al*., 2014).

In another recent study, Cameron and Laing reported that an average of 9% to 89% could be saved by a single-medicine-switch from innovator brands to lowest-priced generic equivalents (Cameron & Laing, 2010). In Pakistan, it is believed an average of 51% of the current private sector spending could be saved across the 9 medicines studied, and the net savings would exceed US$ 12 million. In China a potential US$ 86 million could be saved from the substitution of just four medicines, while saving a patient an average of 65% (Cameron & Laing, 2010).

In a study conducted in Europe by Simoens and De Coster, which aimed to determine the savings from increased substitution of generic for innovator medicines, the methodology used in this study was based on the potential saving from substituting a generic medicine

for an innovator medicine. The study included ten active substances in each country within Europe, which had the highest public expenditure of an innovator brand in 2004. The results revealed that an estimated €3 billion saving for the 11 countries would be achieved by generic substitution (Simoens & De Coster, 2006).

Literature from Shrank and colleagues (2011b) described prior research indicating that while patients generally have favourable views about the quality, cost and value of generic medicines, the majority do not prefer to use them (Shrank *et al.,* 2011b). Although patient perceptions play a vital role in the selection of medication, they rarely communicate with their doctors about out-of-pocket costs of medication and medication choices, and this consequently leaves the doctor with a substantial influence over medication selection (Shrank *et al.,* 2011b). To improve generic medication usage, it would be ideal to understand doctors' perceptions about the quality and efficacy of generic medicines. Therefore, prescribers' attitude towards the use of generic medicines could create a hurdle in the aim of making healthcare more affordable and accessible.

In South Africa, once democracy was achieved in 1994, the governing party, i.e., the African National Congress, was challenged with creating a National Health Plan (NHP) for South Africa to make healthcare accessible and affordable. The aim was to create a system which is able to achieve a unitary, comprehensive, equitable and integrated national health system (Department of Health, 2010). The greatest test of the national government at the time, was not only focussed on providing quality affordable medicines for the majority of the population, but it also had to deal with economic injustices and to increase productivity, while exercising greater control of personal wellness (Yach & Kistnasamy, 2007). With the

construction of a new health system under direction of the NHP, many programmes were introduced in the public sector which culminated and became known as the Reconstruction and Development Programme (RDP) (Kautzky & Tollman, 2008). The RDP was responsible for creating infrastructural development, greater access to water and electrification, availability of social welfare grants to the previously disadvantaged populations, and free maternal and child health care (Kautzky & Tollman, 2008). However, the challenge of affordability and accessibility of medicines is not only felt by the public healthcare sector, but also affects the private healthcare sector.

A major problem facing the private sector is the hasty increase in spending in particular by those patients on medical aid schemes, medical insurances and hospital plans, as the annual spending increases, so do medical aid contributions (van de Merwe, 2014). Often individuals who belong to the medical aid schemes are struck with an above inflation increase in monthly contributions (van de Merwe, 2014). In an attempt to limit the increasing cost of private health care, some medical aid schemes have introduced a generic medicine strategy, whereby the scheme encourages the use of generic medicine (Sheppard & Principal, 2010). Usually, prescription drugs are the most expensive element of any health care plan and the costs generally continue to rise as drug utilisation increases, and new more expensive drugs are introduced into the marketplace (Manulife Financial, 2010).

At the moment, the South African healthcare system is an unbalanced two-tiered system, i.e., the public and the private healthcare systems. However, the public healthcare sector delivers its services to about 80% of the population with limited resources (Ruff *et al*., 2011). To deal with the burden of providing quality healthcare, the South African government is

currently developing a new healthcare system called the National Health Insurance (NHI). The NHI intends to ensure that all South Africans have access to quality healthcare (Naidoo, 2012). The use of generic medicines is the cornerstone of providing quality and affordable healthcare to all South Africans through the NHI. Recent studies have shown that the generic drugs entering the South African market have a 20% - 30% price differential when compared to an innovator drug price, whereas in developed countries a cost differential of up to 90% is seen, due to the domination of expensive generics in the market (Bateman, 2014). As Nicolosi and Gray (2009) stated, the South African government committed itself to the use of generic medicines as a key cost savings mechanism and to promote the availability of safe and effective drugs at the lowest possible cost. Colligan (2009) also reported that generic drugs represent a safe, effective, and affordable method to decrease overall healthcare costs to the state. More importantly, medicines are fundamentally used in the management of many chronic diseases.

According to Bradshaw & Steyn (2001), South Africa is a middle income country that has amongst the most extreme inequalities in wealth in the world. The national statistics suggest that 52% of the households were living in poverty in 1996, although the degree of poverty depends on the poverty line and methodology used (Bradshaw & Steyn, 2001). With increasing pressure on the healthcare system, it is imperative that everyone has access to healthcare facilities while spending the least amount of money on prescription medication and having more money available for other healthcare services. Therefore, the use of generic medicine plays an important role in a patient's lifestyle (Bradshaw & Steyn, 2001). In 2001, more than forty of the world's largest pharmaceutical companies had made an attempt to stop the South African government from trying to introduce legislation aimed at

reducing the price of medicines, and allowing the importation of cheaper drugs in South Africa (Sidley, 2001). A study conducted by Patel *et al.*, to determine patients and health care worker's perceptions about the quality of generic medicines available in South Africa, revealed that generic medicines were acceptable by patients who had chronic illnesses or where cost plays a key factor (Patel *et al.*, 2012).

Nicolosi and Gray (2009) obtained prices of innovator drugs and compared them to the prices of two generic drugs for the twenty five listed chronic conditions set out by the Council for Medical Schemes (CMS). Their results showed that, out of all the generic medicines identified, 67.5% were more than 40% cheaper, per defined daily dose per month, than the innovator product. They also reported that in 16 medicines the cost differentials between generic versions were 1% or less. Some correlation between the number of generics and the size of the cost differential was apparent (correlation coefficient 0.49). There were examples of high-cost differentials in highly competitive areas of the market (Nicolosi & Gray, 2009).

As Aikins and colleagues reported, Africa bears a significant proportion of the global burden of chronic diseases, along with poor countries of Asia and Latin America (Aikins *et al.*, 2010). Africa's chronic disease problem is attributed due to a number of factors that include increased life expectancy, changing lifestyle practices, poverty, urbanisation and globalisation. With an increasing morbidity and mortality rate from chronic diseases, the result is an even greater burden of infectious disease, which accounts for at least 69% of deaths on the continent (Aikins *et al.*, 2010). Most non-communicable diseases are chronic in nature and require treatment indefinitely. This places a huge burden on the country's

financial economy to ensure accessibility and availability of medicines in the primary healthcare system.

The WHO describes non-communicable diseases (NCD) as:

> "chronic diseases which are not passed from person to person. They are of long duration and generally slow progression. The four main types of NCDs are cardiovascular diseases (like heart attacks and stroke), cancers, chronic respiratory diseases (such as chronic obstructed pulmonary disease and asthma) and diabetes" (World Health Organisation, 2014).

The NCDs emerge over an extended period of time and are preceded by an unhealthy lifestyle, resulting in risk factors such as obesity, increased blood pressure, increased blood glucose levels, increased cholesterol levels, physical inactivity, uncontainable alcohol and tobacco use (Puoane *et al.,* 2008). A South African comparative risk assessment conducted in 2000 identified that NCDs often advanced to mortality resulting from diseases such as diabetes mellitus, ischaemic heart disease, stroke and hypertensive disease (Puoane *et al.,* 2008). NCDs are believed to cause disruption to the labour force and productivity output of the country by targeting the working-age populace due to unhealthy lifestyle practices, which are being passed down to the youth and therefore it is critical to prevent further NCDs by identifying individuals at risk and assisting them in changing their behaviour (Bradshaw *et al*., 2010).

Mayosi and colleagues (2009) stated that NCDs are emerging rapidly in both urban and rural areas and are predominantly seen in poor people and this burden is expected to increase significantly over the next decades to come if actions are not taken to halt this trend. With the increasing number of deaths from diabetes, chronic kidney disease, cancer of the cervix and prostate, and neuropsychiatric disorders it is noticeable that the burden of NCDs is rising (Mayosi *et al*., 2009). The WHO estimates that NCDs caused 28% of the total burden of disease, and that the burden is two to three times higher than in developed countries, with similar results seen in sub-Saharan countries (Mayosi *et al*., 2009). To manage the burden, policy amendments have been implemented to control the sale of tobacco and to promote the development of a responsible and sustainable liquor industry (Mayosi *et al*., 2009). Large investments and development into the primary health care system are needed to manage the burden of NCDs, in addition, initiatives to promote good health should be a nationwide phenomenon starting with school sites and proceeding to community based institutions (Mayosi *et al*., 2009).

According to the Medicines and Related Substances Act, 101 of 1965, the level of increase in the single exit price (SEP) of a medicine or scheduled substance is determined by the Minister of Health and based annually on "the average consumer price index for the preceding year; the average producer price index for the preceding year and foreign exchange rates" (Medicines and Related Substances Act, 1965). In a circular published by the CMS (2013), which evaluated the contribution increase assumptions for the year 2013, it was expected that medicine price would increase by 6% on average, which was in line with the approved SEP increase of 5.8%, and that the average cost of medicines within a private hospital would increase by 8.9% (Council for Medical Schemes, 2013).

The aims of this study, therefore, were to compare the prices of the innovator and generic medication required for one month of treatment of a non-communicable disease and to assess the price changes over a period of time.

CHAPTER 2: METHODOLOGY

This chapter details the research methodology used to enable the objectives of this study to be met.

2.1 Research design

This was a cross-sectional retrospective study which assessed and compared the prices of medication required per month for the treatment of non-communicable diseases in South Africa in September 2006 and in July 2014.

2.2 Objectives

The objectives of the study were:

2.2.1 To assess the cost of generic and innovator medicines used to treat common non-communicable diseases in South Africa.

2.2.2 To compare the price differential between generic and innovator medicines in 2006 and in 2014.

2.2.3 To assess the potential cost savings when generic medicines are used instead of innovator medicines to treat common non-communicable diseases in South Africa.

2.3 Methods

The medicines available for the treatment of each of the chosen non-communicable diseases were extracted from the Pharmaceutical Blue books (Pharmaceutical Blue Book. 2006; 2014). Only medicines that were available in the Standard Treatment Guidelines, Primary Heath Care Level (Department of Health, 2008) were used for this study. The single exit price (SEP), inclusive of 14% value added tax (VAT) in the South African currency (the Rand), and the defined daily dose (DDD) of each medicine were used to calculate the monthly costs.

To assess the cost differentials over time, the cost of medicines in 2006 and in 2014 were compared using prices listed in the Pharmaceutical Blue books (Pharmaceutical Blue Book. 2006; 2014).

The innovator drugs along with available generic drugs were selected, and an algorithm was designed to compare the SEP differences. The cost per DDD for a treatment period of 30 days was used as a monthly supply of medication. The DDD is defined as, the assumed average maintenance dose per day for a drug used for its main indication in adults (World Health Organisation Collaborating Centre for Drug Statistics Methodology, 2009). The recommended minimum daily dosage described in the South African Medicines Formulary (2014) for each non-communicable disease was used, and quantity required for a month's supply of medicine was calculated. Since pharmaceutical drugs are available in various strengths and are specific to a disease stages, the different strength prices were also compared where applicable.

The monthly defined daily dosage (MDDD) cost (R) was calculated as follows:

$$Monthly\ defined\ dosage\ cost\ (R) = \frac{(SEPV)x\ 30(days)xDDD/Strength}{Quantity}$$

30 days = Taken as the average number of days in a month

SEPV = Single Exit Price inclusive of VAT

DDD / strength = Number of tablets/capsules required for DDD

Quantity = Number of tablets/capsules in presentation at the SEP

Data were then entered into a Microsoft Excel spread sheet for analysis; validation and proof-reading was done by the researcher to ensure accuracy.

To identify the disease conditions to be investigated, a list was extracted from the CMS (Council for Medical Schemes, 2014) detailing the most common non-communicable chronic diseases in South Africa, and a shortlist was thereafter completed. The following five most common non-communicable chronic diseases in South Africa were chosen (Council for Medical Schemes, 2014):

1. Hypertension
2. Diabetes Mellitus Type 2
3. Asthma
4. Hyperlipidaemia
5. Rheumatoid Arthritis

2.4 Inclusion criteria

Only data pertaining to adults were collected and only medicines administered orally included in the study i.e., persons older than the age of eighteen years.

2.5 Exclusion criteria

Combination drugs (e.g., a combination of an oral blood glucose lowering drug, metformin and sulphonylurea) often, but not invariably, do not have a specified DDD and were therefore excluded.

2.6 Analysis

Data were captured into a spread sheet for analysis. Once entered into a spread sheet, pricing differences, means, standard deviation and percentage differences were calculated. Representational graphs were thereafter generated to explicate the results of the study. All pricing captured are SEPs inclusive of VAT, but excluding dispensing fees, in South African Rand value.

2.7 Ethical considerations

Since all data utilised in this study was available in the public domain, it was not necessary to obtain ethics approval. However, the protocol was given full ethics “exemption” by the Biomedical Research Ethics Committee, University of KwaZulu-Natal, South Africa (BREC Ref.: EXM 295/14) (Appendix B). Informed consent was not required for this study, since no subjects, persons or medical records were utilized. The research was conducted with honesty and the work of other authors, used in this study, was fully acknowledged.

CHAPTER 3: RESULTS

3.1 Introduction

In this chapter, the data are analysed and discussed with reference to the aim and objectives of the study.

3.2 Antihypertensive medicines

For the treatment of hypertension, 12 active ingredients identified were: hydrochlorothiazide; furosemide; spironolactone; enalapril; perindopril; ramipril; captopril; amlodipine; methyldopa; atenolol; bisoprolol and propranolol.

As shown in Figure 1, there was 49.68% difference in cost for hydrochlorothiazide 25mg between the innovator and the cheapest generic drug price. In the case of furosemide in 2014, there was a major price difference of 97.14% (R132.25) between the innovator and the cheapest generic. The difference between the mean generic price and cheapest generic price is 66.29% (R7.67). It would work out much more cost effective if a patient were to receive a 120, 25mg spironolactone tablets instead of 30, 100mg spironolactone tablets (a saving of R83.46 as seen with the cheapest generic). With other diuretics, there was a difference of 4.45% (R1.58) between the spironolactone 25mg innovator and cheapest generic.

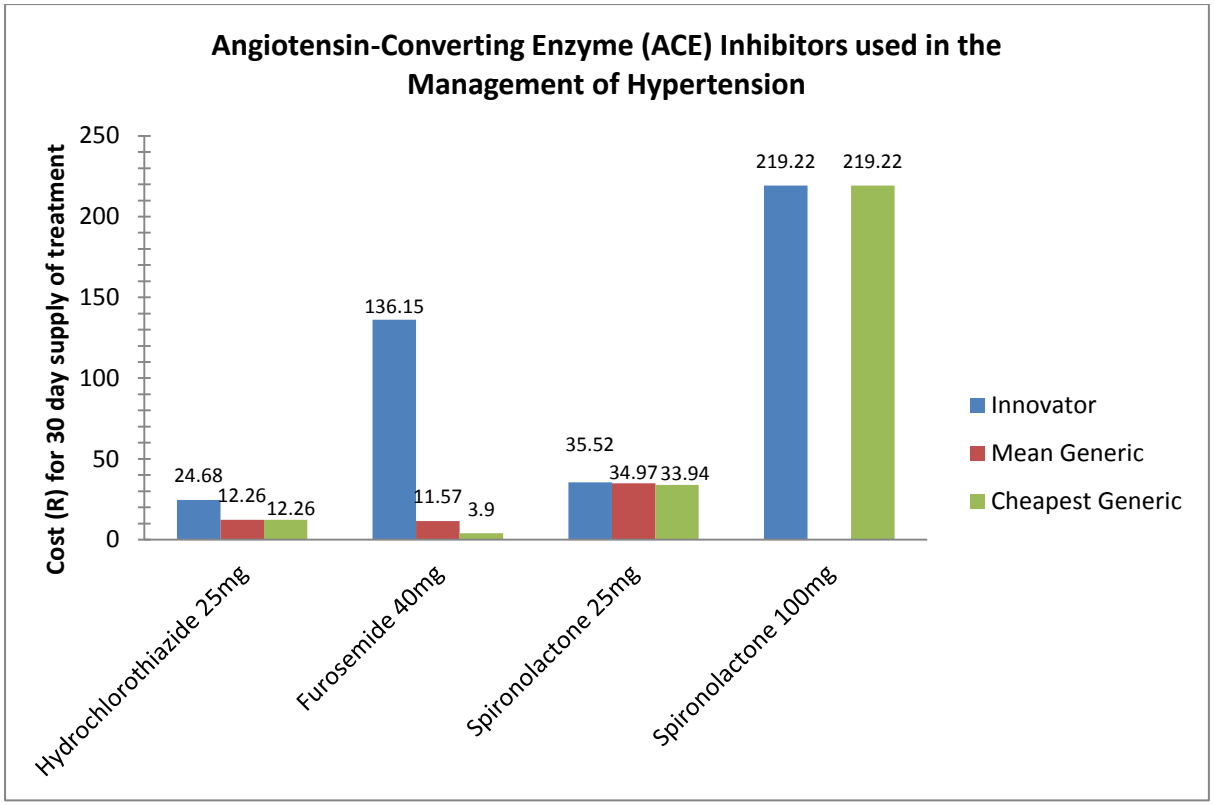

Figure1: Prices of antihypertensive medication – diuretics in 2014.

For enalapril, a similar pattern of price differences is seen amongst all the strengths as shown in Figure 2, except for the enalapril 10mg, in which there was only 4.1% (R1.90) difference between the innovator and mean generic price. As for ramipril 5mg, a price difference of 65.48% (R195.15) existed between the innovator and cheapest generic, and 50.97% (R151.90) between the innovator and the mean generic price. This means that a patient could purchase almost 3 months' supply of the cheapest generic of ramipril 5mg for the price of one month's supply of ramipril innovator. The captopril 25mg had a difference of 92.17% (R156.16) between the innovator and cheapest generic, and 80.37% (R136.16) between the innovator and mean generic price.

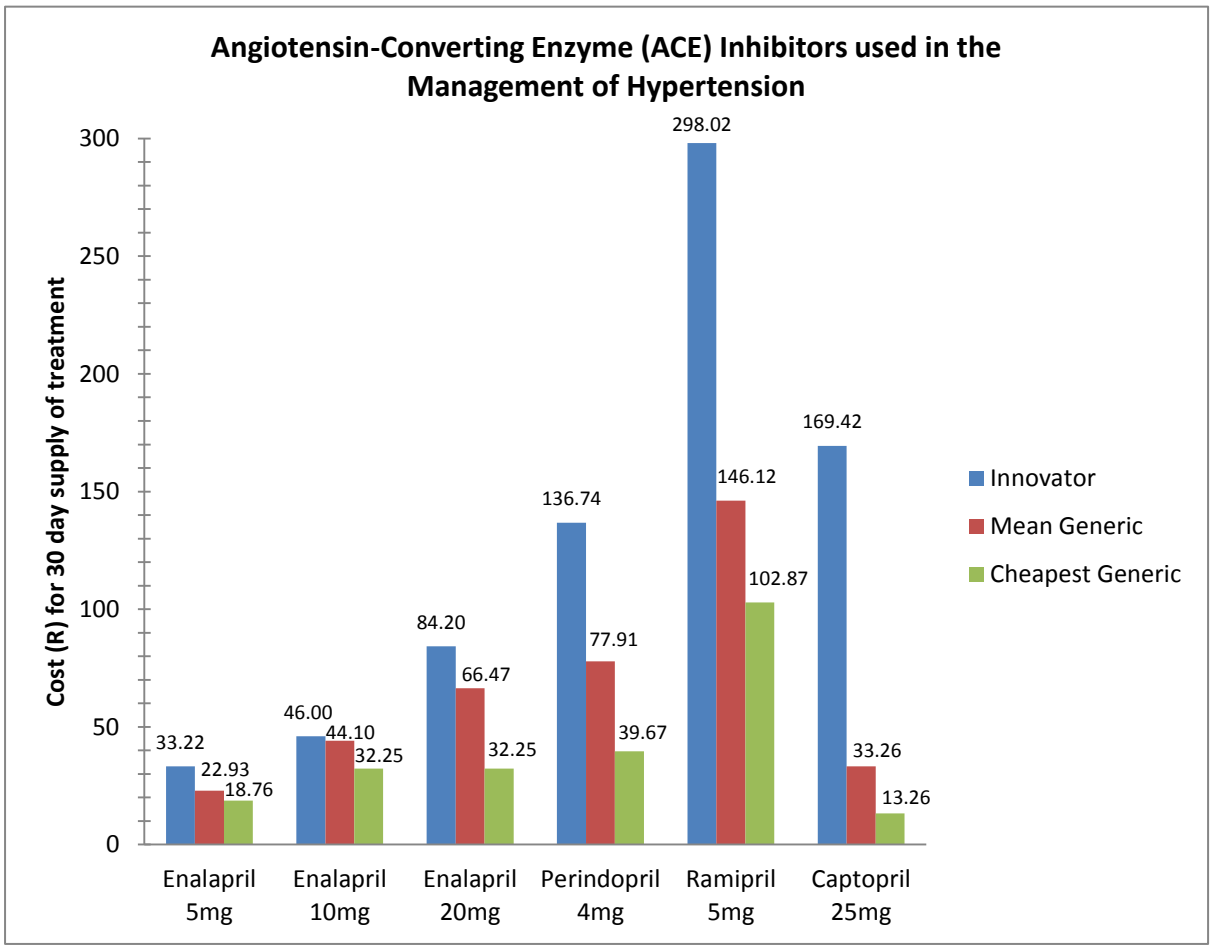

Figure 2: Prices of antihypertention medication – ACE inhibitors in 2014.

There was a trend of saving for the two strengths of the amlodipine range from the use of generic medicines. A saving of 78.51% (R129.09) between the innovator and cheapest generic, and 58.52% (R96.23) between the innovator and mean generic price was seen for amlodipine 5mg, and 48.18% (R32.86) between the mean and cheapest generic. The amlodipine 10mg has a saving of 72.16% (R162.50) between the innovator and cheapest generic, and 40.65% (R42.94) between the mean generic and cheapest generic price. Methyldopa has a saving of 42.95% (R14.16) between the innovator and cheapest generic as seen in Figure 3, below.

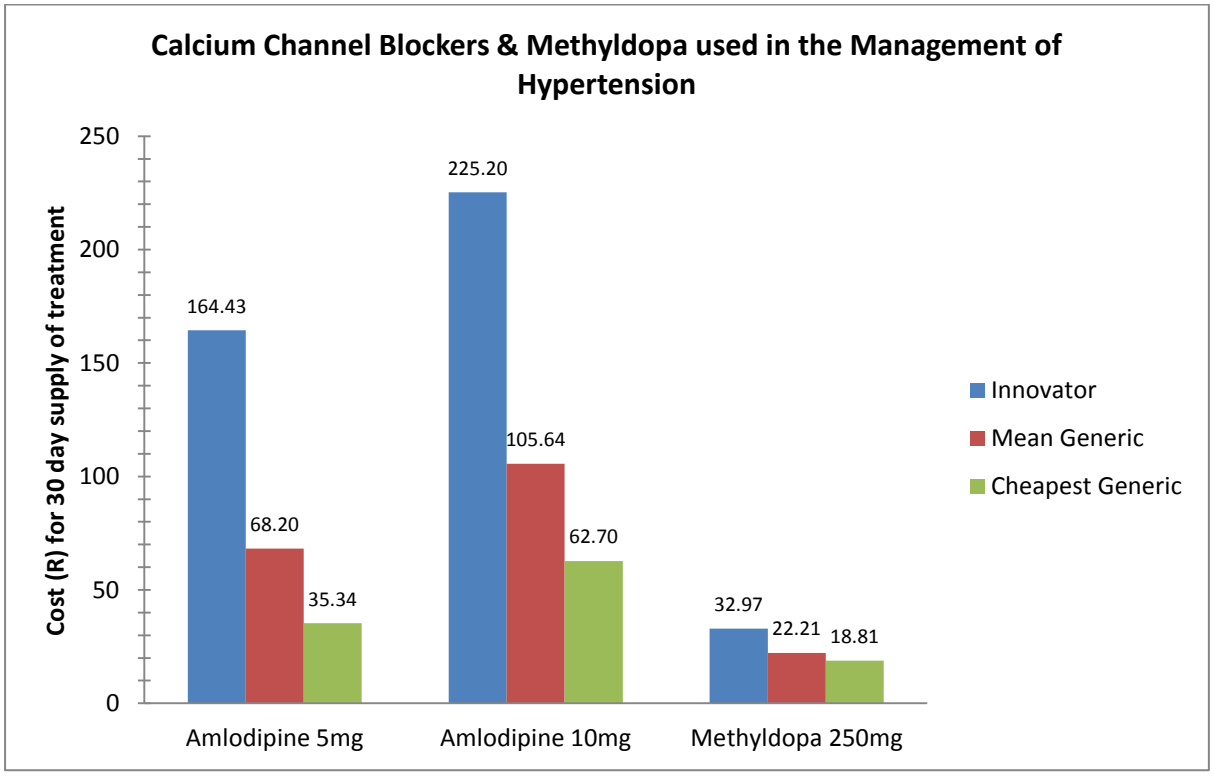

Figure 3: Prices of antihypertensive medication – calcium channel blockers & methyldopa in 2014.

As shown in Figure 4, there were more considerable savings from the use of generic beta-blockers in the treatment of hypertension. The atenolol 50mg had a saving of 90.74% (R158.44) between the innovator and cheapest generic, 86.72% (R151.43) between the innovator and mean generic price, and 30.24% (R7.01) between the mean generic price and the cheapest generic. For atenolol 100mg, a saving of 90.28% (R256.31) between the innovator and cheapest generic, 86.20% (R244.78) between the innovator and mean generic, and 29.47% (R11.53) between the mean generic and cheapest generic. The bisoprolol 5mg and 10mg had a saving of 54.21% (R53.37) and 51.27% (R79.82) between the innovator and cheapest generic respectively. Propranolol had a similar savings potential of 94.81% (R45.29) and 96.40% (R115.26) for the 10mg and 40mg tablets respectively.

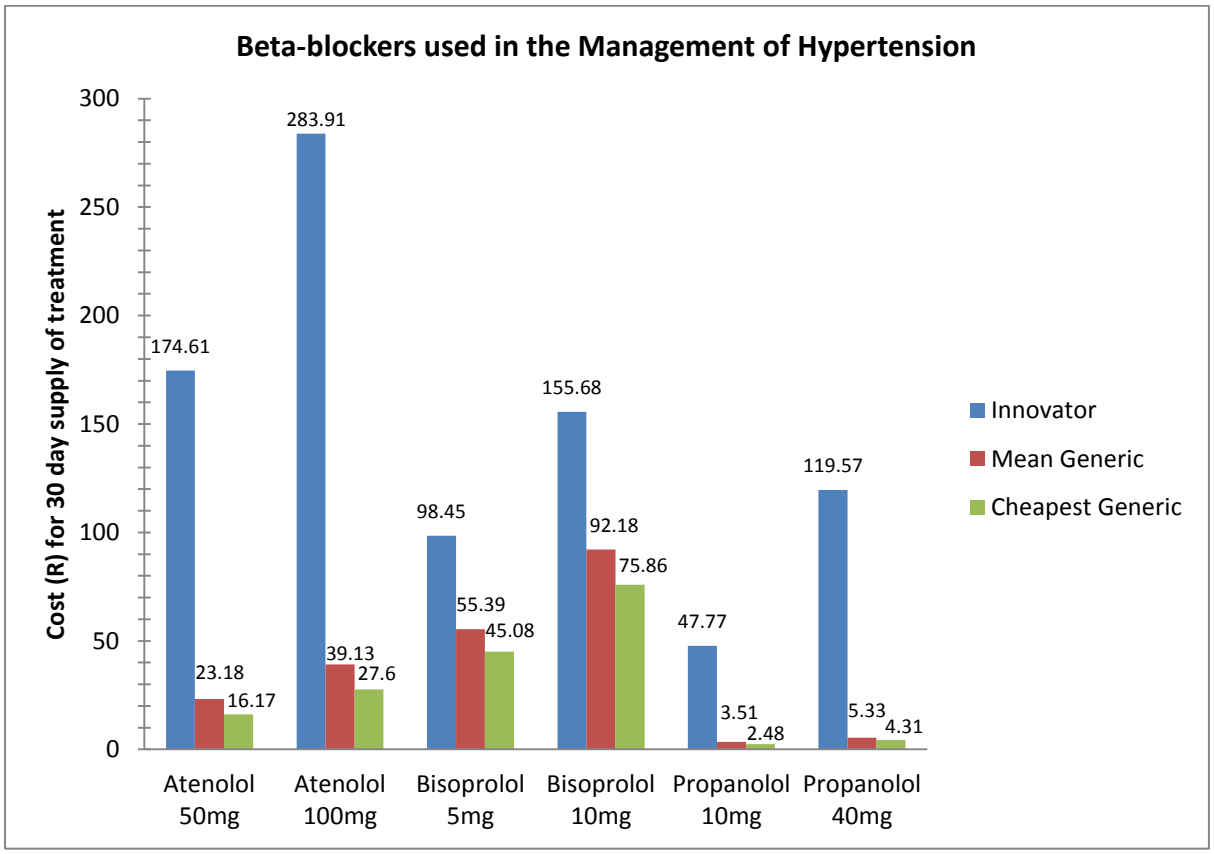

Figure 4: Prices of antihypertensive medication – β-blockers in 2014.

3.3 Diabetes Mellitus Type 2 medicines

The oral antidiabetic medicines included in this study belonged to two pharmacological classes - that is, the biguanides and sulphonylureas. A total of four active ingredients were identified - i.e. metformin; glibenclamide; gliclazide and glimepiride.

As shown in Figure 5, there was a noticeable trend in the metformin price among the two strengths. A saving of 39.66% (R6.52) existed between the innovator and the cheapest generic, 30.90% (R5.08) between the innovator and the mean generic price, and 12.68% (R1.44) between the mean generic and cheapest generic for a month's supply of metformin 500mg. For metformin 850mg, a saving of 38.21% (R11.21) between the innovator and cheapest generic, 29.62% (R8.69) between the innovator and mean generic, and 12.20% (R2.52) between the mean generic and cheapest generic existed.

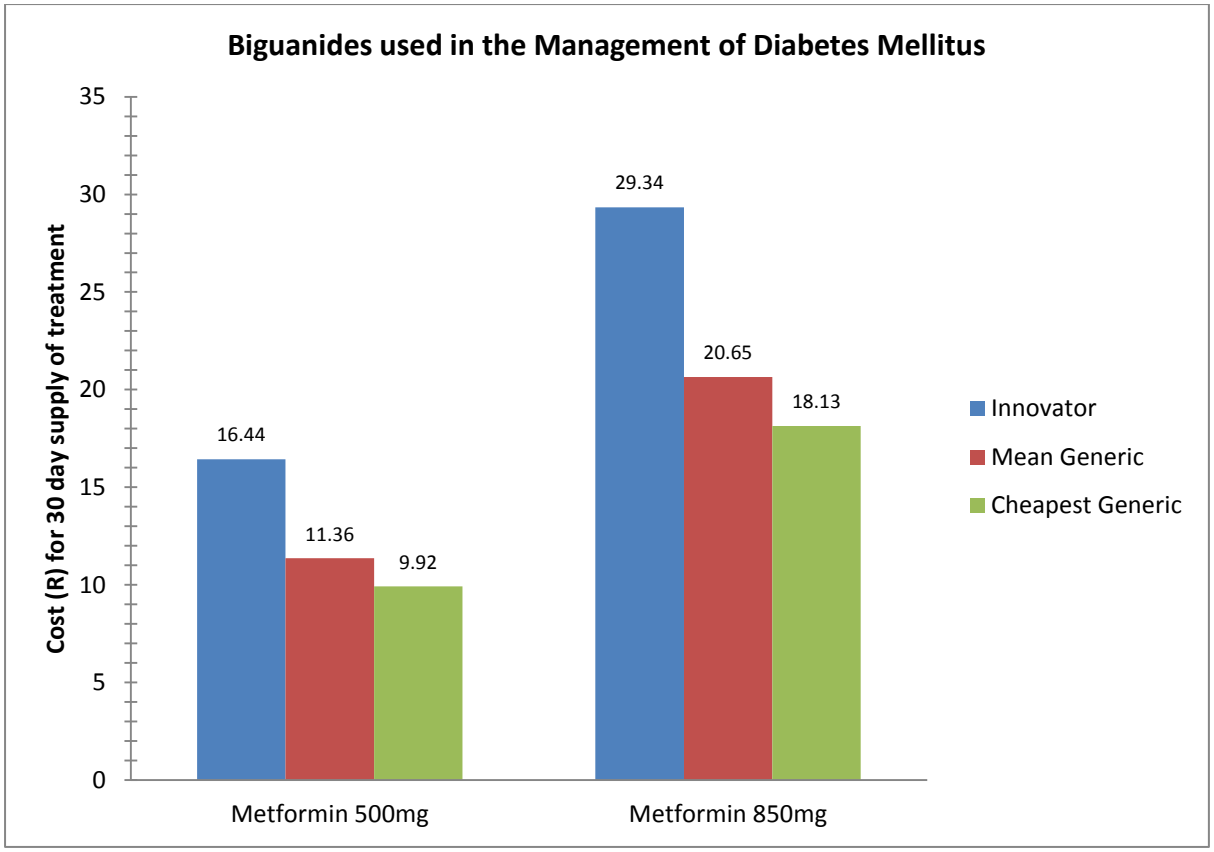

Figure 5: Prices of diabetes mellitus type 2 medication – biguanides in 2014.

Glibenclamide had the largest variation in price when compared with the available brands as seen in Figure 6. A saving of 95.70% (R153.11) existed between the innovator and cheapest generic, 95.46% (R152.73) between the innovator and mean generic, and 5.23% (R0.38) between the mean generic and cheapest generic. The innovator had therefore priced itself significantly higher than all available generic brands, and will most likely have the least market share. The gliclazide 80mg had a saving of 57.94% (R25.65) between the innovator and cheapest generic, glimepiride 1mg and 2mg have a saving of 53.79% and 51.87% between the innovator and cheapest generic respectively.

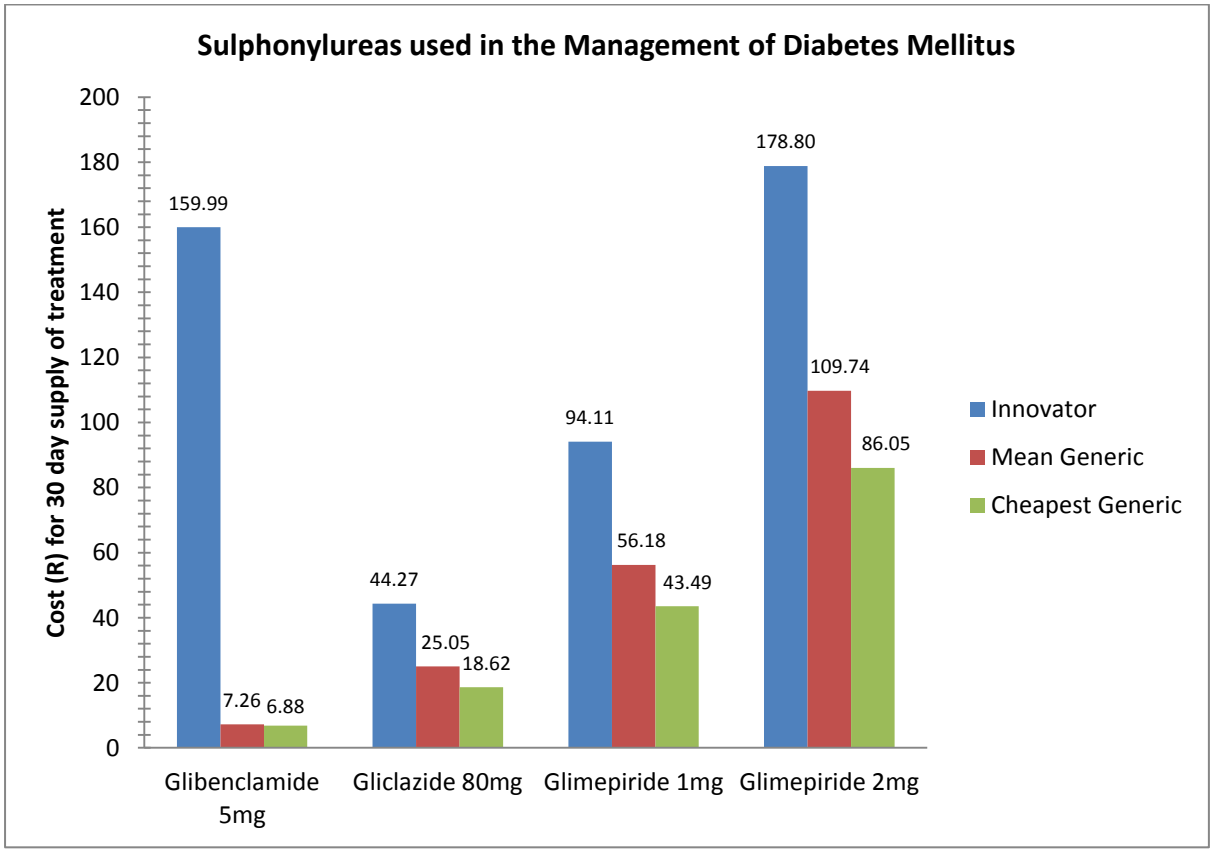

Figure 6: Prices of diabetes mellitus type 2 medication – sulphonylureas in 2014.

3.4 Asthma medicines

Asthma medicines included in this study consisted of 3 pharmacological classes and four active ingredients, i.e., salbutamol; theophylline; budesonide and beclomethasone were available for analysis.

As shown in Figure 7, a salbutamol 100µg 200 dose unit had a saving of 65.39% (R42.63) between the innovator and cheapest generic, 45.21% (R29.47) between the innovator and mean generic, and 36.84% (R13.16) between the mean generic and cheapest generic. Theophylline had a single generic drug for each strength of the active ingredient available. There was a saving of 70.95% (R107.38) and 63.36% (R111.23) for the 200mg and 300mg respectively.

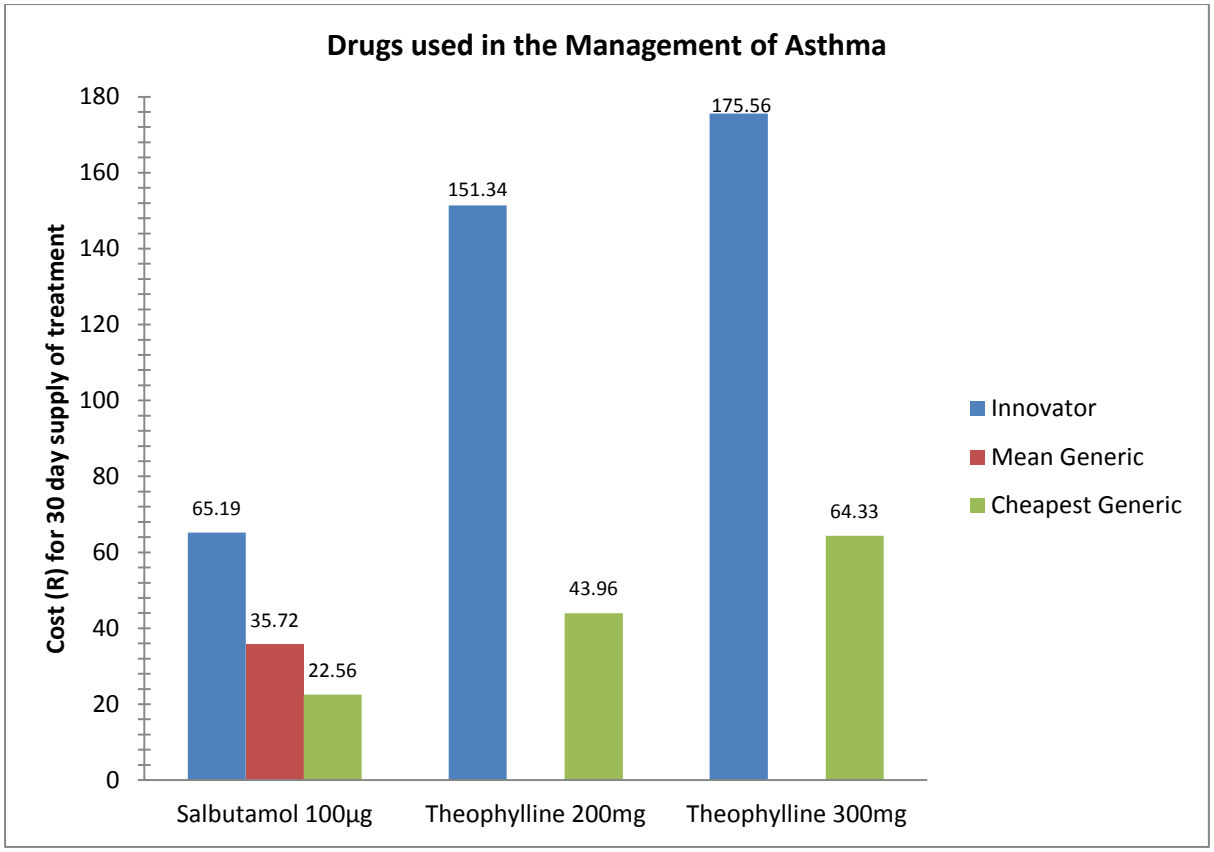

Figure 7: Prices of asthma medication in 2014.

The cheapest generic for budesonide 100mg costs 23.79% (R45.51) less than the innovator (Figure 8). The innovator of budesonide 200µg is 14.68% (R32.90) cheaper than the mean generic price and 8.06% (R16.76) cheaper than the cheapest generic. More importantly, it is noted that the innovator of budesonide 100µ and 200µ was the same price. The beclomethasone 100µg has a saving of 61.49% (R126.49) between the innovator and cheapest generic.

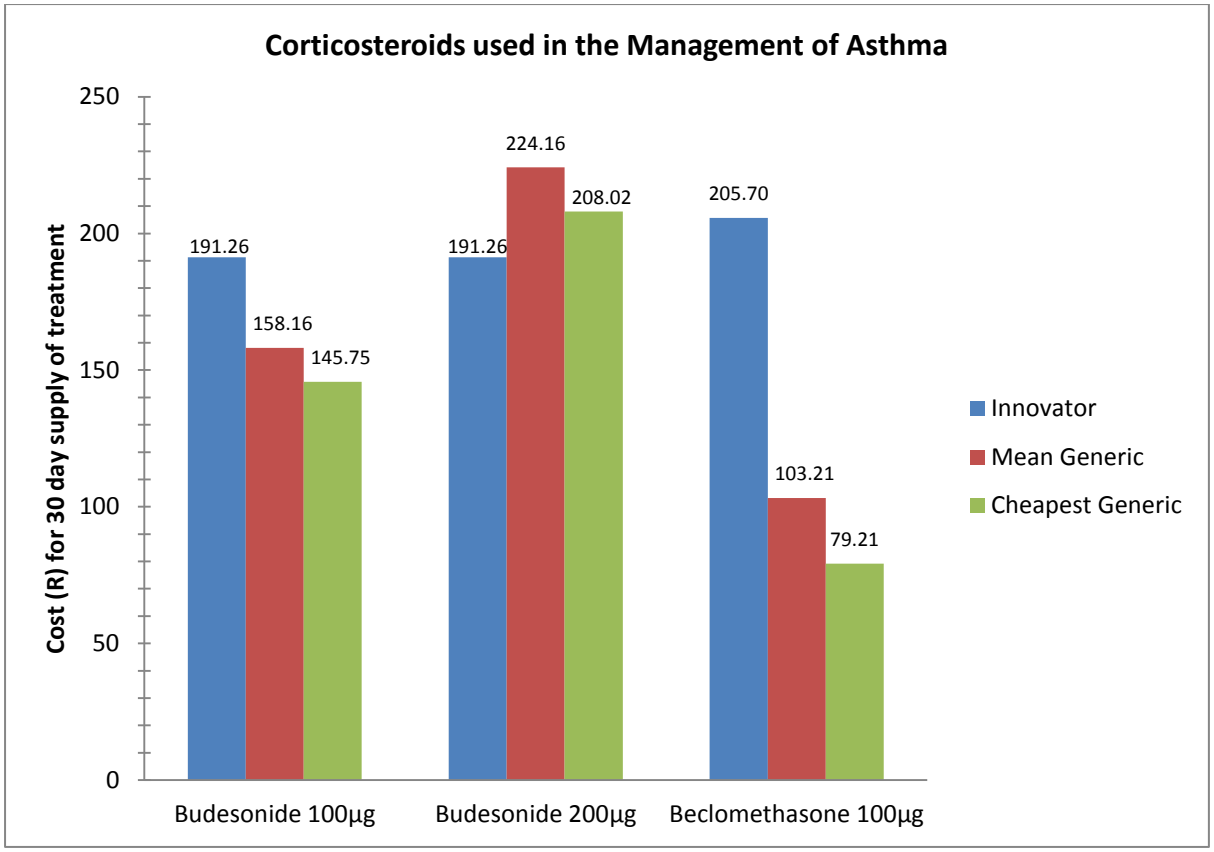

Figure 8: Prices of asthma medication – corticosteroids in 2014.

3.5 Hyperlipidaemia medicines

One class of hyperlipidaemia medicines was identified, i.e., the HMG-CoA reductase inhibitors and the following active ingredients were available for analysis; simvastatin; atorvastatin and pravastatin.

The entire statin range had a similar pattern of price distribution, with the mean generic and cheapest generic having a minimum of 39% cheaper price than the innovator (refer to Figure 9). The simvastatin 10mg had a price difference of 77.70% (R75.69) between the innovator and cheapest generic. The simvastatin 20mg had a price difference of 79.76% (R88.80) between the innovator and cheapest generic. The atorvastatin 10mg had a saving of 85.29% (168.78) between the innovator and cheapest generic, and 33% (14.33) between the mean generic and cheapest generic. And the pravastatin 10mg has a saving of 43.96% (R100.78) between the innovator and cheapest generic.

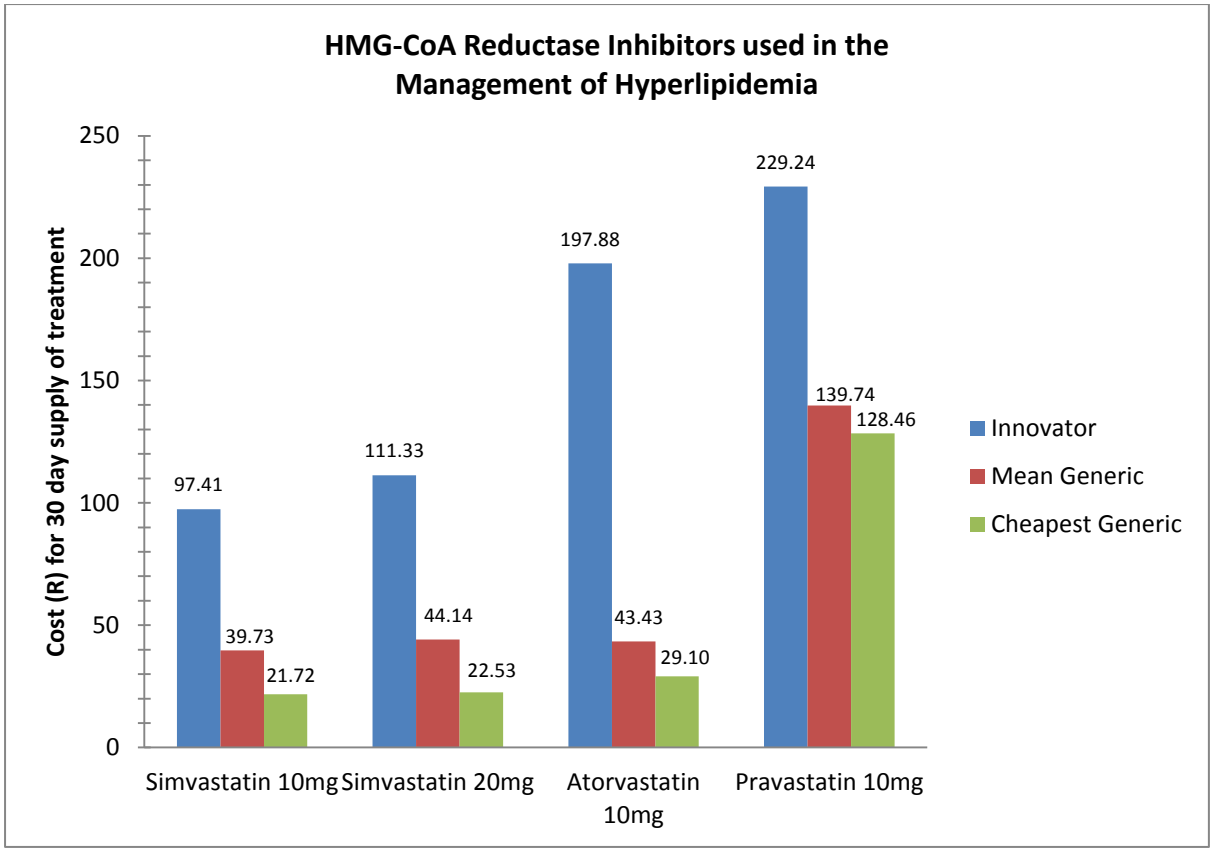

Figure 9: Prices of hyperlipidemia medication – HMG-CoA reductase inhibitors in 2014.

3.6 Anti-rheumatic medicines

Anti-rheumatic medicines included in this study were from five different pharmacological classes of drugs, i.e., the disease-modifying anti-rheumatic drugs, corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs) and the anilide. The active ingredients identified were: chloroquine, methotrexate; prednisone; ibuprofen; diclofenac; naproxen and paracetamol.

As shown in Figure 10, chloroquine had a saving of 54.61% (R38.58) between the innovator and cheapest generic. Methotrexate had a saving of 25.98% (R13.00) between the innovator and cheapest generic, and 2.83% (R1.08) between the mean generic and cheapest generic price. Prednisone had a saving of 97.11% (R112.37) between the innovator and cheapest generic, and 97.06% (R112.31) between the innovator and mean generic. It is was interesting to find that prednisone had three different generic brands available in South Africa with an average price of R3.40 per month, which was substantially cheaper than the innovator drug, which was about R116 per month.

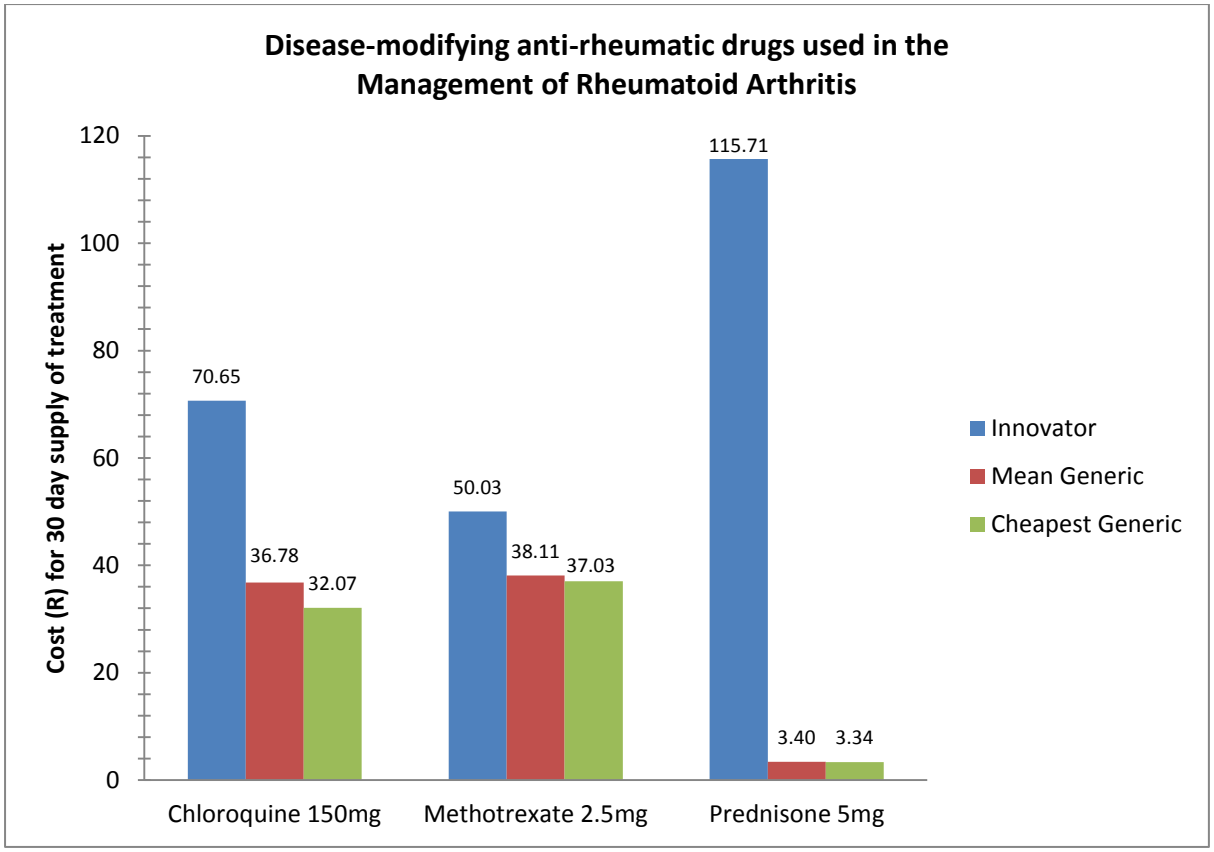

Figure 10: Prices of anti-rheumatic medication in 2014.

As shown in Figure 11, it is clear that there is great potential savings from the use of generic medicines. For example, the ibuprofen 400mg had a saving of 90.36% (R35.70) between the innovator and cheapest generic, the diclofenac 25mg had 89.36% (R21.33), the diclofenac 50mg had 93.33% (R45.31), the naproxen 250mg had 77.29% (R28.99) and the paracetamol 500mg had 69.89% (R7.52) savings. More importantly, the paracetamol 500mg generic brands had similar prices.

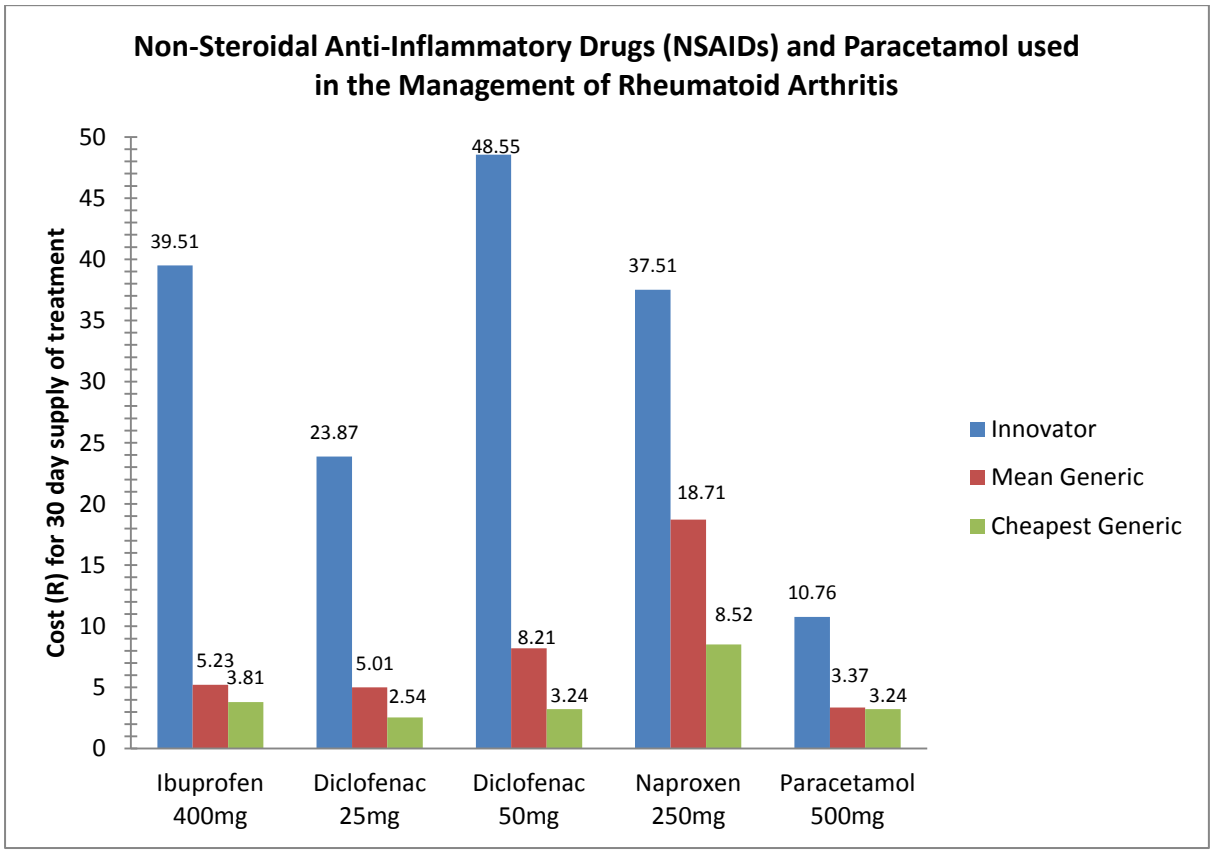

Figure 11: Prices of NSAIDs and paracetamol in 2014.

3.7 Cross-sectional treatment cost comparison for September 2006 and July 2014

Figure 12, shows that all innovator medicine prices have increased, with the greatest increase being that of the captopril 25mg at 71.92% (R121.87). Interestingly, it was also discovered that hydrochlorothiazide 25mg did not have a generic alternative in 2006 and the amlodipine 5mg was the only antihypertensive drug to have had a price decrease (of 54.26% or R41.92) between 2006 and 2014.

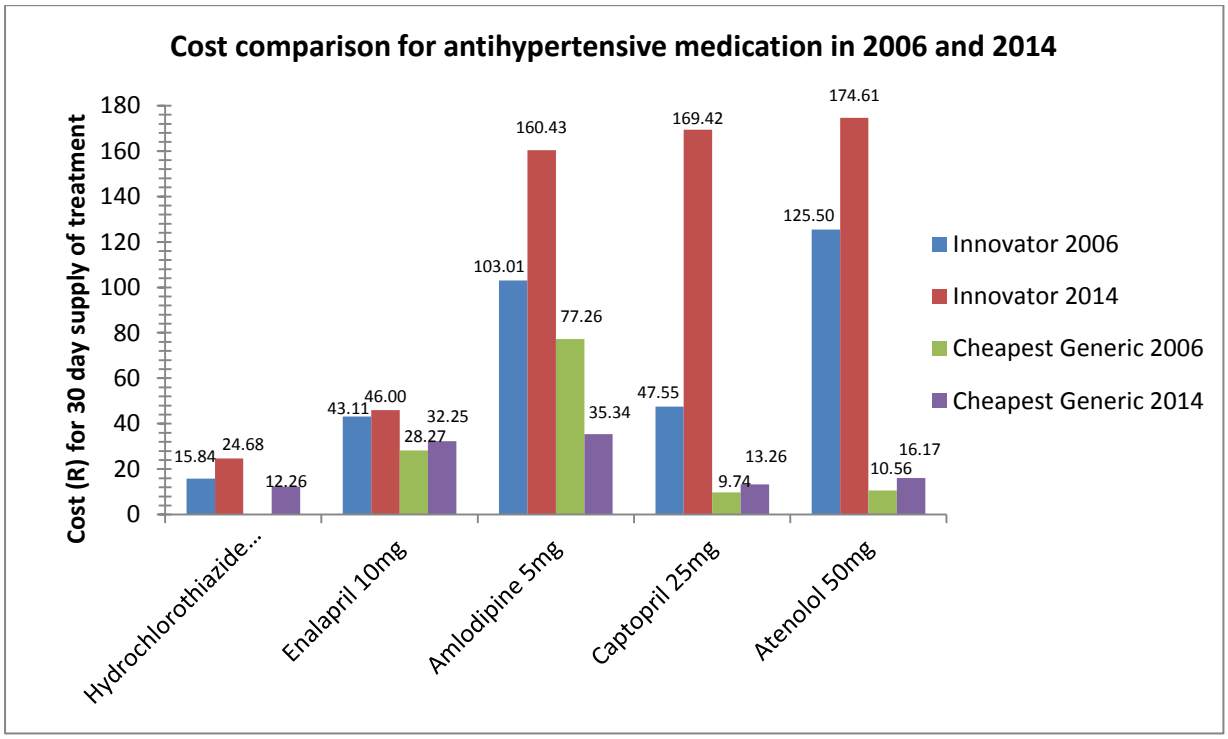

Figure 12: Cross-sectional treatment cost comparison for antihypertensives

A similar trend of price increase was seen with the oral anti-diabetes medicines (refer to Figure 13). There was a huge increase in the innovator price for glibenclamide 5mg (35.80%), and with gliclazide 80mg there was a 17.08% increase – while the metformin 500mg had an overall price increase of 7.06% over a period of 8 years for the generic brand.

The cheapest generic for glibenclamide 5mg, had the greatest price increase of 28.05% between 2006 and 2014

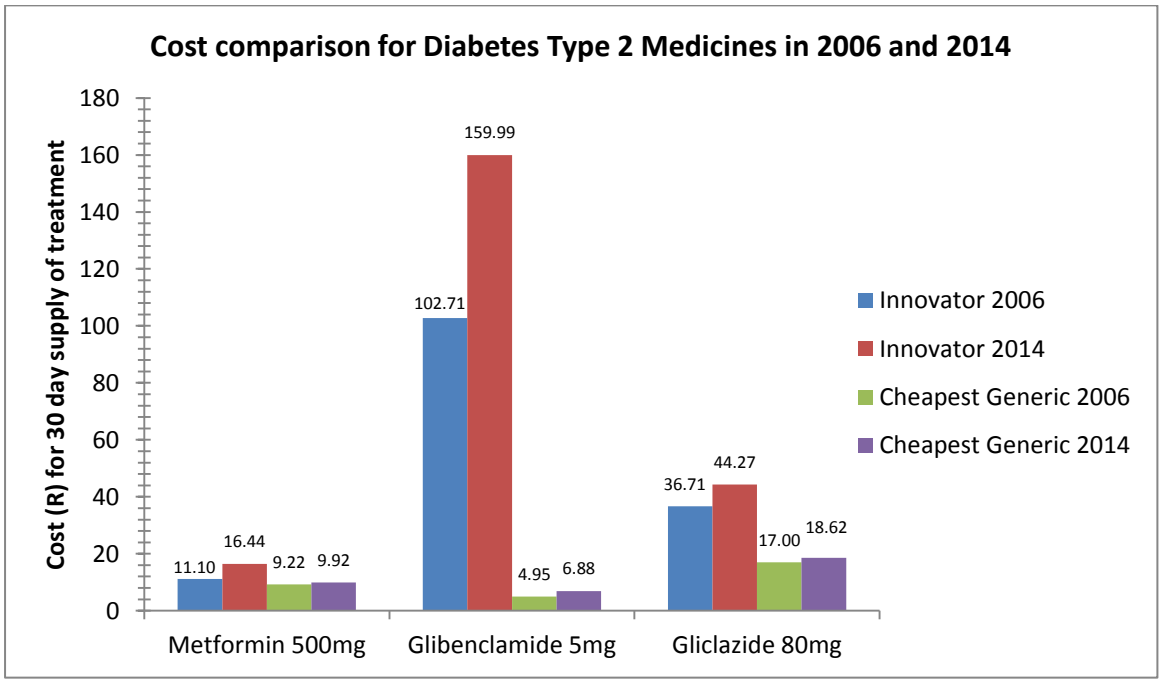

Figure 13: Cross-sectional treatment cost comparison for diabetes type 2 medicines

All the active ingredients for the management of asthma, as depicted in Figure 14 have a similar trend, showing an increase in all drug prices. However, the innovator of salbutamol 100µg had the lowest price increase of 21.15%, while budesonide 100µg had the highest with 39.25% over the studied period as seen in Figure 14. Interestingly, the innovator and cheapest generic of theophylline 200mg had increased by 33% over the comparison period.

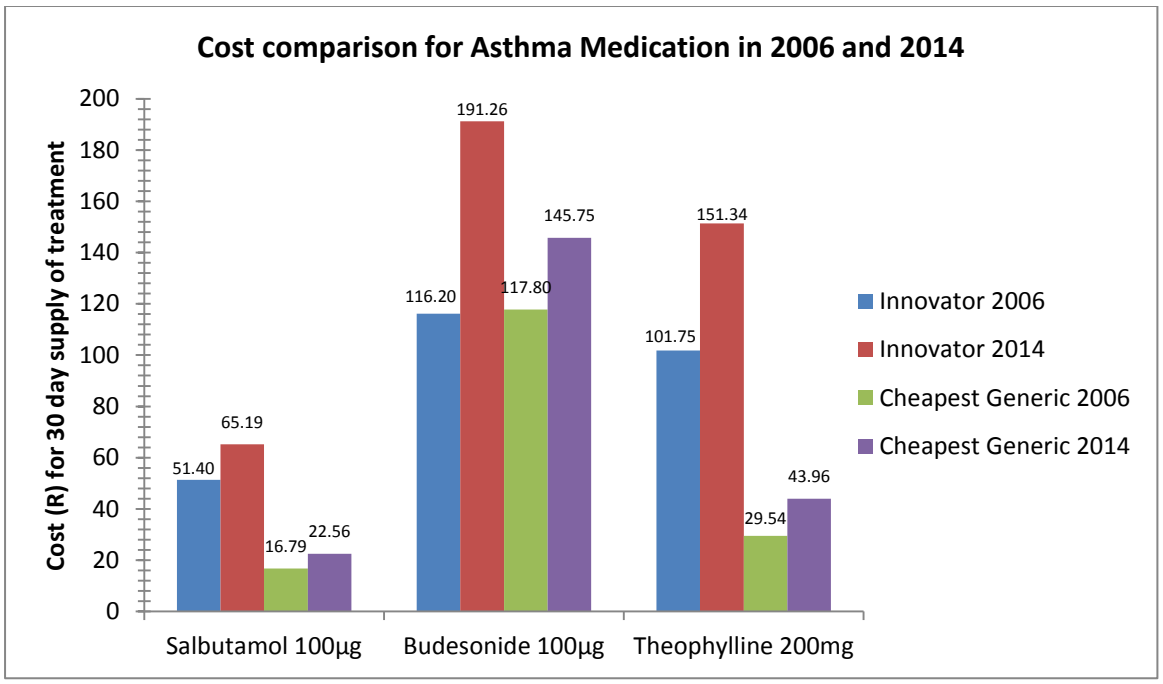

Figure 14: Cross-sectional treatment cost comparison for asthma medicines

Remarkably, as seen in Figure 15, the price of simvastatin for both the 10mg and 20mg of the innovator and cheapest generic has decreased remarkably over the comparison period. The innovator brands of simvastatin 10 and 20mg had decreased by 25.44% and 32.83%, while the cheapest generics had plummeted by 69.95% and 72.32% respectively. Also of note is that in 2006, atorvastatin did not have a generic alternative.

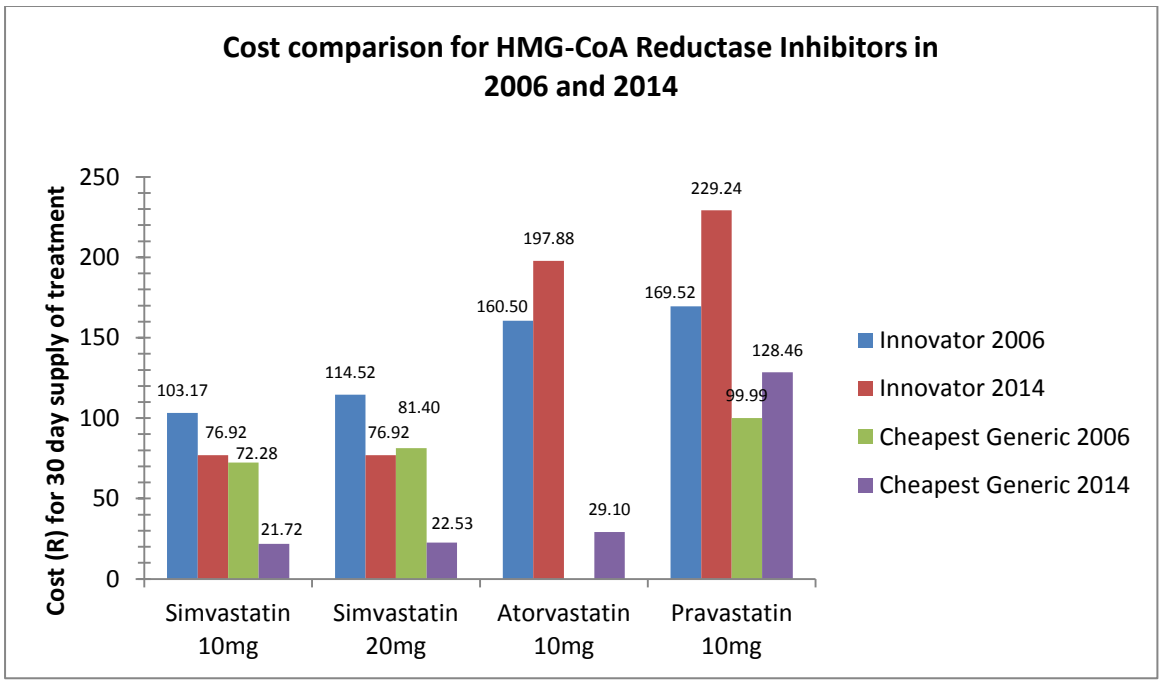

Figure 15: Cross-sectional treatment cost comparison for hyperlipidaemia medicines

In Figure 16 it is seen that large price increases have occurred over the evaluation period. Of all the innovator medicines, prednisone 5mg had the greatest increase (35.67%). Methotrexate 2.5mg cheapest generic had the biggest price upsurge of 75.70%.

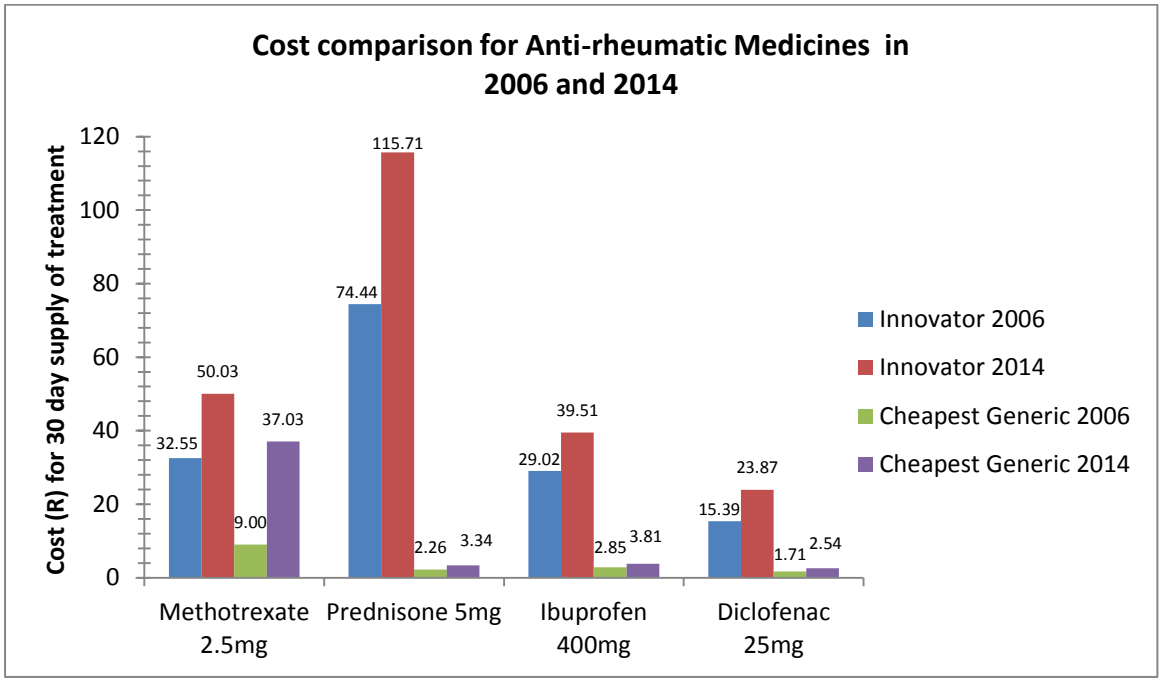

Figure 16: Cross-sectional treatment cost comparison for anti-rheumatic medicines

CHAPTER 4: DISCUSSION

4.1 Introduction

This study quantitatively assessed the potential saving from the use of generic medicines for the treatment of the most common non-communicable diseases among adults in South Africa. The main objective of this study was to determine if there was a cost saving by using generic medicines for the treatment of each chronic disease based on the single exit price and the monthly defined daily dosage. The saving potential was constructed around the innovator price, the mean generic price and the cheapest generic price. The second objective was to compare the current drug prices with data from eight years ago.

Forty three drugs were investigated, forty one (95.3%) were found to have a cheaper generic alternative available. One (2.3%) generic drug was the same price as the innovator, and one (2.3%) innovator drug was cheaper than the generic. These results further illustrate the advantages of generic substitution as Shrank and partners (2011a) reported that generic medicines are cost-effective and can save lives by increasing the affordability and accessibility of quality healthcare to the population.

4.2 Cost Savings When Generic Medicines are used to treat Hypertension

This study has shown that, with regards to diuretics, there was about 50% and 97% savings for hydrochlorothiazide and furosemide respectively when generic medicines are utilised to treat hypertension instead of innovator products. This is in line with Farfan-Portet and colleagues (2012) who found that there is a price difference of €2.47 for furosemide, based on the generic price reference system of Belgium, also, they mentioned that patients

registered with a PHC centre had a better chance of receiving generic alternatives due to good prescribing habits (Farfan-Portet *et al.*, 2012). Interestingly, if a patient was to be treated with a dosage of spironolactone 100mg, it would compute 38% cheaper to purchase a hundred and twenty of the 25mg generic tablets rather than the thirty of the 100mg, but patient adherence to treatment may thereafter become a factor.

Concurring with our findings, García and partners (2004) reported that the use of generic drugs reduced the expenditure on ACE inhibitors by almost 7% even though the sales had increased by approximately 18% (García *et al*., 2004). In this study there was a potential savings of 44%, 30% and 62% for each of the 5mg, 10mg and 20mg tablets, respectively, for enalapril. Another ACE inhibitor, ramipril, had a saving of 65% between the innovator and cheapest generic drug price. However, captopril had an even greater price difference of 92%. This is in line with findings from Nicolosi and Gray (2009), who reported a saving of 42% for ramipril and 86% for captopril.

In the case of amlodipine 5mg a saving of 59% was seen in our study, and this was in line with the findings of Olusola *et al*. (2012), who investigated the equivalence of two generic brands of amlodipine and found a 65% price difference between the innovator and cheapest generic alternative. Unfortunately, Federman and partners (2006) reported that patients diagnosed with hypertension do not fully utilise generic medicines, seen with 3 of the 5 cardiovascular pharmacological drug classifications, and therefore they are not enjoying the benefits associated with generic medicines of which out-of-pocket costs is a major advantage (Federman *et al.*, 2006).

4.3 Cost Savings When Generic Medicines are used to treat Diabetes Mellitus Type 2

With regards to the biguanides, a saving of approximately 38% to 39% was seen for both strengths of metformin. In the category of sulphonylureas, glibenclamide had a substantial saving of 96% when generic medicine were used, while gliclazide came in second with a saving of 58%, however in Poland a saving of only 4% was found for gliclazide, but this marginal difference is most probably due to the Polish generic market element, which is driven by supply measures (Simoens, 2009).

Interestingly glimepiride had an average difference of 52% between the innovator and generic brand. With the promising saving from the use of generic medicines for the treatment of type 2 diabetes, the switch from innovator to generic medicines may contribute to better treatment adherence due to fewer out-of-pocket costs as seen with innovator medicines (Piette *et al*., 2004).

4.4 Cost Savings When Generic Medicines are used to treat Asthma

The potential saving from the use of generic medicine for the management of asthma varied widely for each active ingredient. The major saving was that of theophylline, 71% (200mg) and 63% (300mg) respectively. Salbutamol is often used as a bronchospasm reliever for many asthma sufferers, the generic alternative costs 65% less than the innovator, nonetheless this finding is seen in relation to Ghanname *et al.*, (2014), who reported that even though the innovator price is aligned with its international price, and the generic costs 29% less in Morocco, the sales of the innovator remain higher than the generic due to poor prescribing habits.

Unexpectedly the innovator of budesonide 200µg, costs 15% less than the mean generic price and 8% lower than the cheapest generic. Also, in this study it was discovered that budesonide 100µg and 200µg cost the same. The reason for this is unknown, but a possible explanation is that the innovator is attempting to gain market share to improve sales turnover. In Poland, a saving of 61% was seen from the use of a generic budesonide inhaler, whereas in this study a saving of 24% was calculated for the budesonide 100µg (Simoens, 2009).

4.5 Cost Savings When Generic Medicines are used to treat Hyperlipidaemia

In this study we have shown that the pattern of prices of statin drugs were similar. The standout drug is atorvastatin of which there was an 85% saving from the use of generic medicine. Simvastatin had an average saving of 78%, while the pravastatin generic saved the consumer 44%. In this regard, our findings were in line with those of Cullen *et al*., (2014), who reported that generic statins have a lower cost, similar effectiveness and would support the health system by lowering overall medicines costs.

The lower cost of drugs from the use of generic medicines has advantages of better adherence, and fewer therapy discontinuations, as Casula and team (2012), had discovered that patients fail to comply due to multiple factors, but most importantly out-of-pocket cost was a key aspect (Casula *et al.,* 2012). Similar results were also seen in a study conducted in Europe (Godman *et al*., 2010) where the healthcare system was capable of providing quality healthcare with minimal resources propelled by the utilisation of generic medicines.

4.6 Cost Savings When Generic Medicines are used to treat Rheumatoid Arthritis

The management of rheumatoid arthritis consisted of two categories of drugs, the disease-modifying anti-rheumatic drugs and non-steroidal anti-inflammatories. Of all the drugs investigated in this study for the treatment of rheumatoid arthritis, the generic alternative was found to be cheaper than the innovator.

Prednisone remarkably, had a price difference of 97.1% when the innovator was compared to the cheapest generic. This was a substantial saving of note although prednisone has 3 generic alternatives, the innovator price is significantly higher, as seen by a price difference 97% between the innovator and mean generic price. This will be of great advantage for patients that used prednisone for conditions other the rheumatoid arthritis. In Canada, similar results were shown whereby generic substitution of NSAIDs produced approximately $1 million (CAN) in annual savings (Grootendorst, 2005).

4.7 Changes of prices of medication over time

Over a period of eight years, nominated innovator and generic drug prices were formulated for a comparison. An overview of the results in this study acclimate the drug price increase to that in line with the average inflation rate of South Africa for most medicines.

In the treatment of hypertension, major price increases were seen for amlodipine, captopril and atenolol. The amlodipine innovator had a price increase 36% over the period of 8 years, surprisingly the generic price had decreased by 54% over the same period, however, a possible reason for this decrease in 2014, is in 2006 only one alternative generic for amlodipine was available on the market. These findings are dissimilar to that of a study

conducted by Wenjie in China, where the price of generic amlodipine had increased between 2006 and 2011, although the usage had increase by 6 folds (Wenjie, 2013). The captopril innovator had a price increase of 72% which is aligned with Alpern and colleagues (2014) in which they found that the price of captopril increased by 2800% over a period of 2 years in the US, this however is substantially higher than the price increase seen in South Africa.

For the treatment of diabetes type 2, the highest possible increase was seen in glibenclamide 36%, however the generic price remained fairly low in comparison to the innovator over the period of 8 years. The metformin generic price appeared to have stabilised with a minimal increase over the 8 year period and well within inflation rates. In the management of asthma, all medicine prices had increased over the 8 year period and percentile increase seemed to be within inflation rates.

The innovator of simvastatin had a price decrease over the 8 year period, this is possibly due to the patent expiry and arrival of many new generic alternatives. More importantly, the generic prices of simvastatin have decreased over time, which is due to tough competition for market share in the healthcare environment. Also, in 2006, atorvastatin did not have a generic available due to the patent protection, currently there are generic alternatives available with the cheapest one being 85% cheaper than the innovator. In China, the price of generic atorvastatin had decreased between 2006 and 2011 although the usage increased (Wenjie, 2013)

In the treatment of rheumatoid arthritis, there has been a significant increase in the price of the generic methotrexate (76%). Ibuprofen and diclofenac generics have had smaller price increases which are within inflation rates.

The findings of this study are in line with Huckfeldt and Knittel (2011) who reported that an innovator usage declines promptly upon the release of a generic product. In another study conducted by Wenjie (2013) in China, between 2006 and 2011, the market share was dominated by innovator drugs based on volume and monetary value.

4.8 Limitations

An important limitation to the study is that only medicines recorded in the Pharmaceutical Blue Book were studied. It is possible that there were more generic alternatives available on the market at the time of the study. Prescribing patterns were not investigated in this study.

CHAPTER 5: CONCLUSION AND RECOMMENDATIONS

This study assessed the potential savings from the use of generic medicines for the treatment of five of the most common non-communicable diseases in adults in South Africa. The main objective of the study was to determine the cost differential between innovator and generic medicines used in the treatment of the most common NCDs and to compare the price differential between generic and innovator medicines in 2006 and 2014. The cost saving was calculated based on the SEP and DDD of each drug.

The SEP was introduced into South Africa in 2004, after plentiful criticism from the pharmaceutical industry to overrule its instatement. The SEP structure lists the maximum price that a medicine can be charged for taking into consideration the fixed dispensing fee added to the mark-up charged on the SEP. In South Africa, the private sector provides healthcare for approximately 8 million citizens most of whom belong to a medical scheme, while the government manages the other 42 million residents that are unable to afford private healthcare (Gray, 2014). Therefore the government needs to review its procurement procedure by suggesting a tender renewal every 6 months for all drugs supplied in the state sector. This outcome would yield greater competition among local drug manufacturers and moreover provide an enticement for international pharmaceutical companies who could also supply the local market which is also known as parallel importation.

The public's perception towards generic medicine needs to be changed, most patients believe that generic medicines do not work as well as their innovator counterparts. This perception needs to be corrected at ground level and should be introduced at senior school

level just prior to entering the tertiary world as they would soon be purchasing their own medicine. Furthermore, drug advertising, and generic substitution should be introduced to undergraduate healthcare students as it would be the perfect period to instil the positives of generic medicines in the future leaders of society and the healthcare fraternity.

Generic substitution needs to be perpetuated in all healthcare sectors, the benefits clearly overshadow the controversial speculations that are made by certain persons. A generic drug is made of the same active ingredient as the innovator and the bioequivalence is expected to be of similar standards. The use of generic medicines is therefore encouraged to allow for greater access and affordability of quality healthcare.

Pharmacists play a crucial role in driving the generic substitution mandate and it is therefore vital that each and every one helps to maintain and promote this advantageous model. The prescribing patterns of medical practitioners need to change, as their prescribing trends are quite often influenced by sales representatives and outdated research. Prescribers need to revitalise their methods of prescribing and where possible adjust their attitude towards generic medicines as it is here to stay.

In this study it has shown that there is a significant saving potential from the use of generic medicines over innovator medicines for the treatment of the most common non-communicable diseases in adults in South Africa. This has been proven by comparing the single exit price of innovator medicines against that of generic alternatives. Secondly, this study has shown that over a period of eight years, most generic drug prices have increased

in line or below, with the countries inflation rate, and some generic medicine prices had actually decreased over time.

It is recommended that further research be undertaken to assess disease specific cost saving potential from the use of generic medicines instead of innovator medicines, and how the price has evolved over a period of time.

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APPENDICES

APPENDIX A - RESULTS

Appendix A – 1: Hydrochlorothiazide brands in 2014

Appendix A – 2: Furosemide brands in 2014

Appendix A – 3: Spironolactone 25mg brands in 2014

Appendix A – 4: Spironolactone 100mg brands in 2014

Appendix A – 5: Enalapril 5mg brands in 2014

Appendix A – 6: Enalapril 10mg brands in 2014

Appendix A – 8: Perindopril 4mg brands in 2014

Appendix A –7: Enalapril 20mg brands in 2014

Appendix A –9: Ramipril 5mg brands in 2014

Appendix A – 10: Amlodipine 5mg brands in 2014

Appendix A –11: Amlodipine 10mg brands in 2014

Appendix A – 12: Atenolol 50mg brands in 2014

Appendix A – 13: Atenolol 100mg brands in 2014

Appendix A – 14: Bisoprolol brands in 2014

Appendix A – 15: Bisoprolol 10mg brands in 2014

Appendix A – 16: Propranolol 10mg brands in 2014

Appendix A – 17: Propranolol 40mg brands in 2014

Appendix A – 18: Methyldopa brands in 2014

Appendix A – 19: Metformin 500mg brands in 2014

Appendix A – 20: Metformin 850mg brands in 2014

Appendix A – 21: Glibenclamide 5mg brands in 2014

Appendix A – 22: Gliclazide 80mg brands in 2014

Appendix A – 23: Glimepiride 1mg brands in 2014

Appendix A – 24: Glimepiride 2mg brands in 2014

Appendix A – 25: Salbutamol 100µg brands in 2014

Appendix A – 26: Budesonide 100µg brands in 2014

Appendix A –27: Budesonide 200µg brands in 2014

Appendix A – 28: Beclomethasone 100µg brands in 2014

Appendix A –29: Theophylline 200mg brands in 2014

Appendix A –30: Theophylline 300mg brands in 2014

Appendix A –31: Simvastatin 10mg brands in 2014

Appendix A – 32: Simvastatin 20mg brands in 2014

Appendix A –33: Atorvastatin 10mg brands in 2014

Appendix A – 34: Pravastatin 10mg brands in 2014

Appendix A – 35: Chloroquine brands in 2014

Appendix A – 36: Methotrexate brands in 2014

Appendix A – 37: Prednisone brands in 2014

Appendix A – 38: Paracetamol brands in 2014

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Appendix A – 40: Diclofenac 25mg brands in 2014

Appendix A – 41: Diclofenac 50mg brands in 2014

Appendix A – 42: Naproxen brands in 2014

Appendix A – 43: Available generic drugs per active ingredient for the treatment of Hypertension in 2014

Appendix A – 44: Available generic drugs per active ingredient for the treatment of Diabetes Mellitus in 2014

Appendix A – 45: Available generic drugs per active ingredient for the treatment of Asthma in 2014

Appendix A – 46: Available generic drugs per active ingredient for the treatment of Hyperlipidemia in 2014

Appendix A – 47: Available generic drugs per active ingredient for the treatment of Rheumatoid Arthritis in 2014

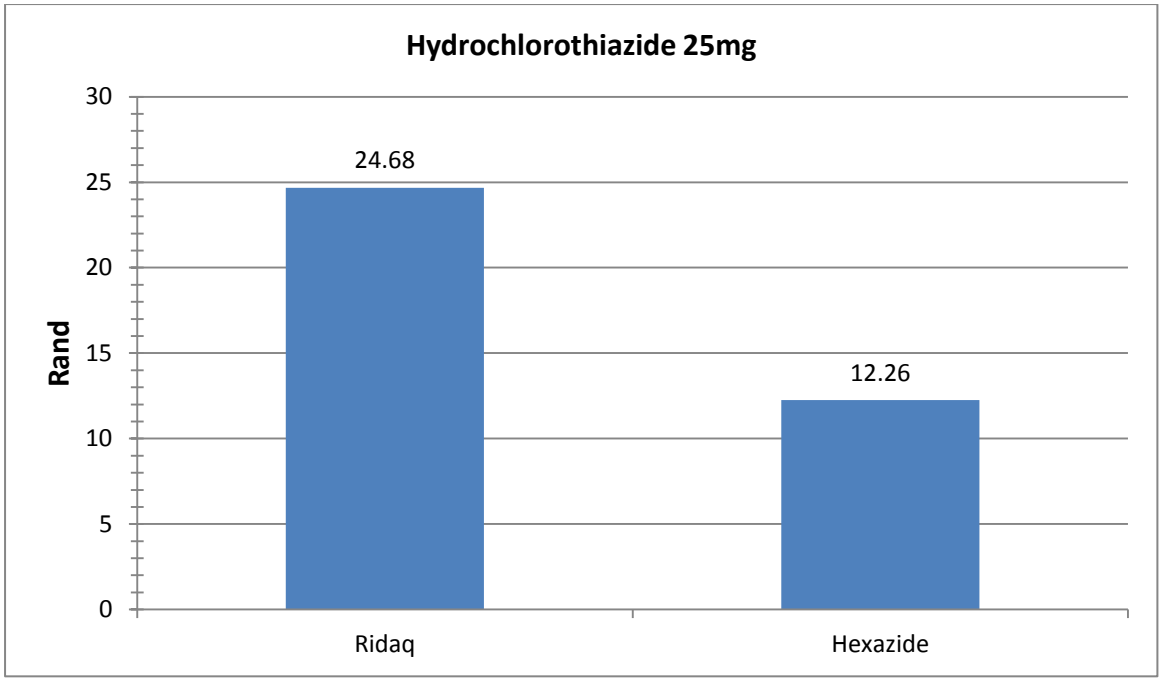
Appendix A – 52: Data capture sheet – Rheumatoid Arthritis

Appendix A – 51: Data capture sheet – Hyperlipidemia

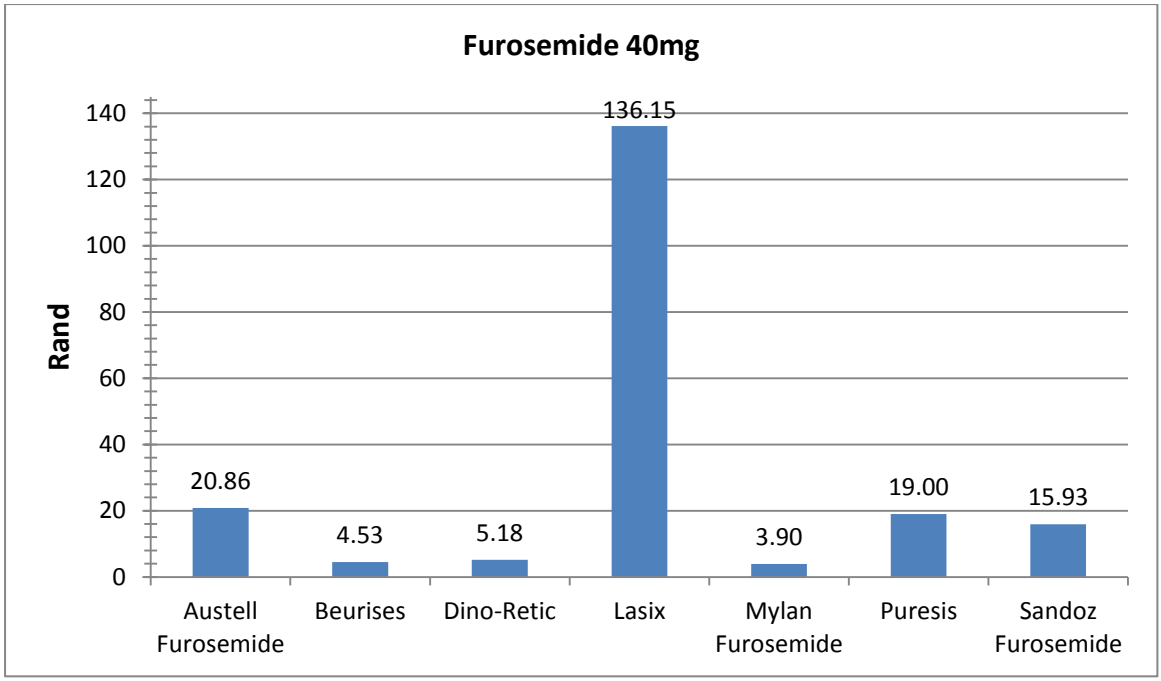
Appendix A – 50: Data capture sheet - Asthma

Appendix A – 49: Data capture sheet – Diabetes Mellitus Type 2

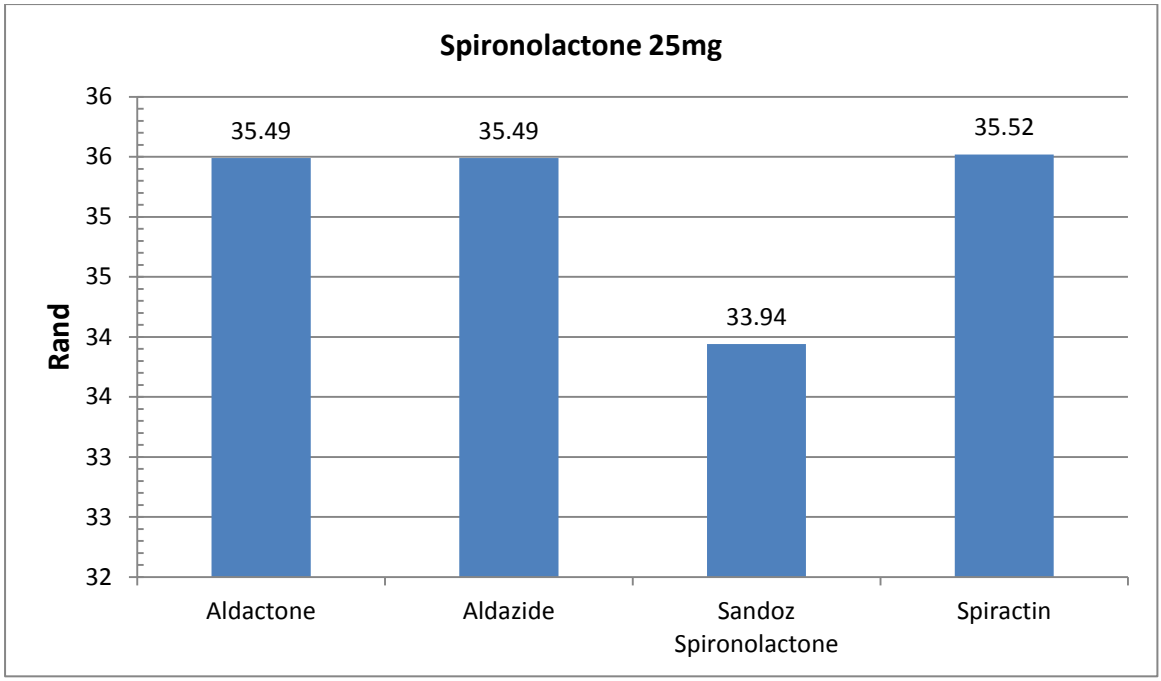
Appendix A – 48: Data capture sheet - Hypertension



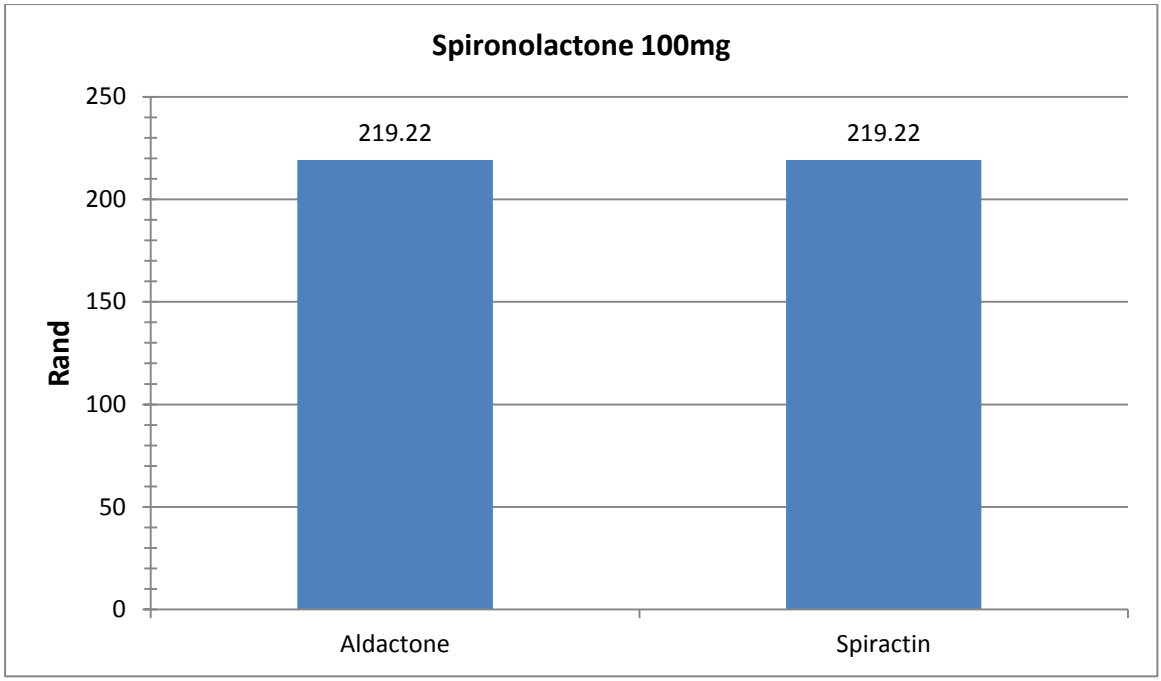
Appendix A – 1: Hydrochlorothiazide brands in 2014



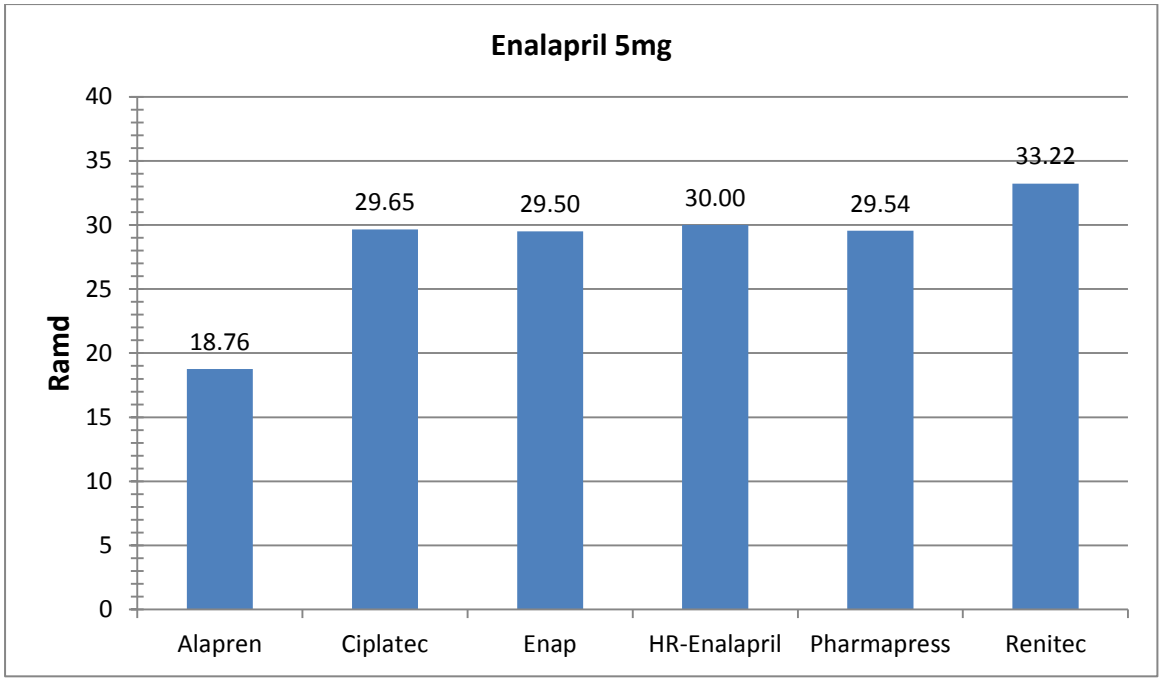
Appendix A – 2: Furosemide brands in 2014



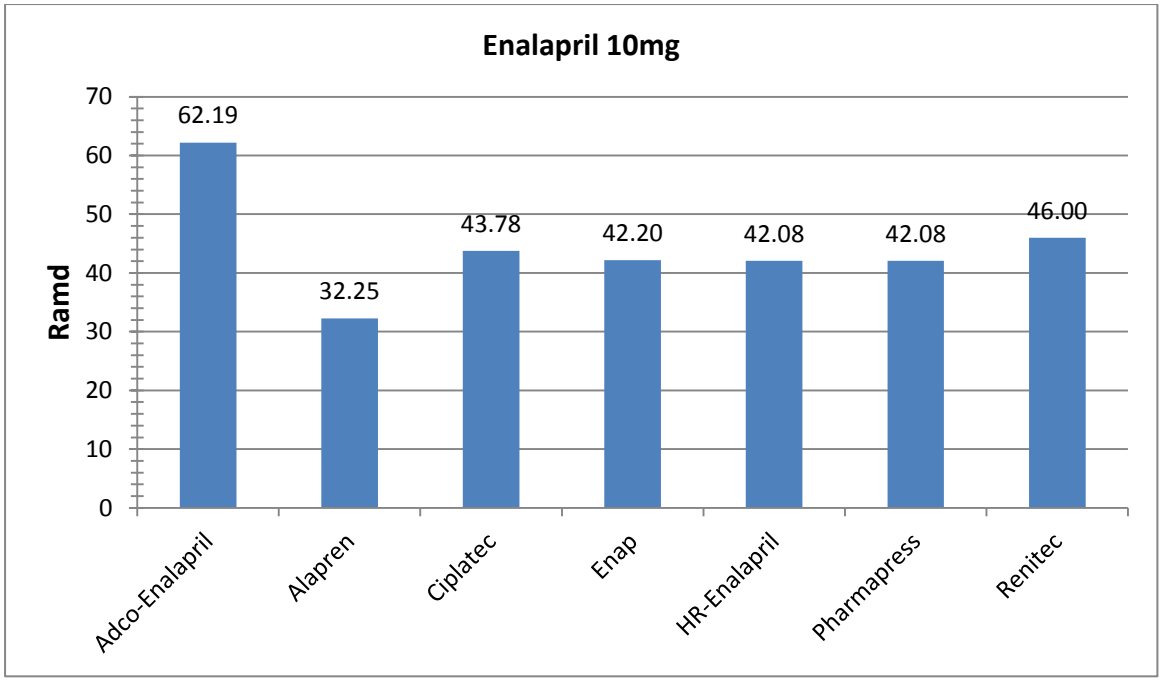
Appendix A – 3: Spironolactone 25mg brands in 2014



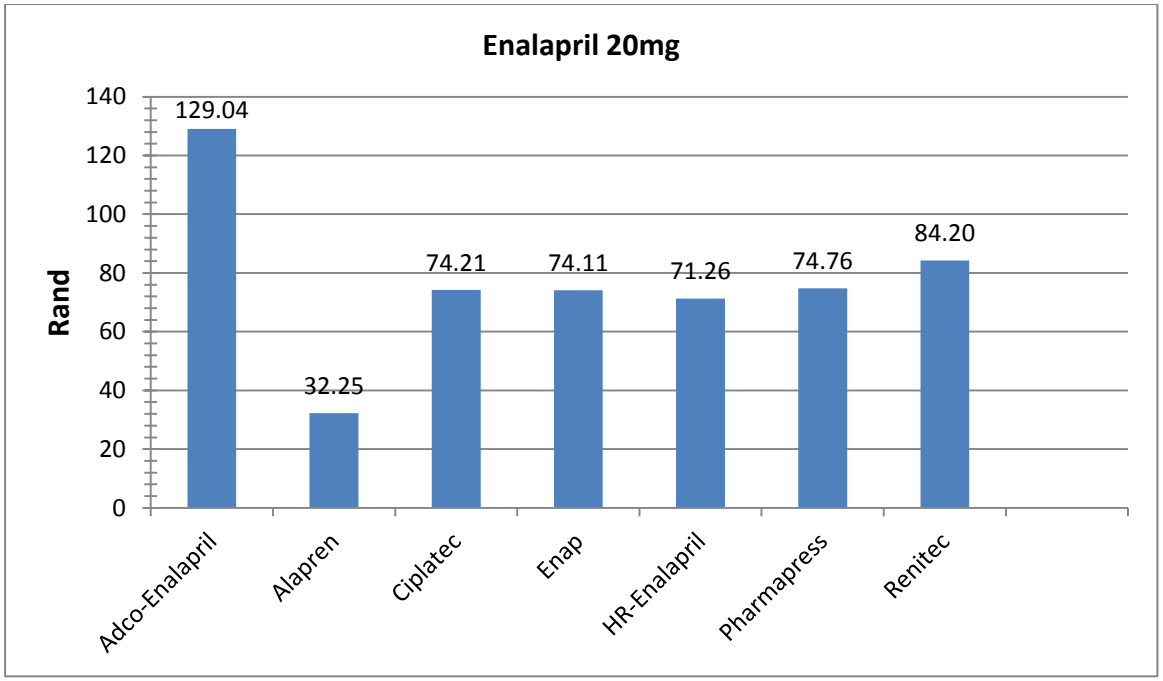
Appendix A – 4: Spironolactone 100mg brands in 2014



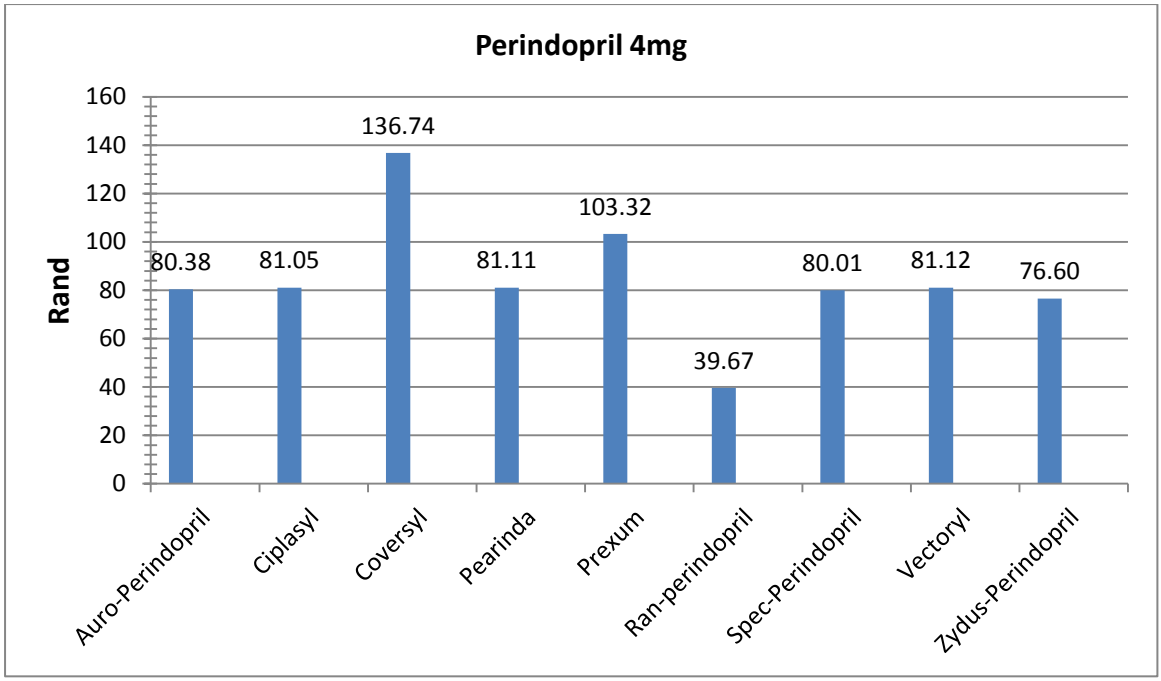
Appendix A – 5: Enalapril 5mg brands in 2014



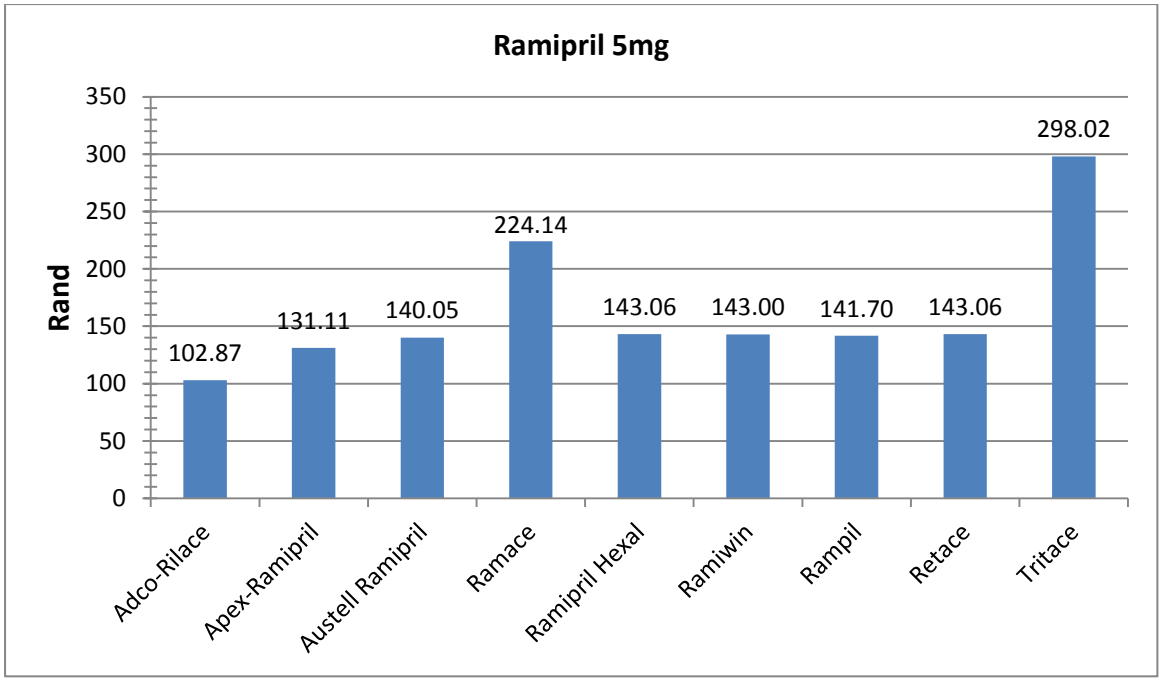
Appendix A – 6: Enalapril 10mg brands in 2014



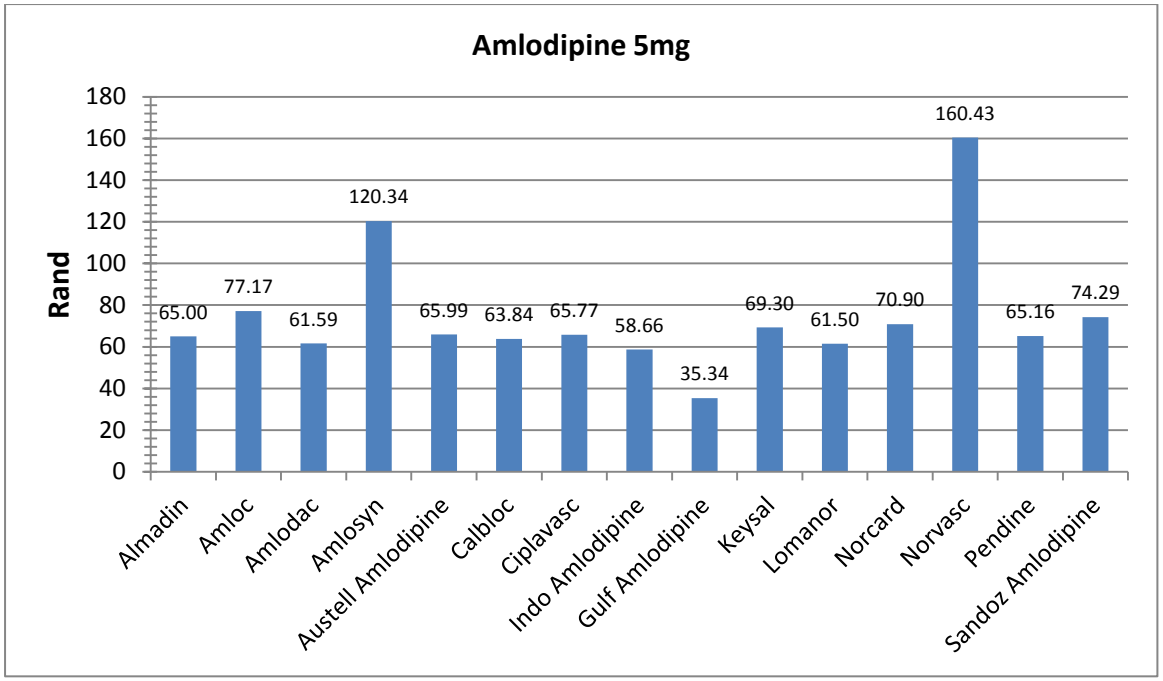
Appendix A –7: Enalapril 20mg brands in 2014



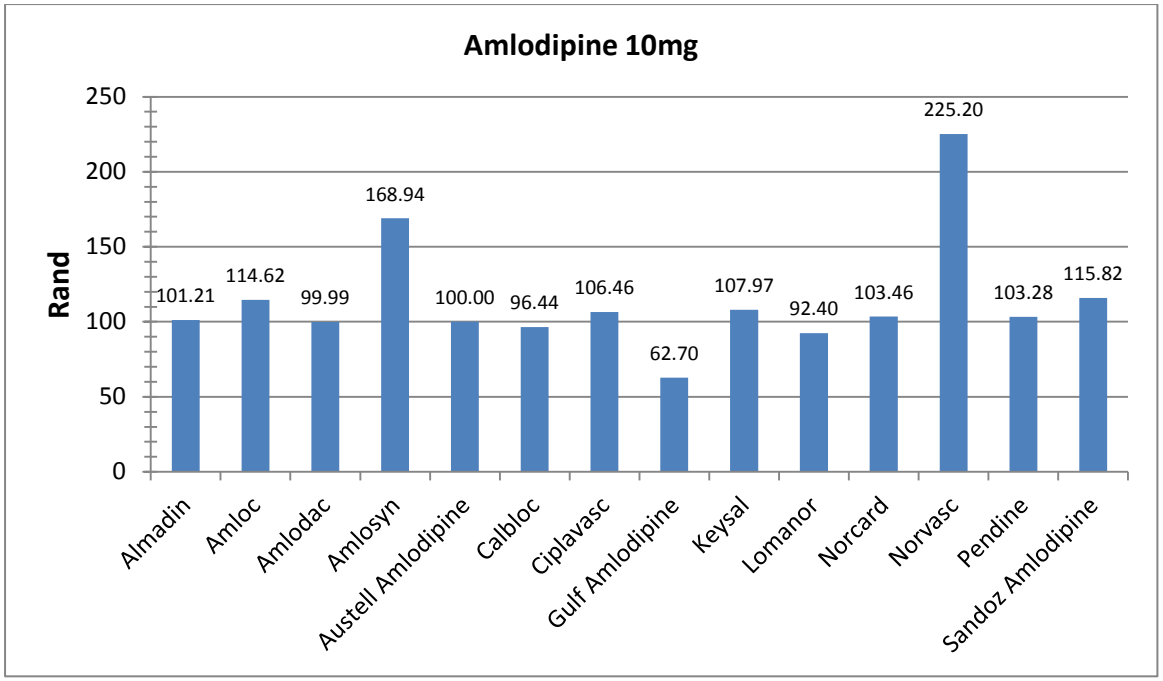
Appendix A – 8: Perindopril 4mg brands in 2014



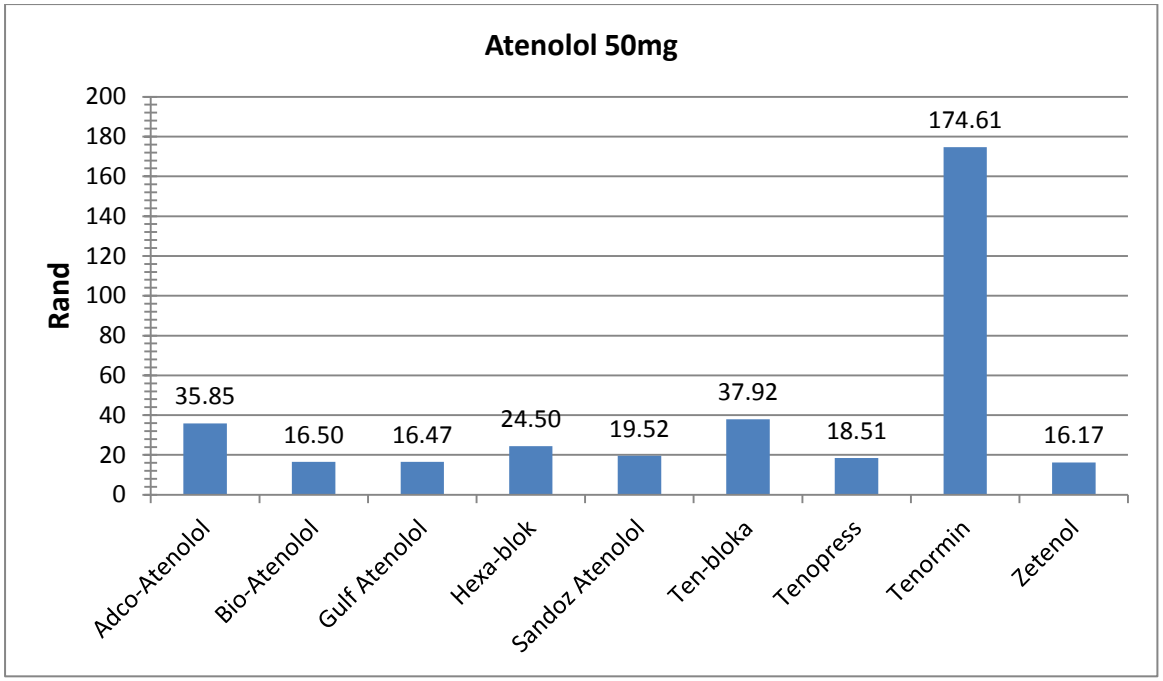
Appendix A –9: Ramipril 5mg brands in 2014



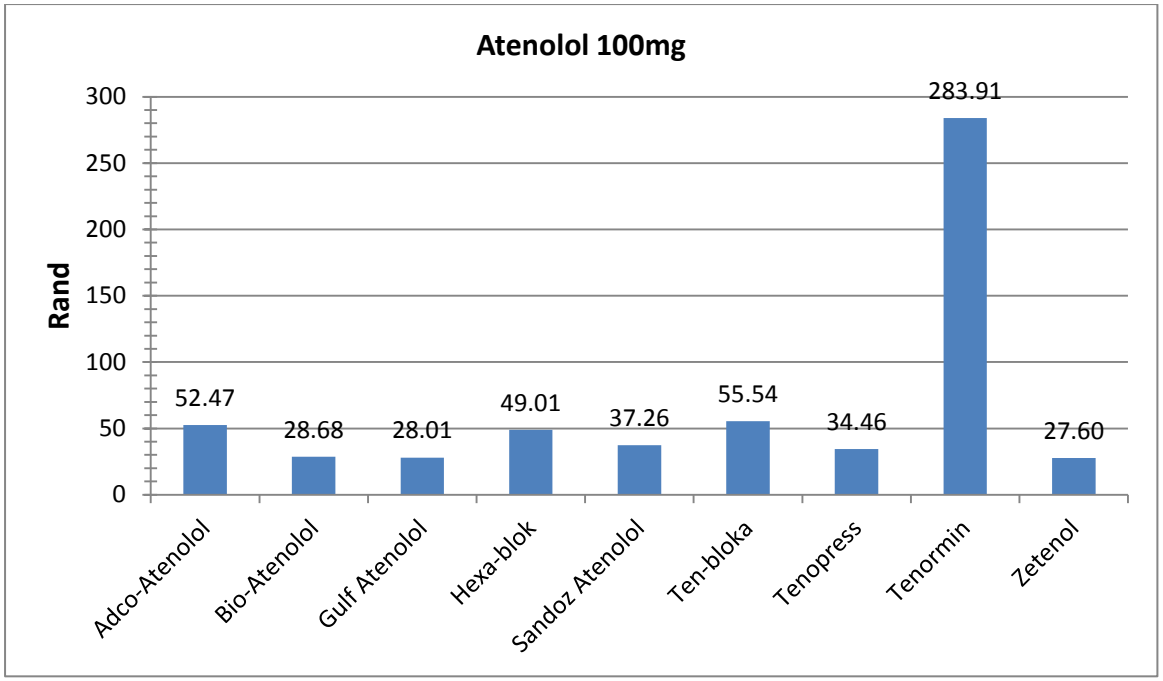
Appendix A – 10: Amlodipine 5mg brands in 2014



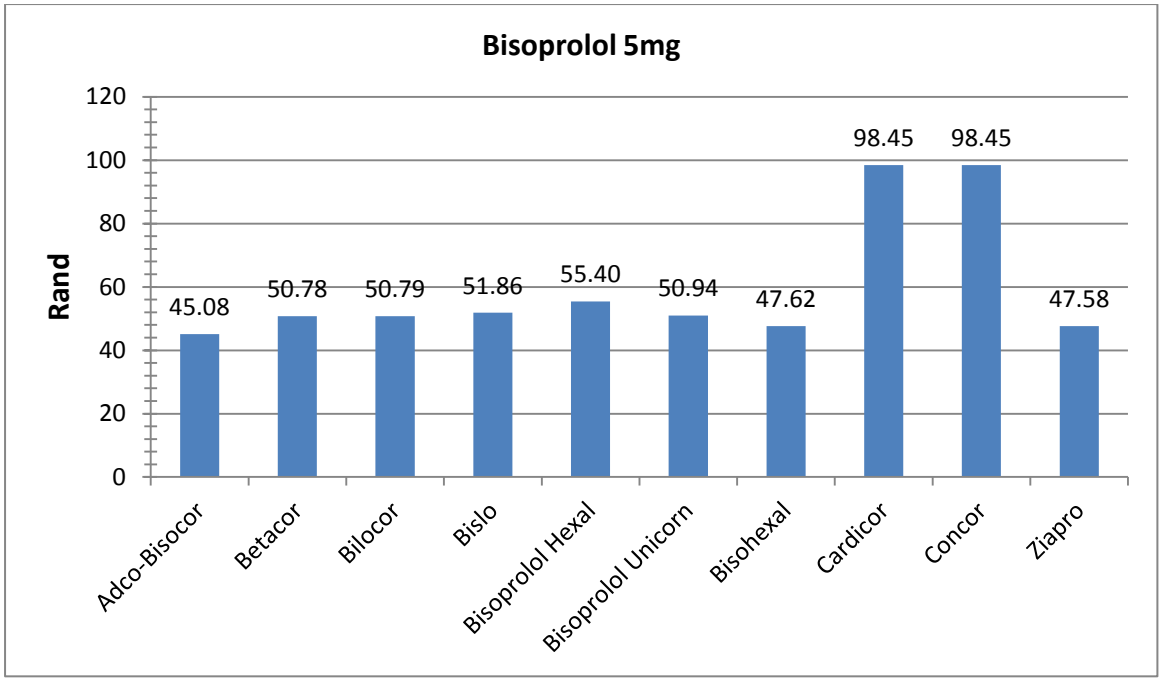
Appendix A –11: Amlodipine 10mg brands in 2014



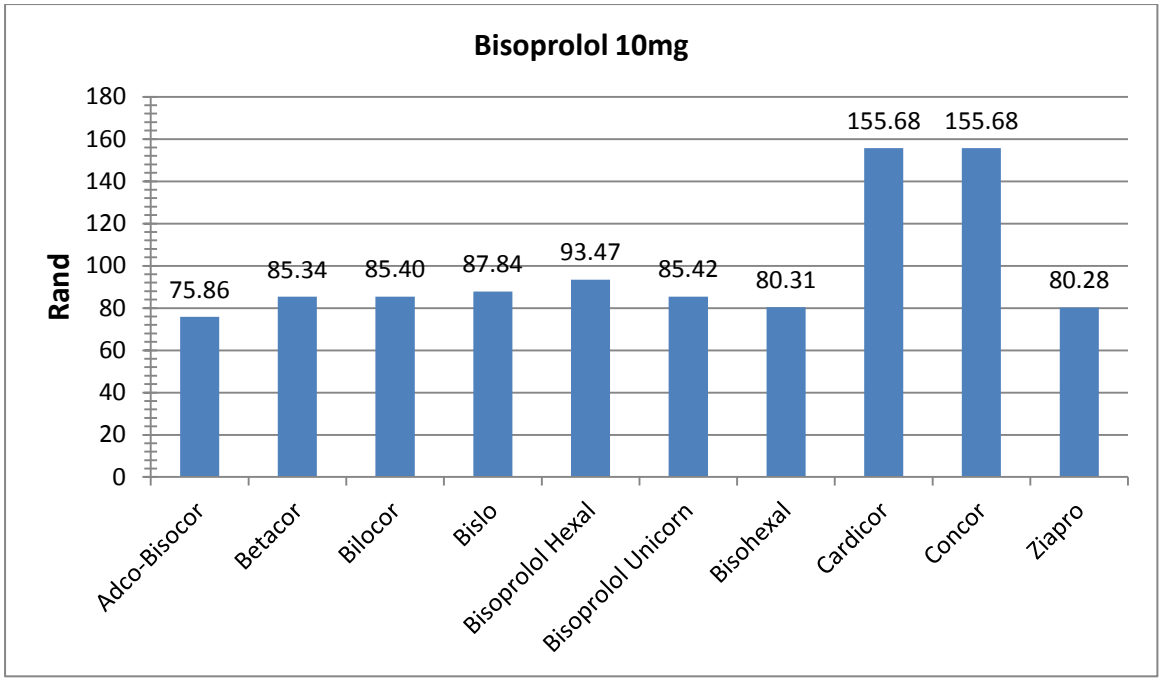
Appendix A – 12: Atenolol 50mg brands in 2014



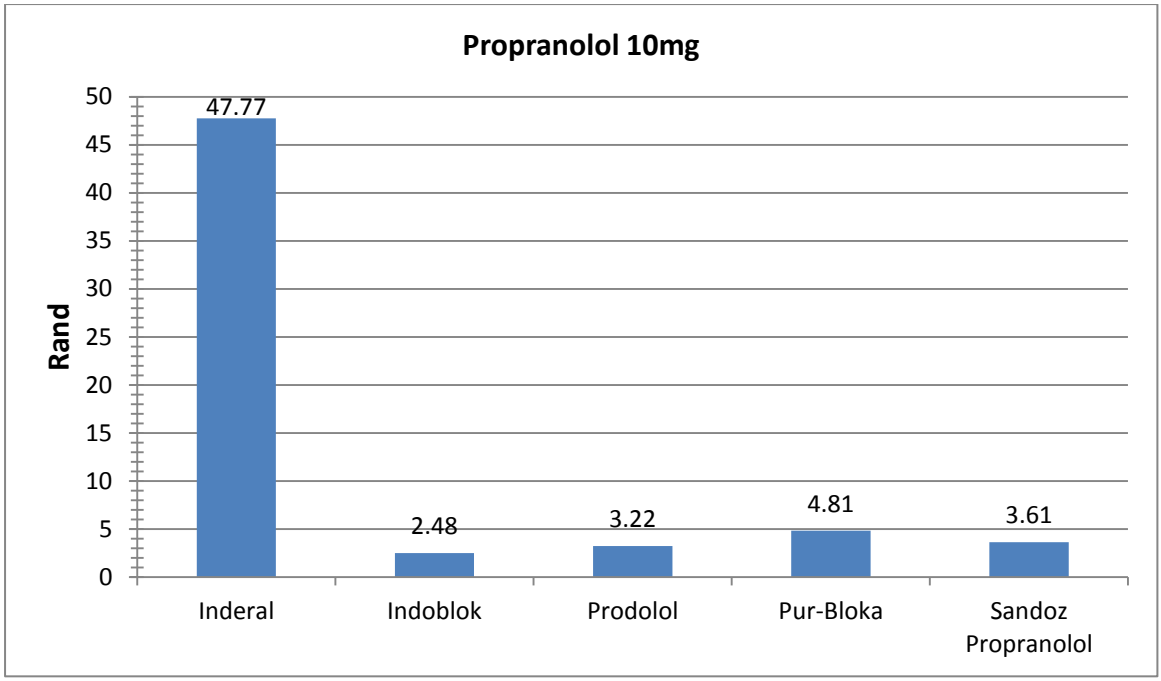
Appendix A – 13: Atenolol 100mg brands in 2014



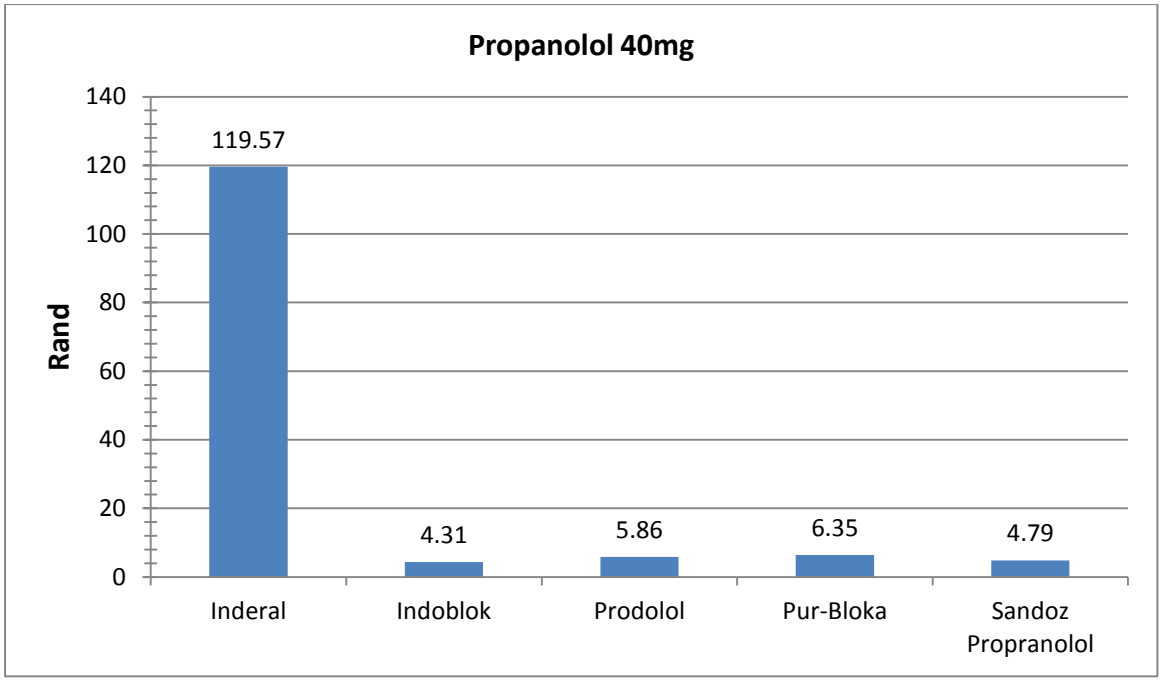
Appendix A – 14: Bisoprolol brands in 2014



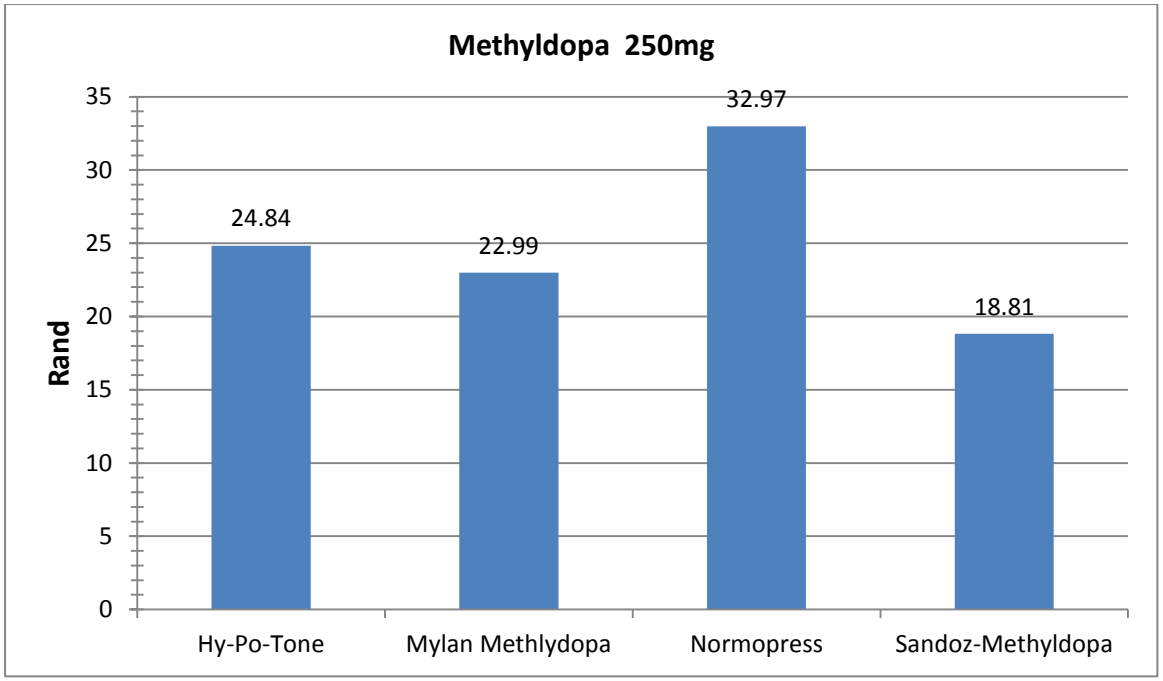
Appendix A – 15: Bisoprolol 10mg brands in 2014



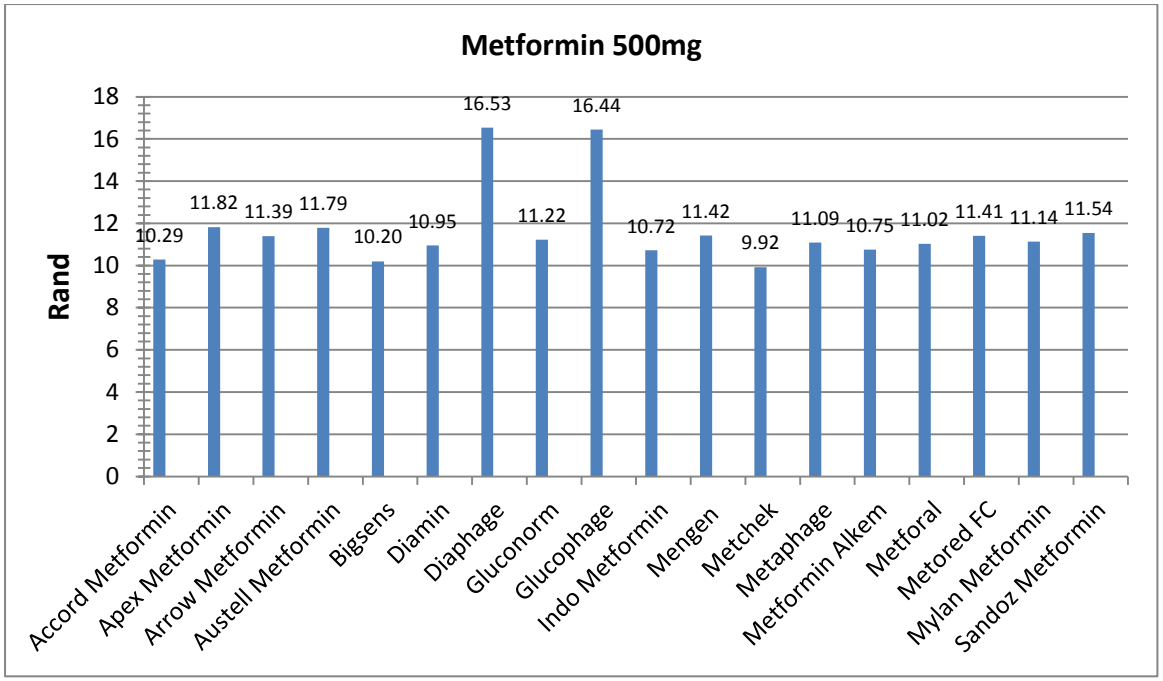
Appendix A – 16: Propranolol 10mg brands in 2014



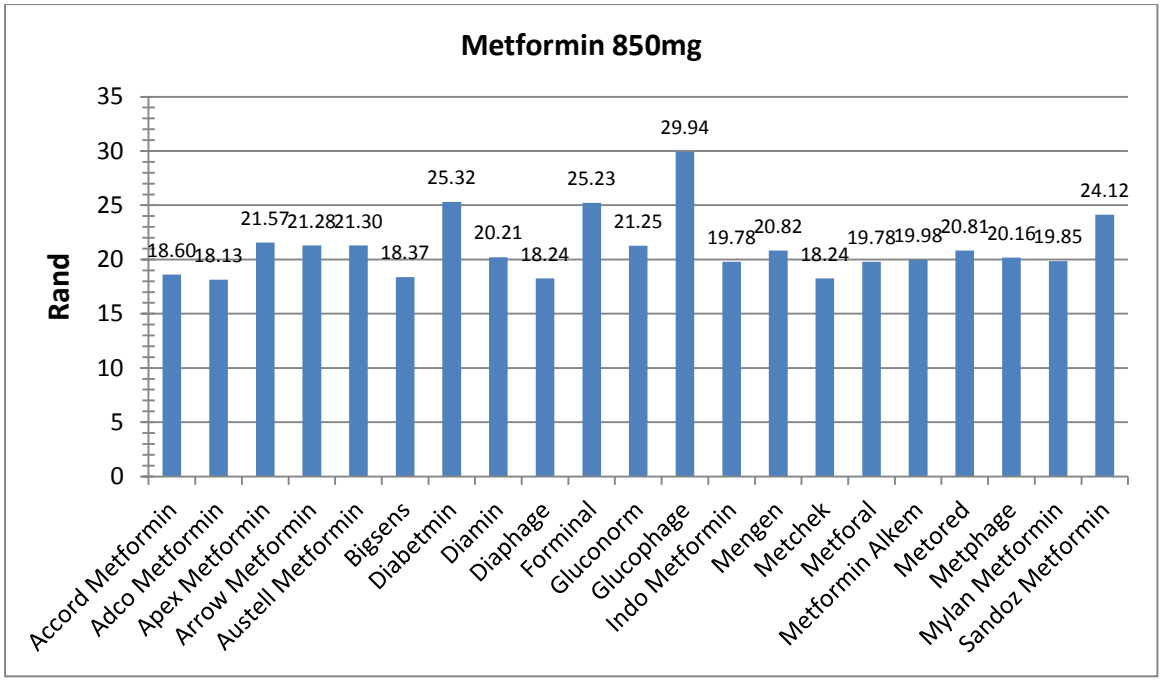
Appendix A – 17: Propranolol 40mg brands in 2014



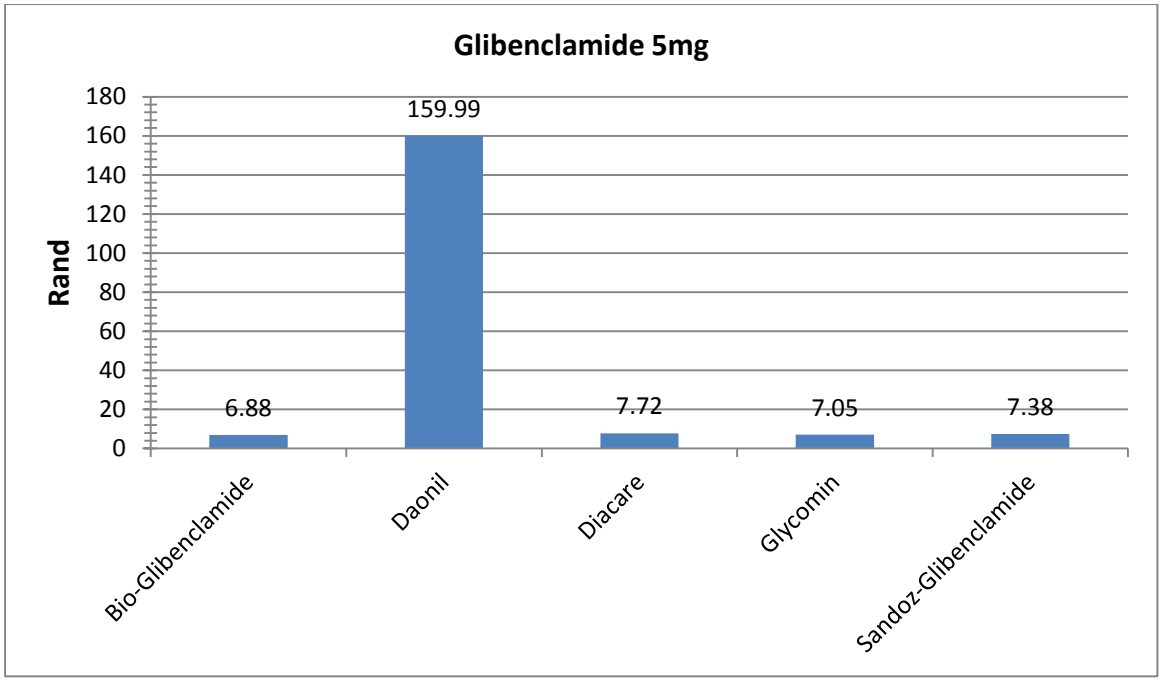
Appendix A – 18: Methyldopa brands in 2014



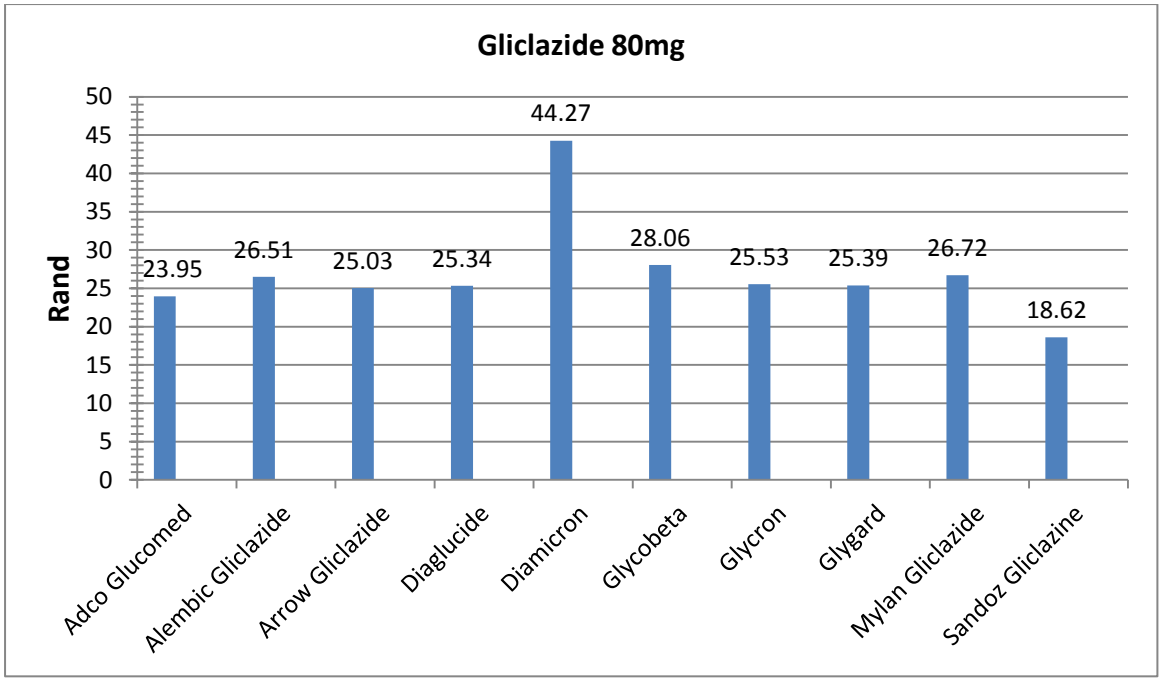
Appendix A – 19: Metformin 500mg brands in 2014



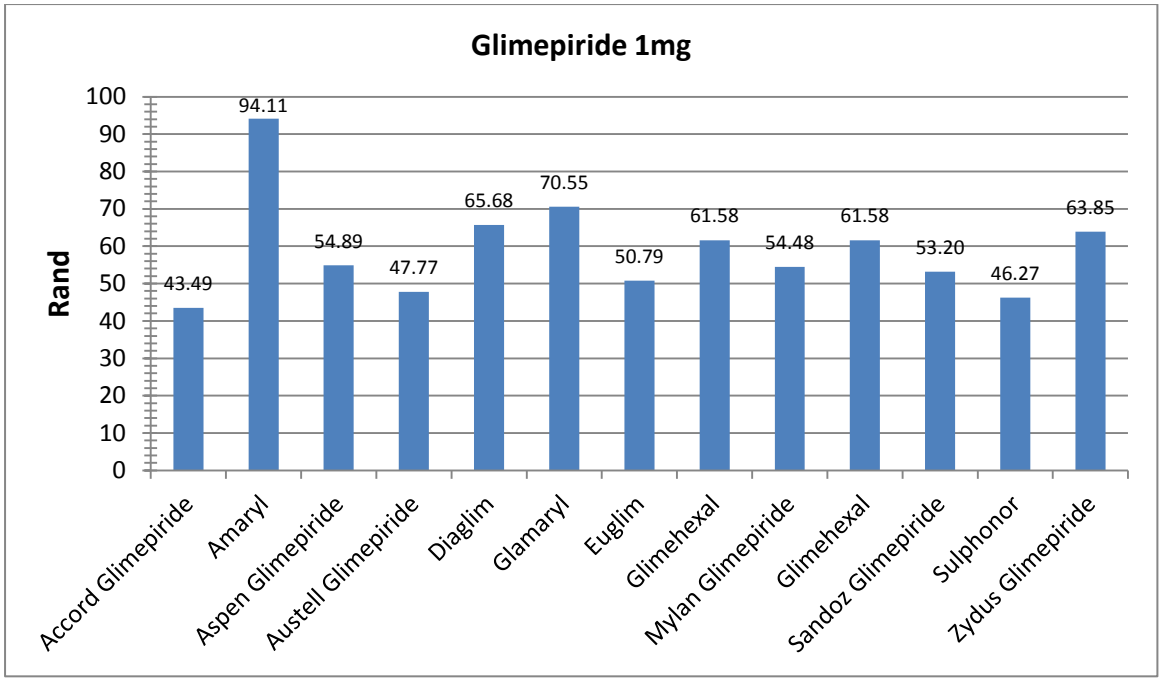
Appendix A – 20: Metformin 850mg brands in 2014



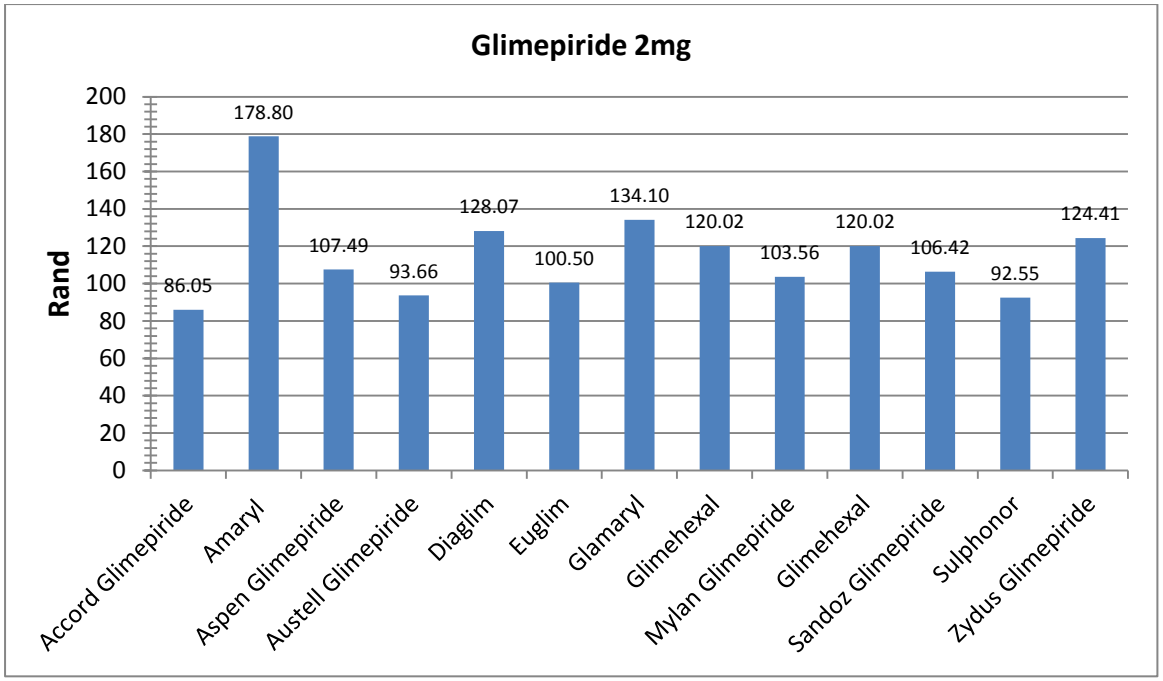
Appendix A – 21: Glibenclamide 5mg brands in 2014



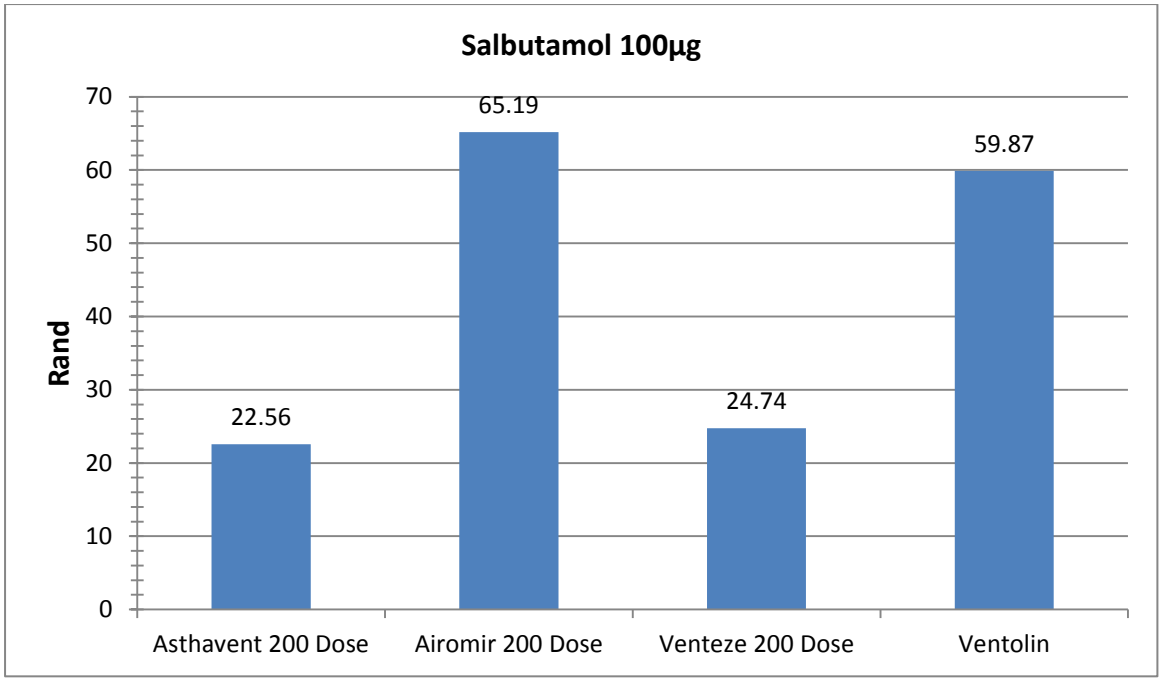
Appendix A – 22: Gliclazide 80mg brands in 2014



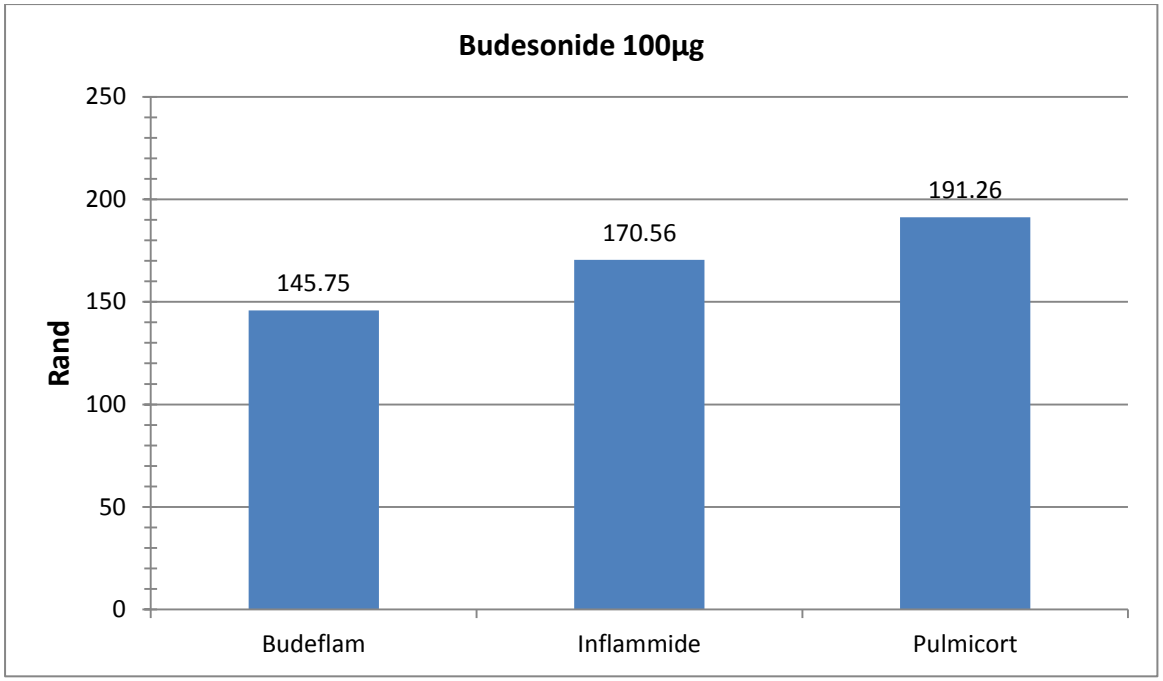
Appendix A – 23: Glimepiride 1mg brands in 2014



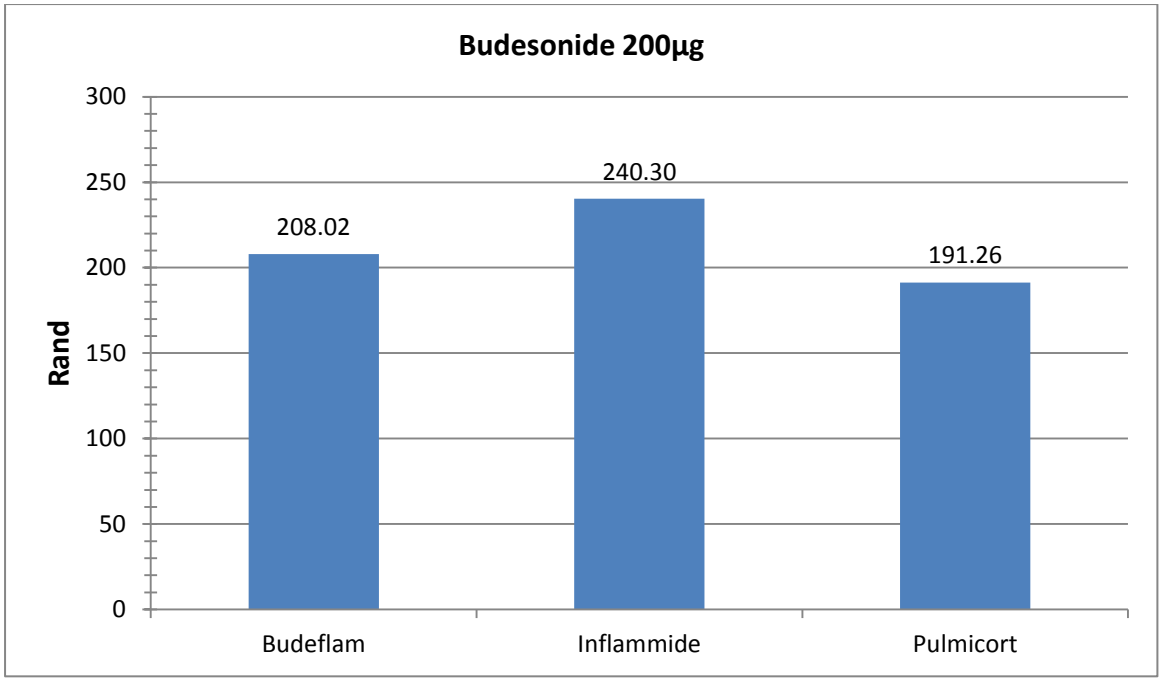
Appendix A – 24: Glimepiride 2mg brands in 2014



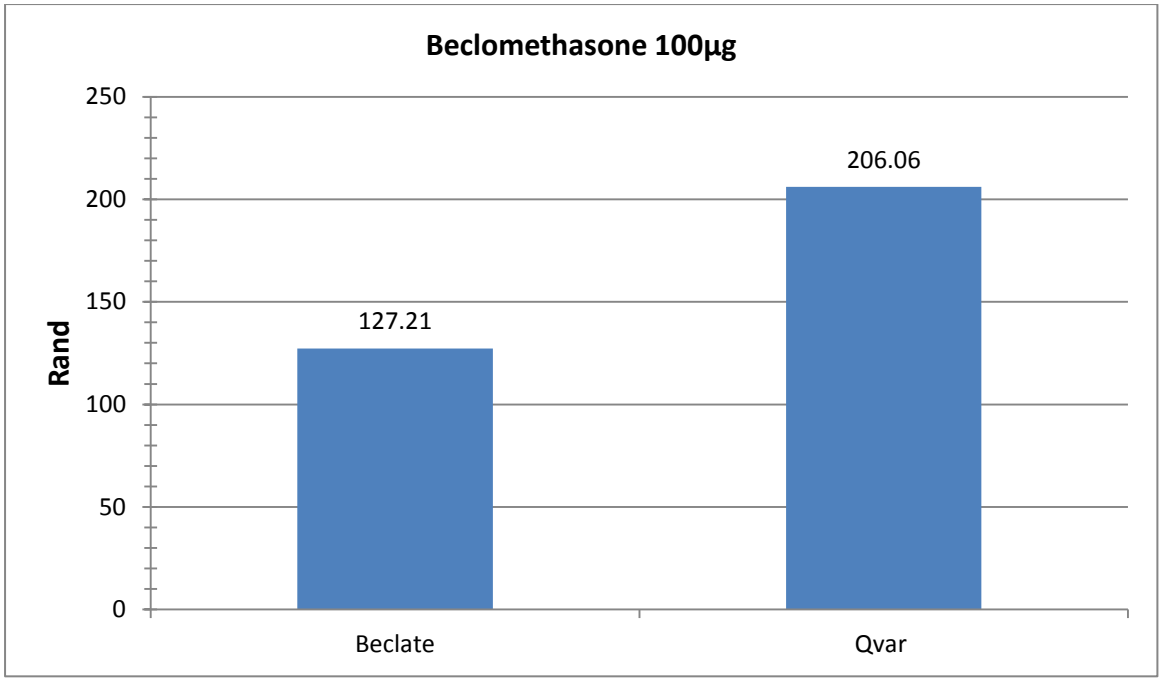
Appendix A – 25: Salbutamol 100µg brands in 2014



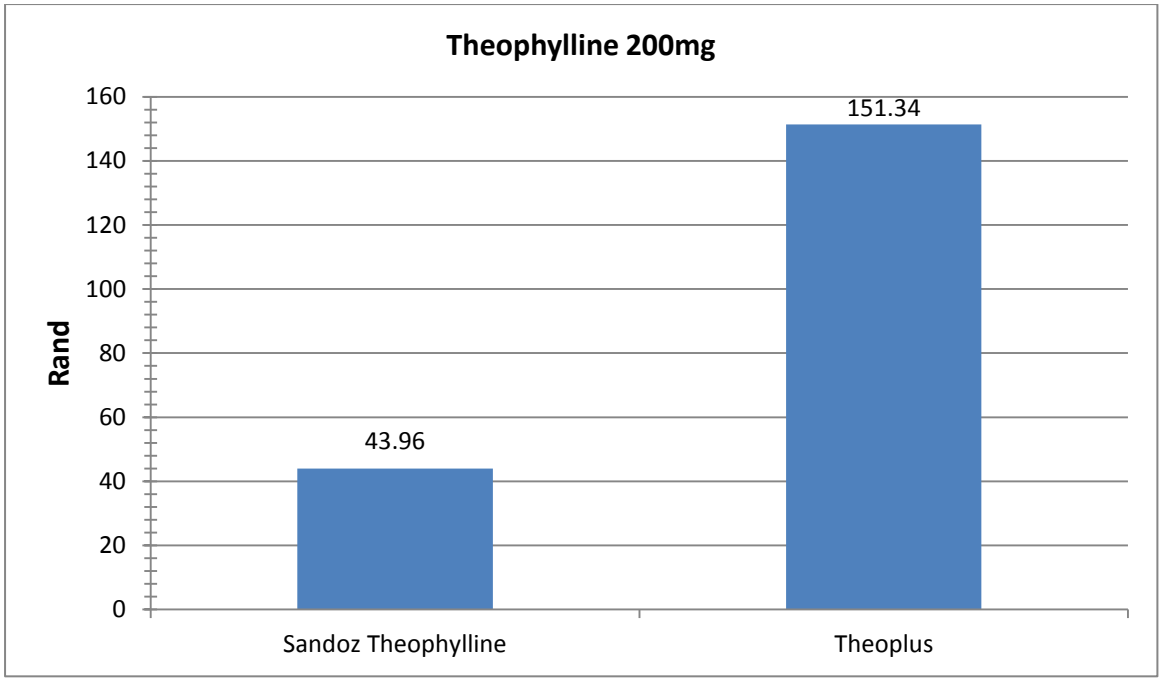
Appendix A – 26: Budesonide 100µg brands in 2014



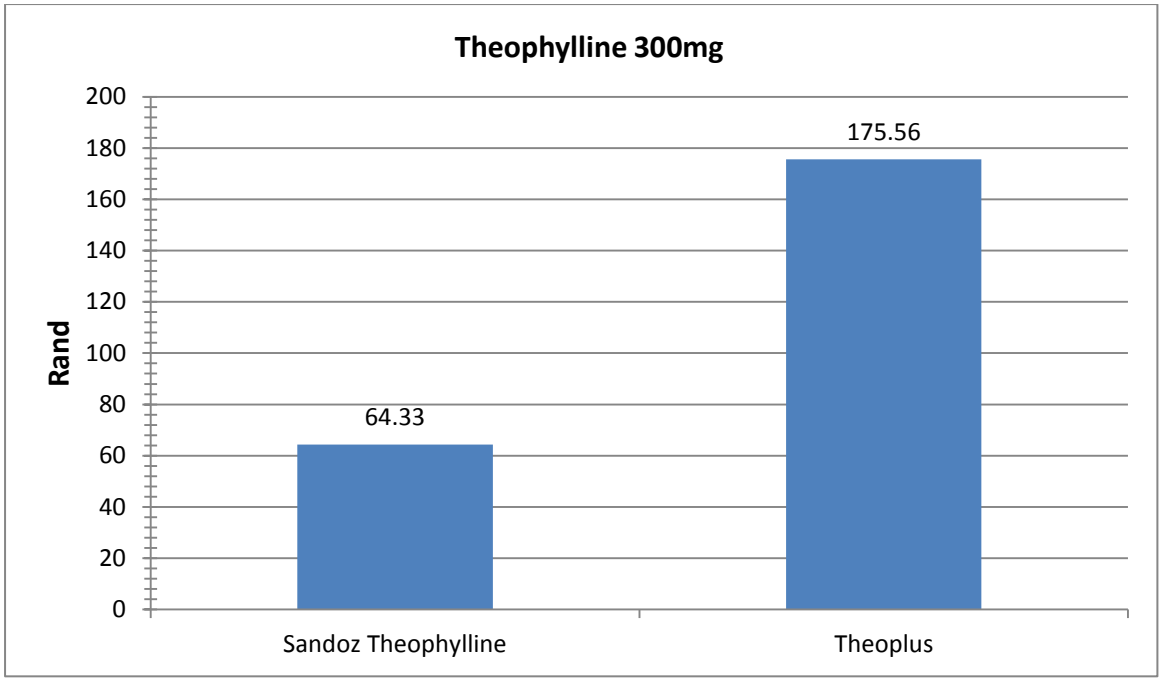
Appendix A –27: Budesonide 200µg brands in 2014



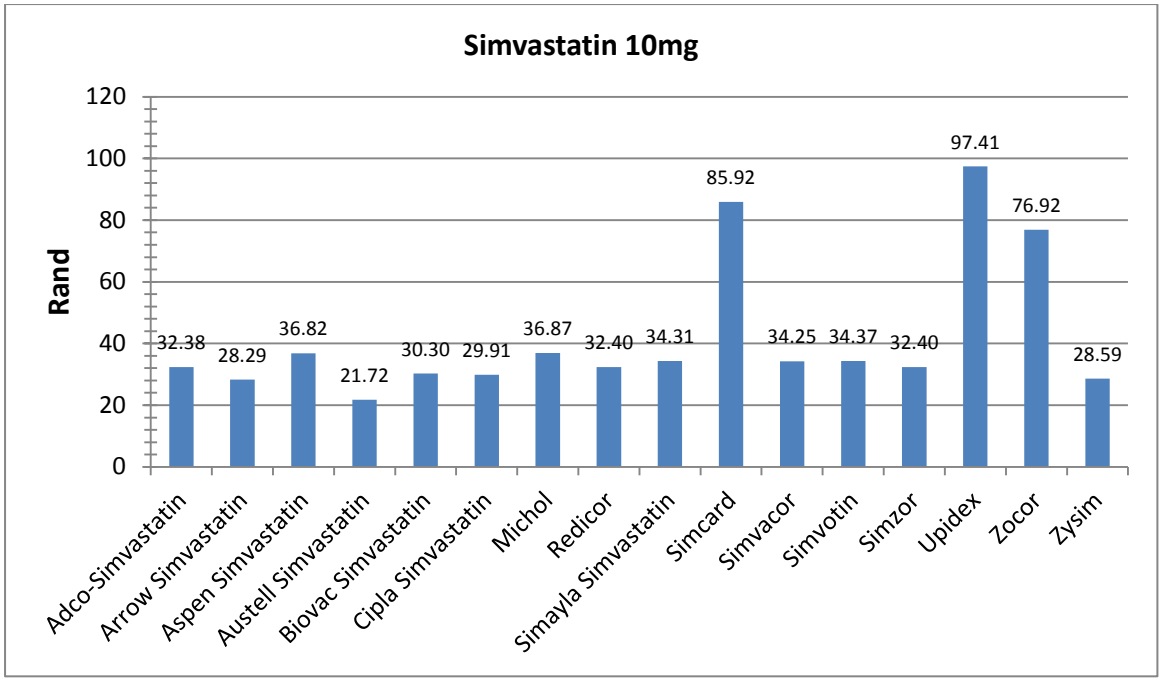
Appendix A – 28: Beclomethasone 100µg brands in 2014



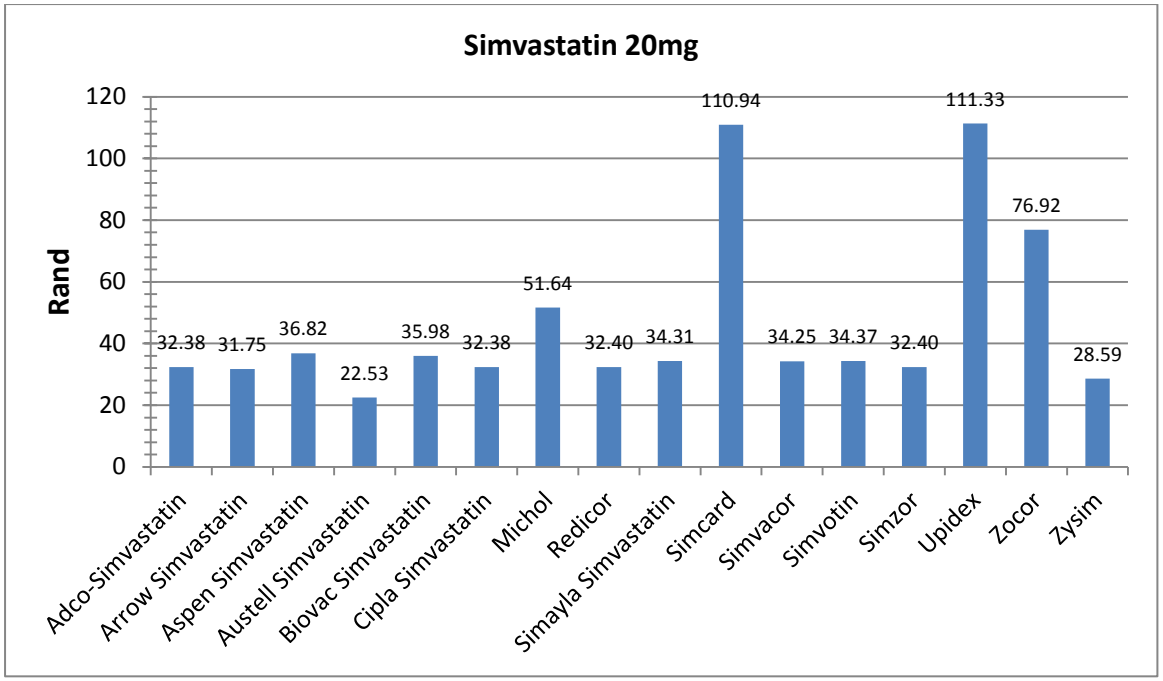
Appendix A –29: Theophylline 200mg brands in 2014



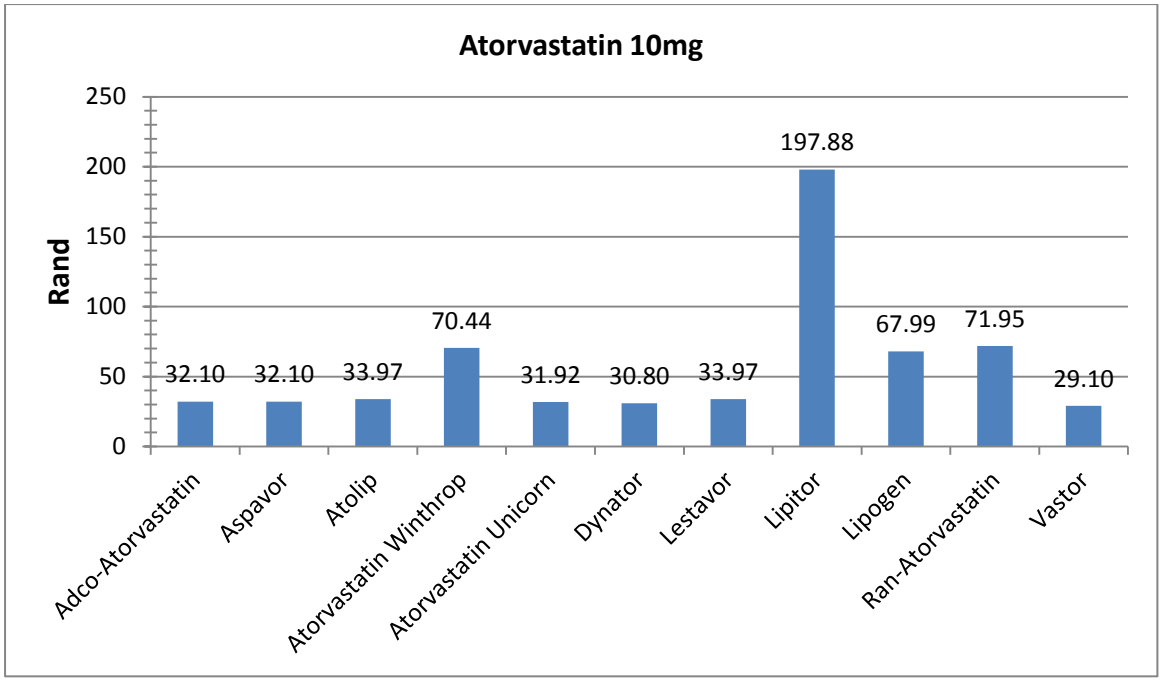
Appendix A –30: Theophylline 300mg brands in 2014



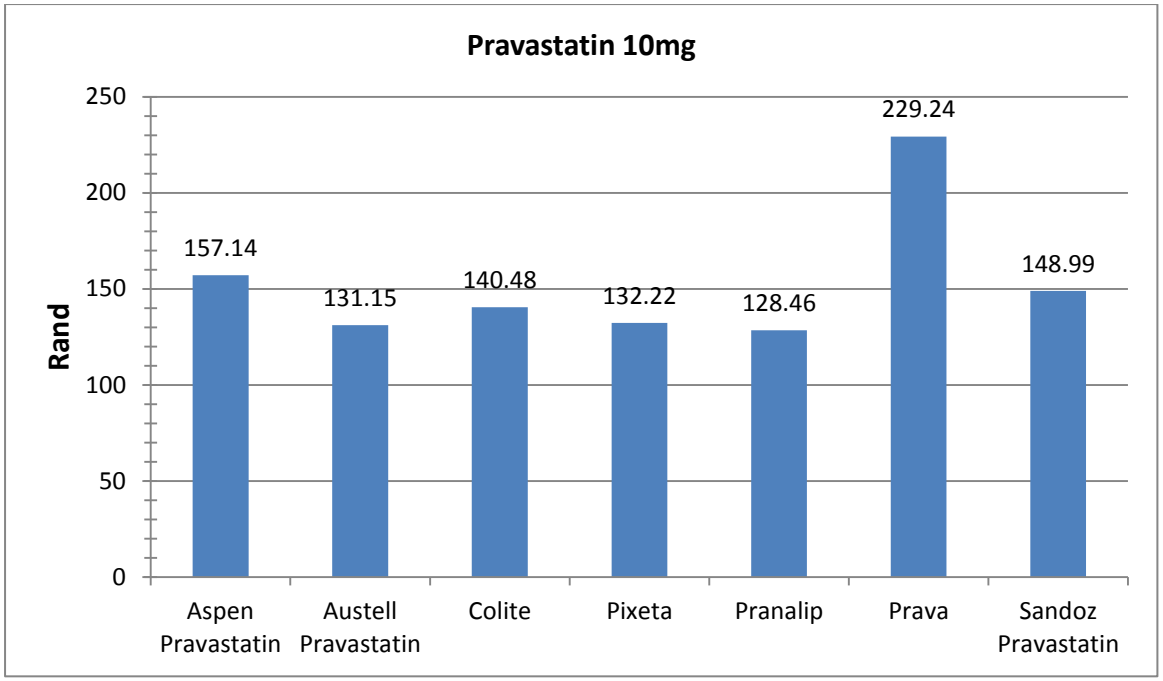
Appendix A –31: Simvastatin 10mg brands in 2014



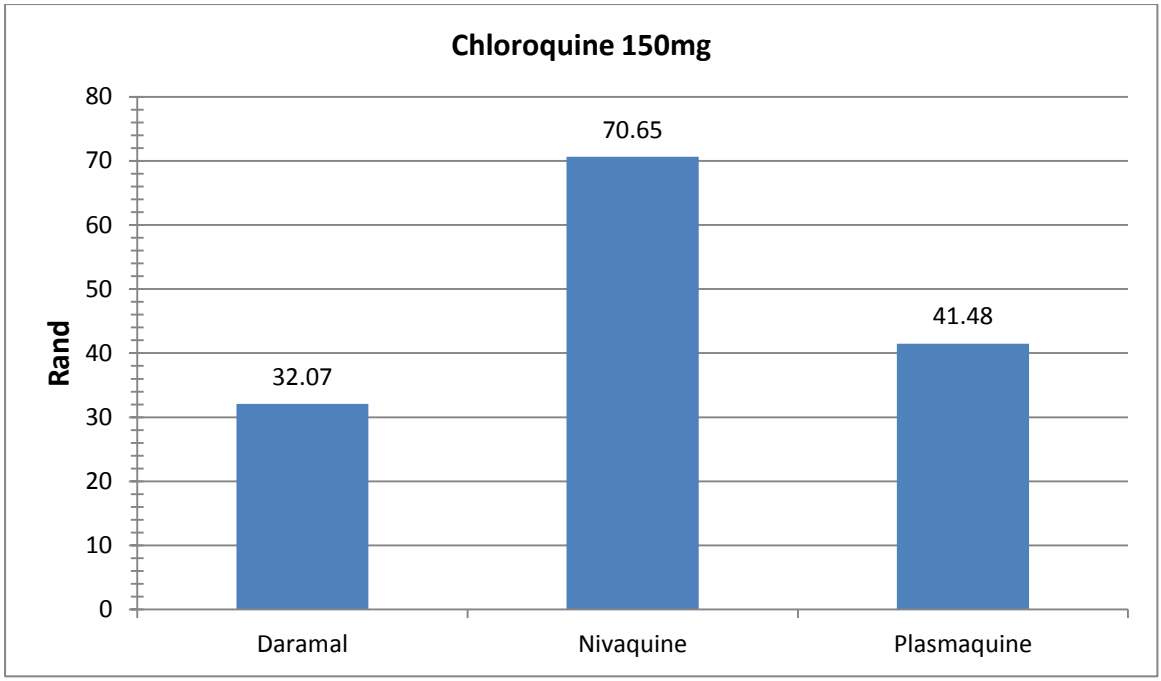
Appendix A – 32: Simvastatin 20mg brands in 2014



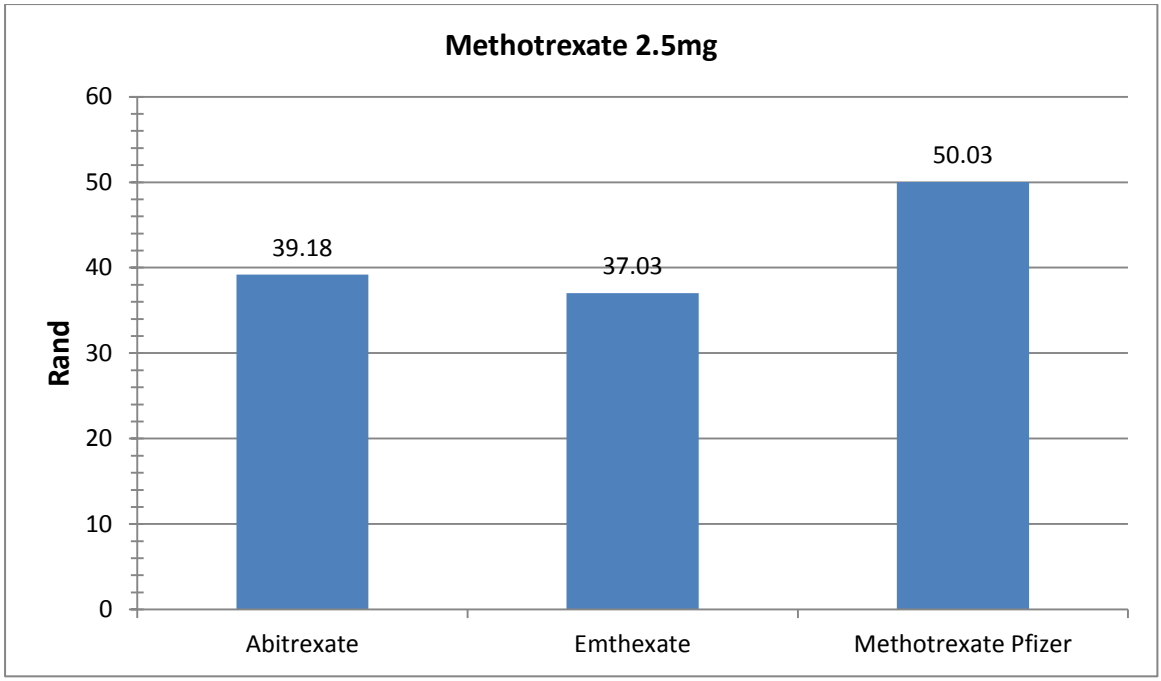
Appendix A –33: Atorvastatin 10mg brands in 2014



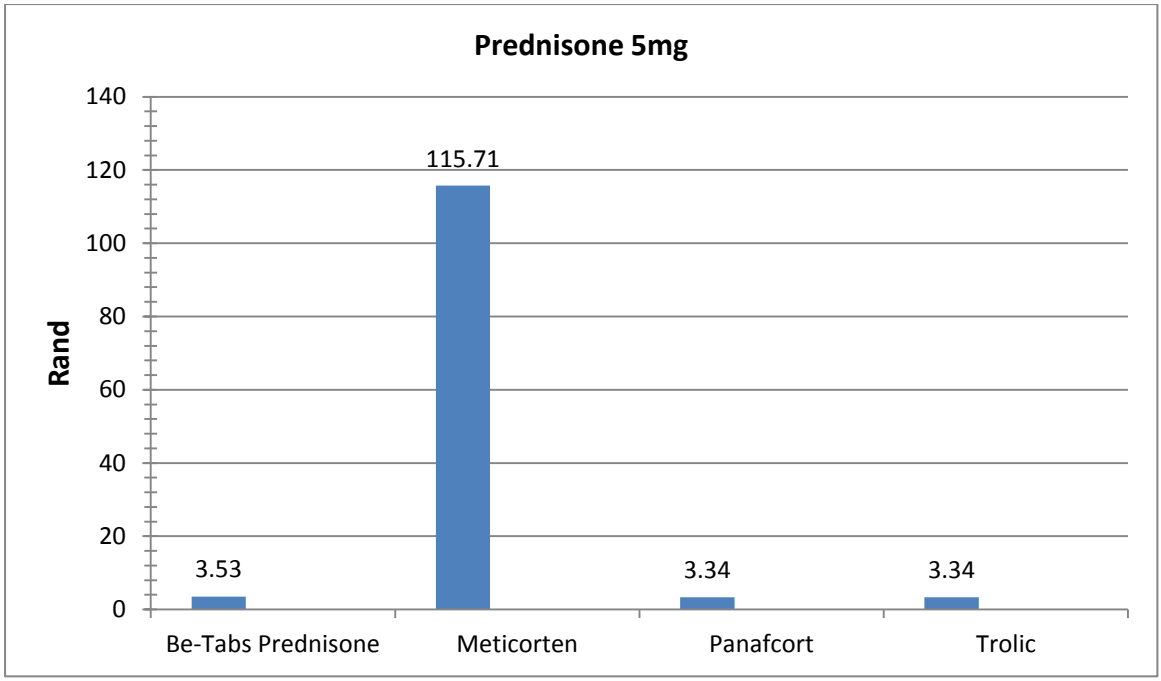
Appendix A – 34: Pravastatin 10mg brands in 2014



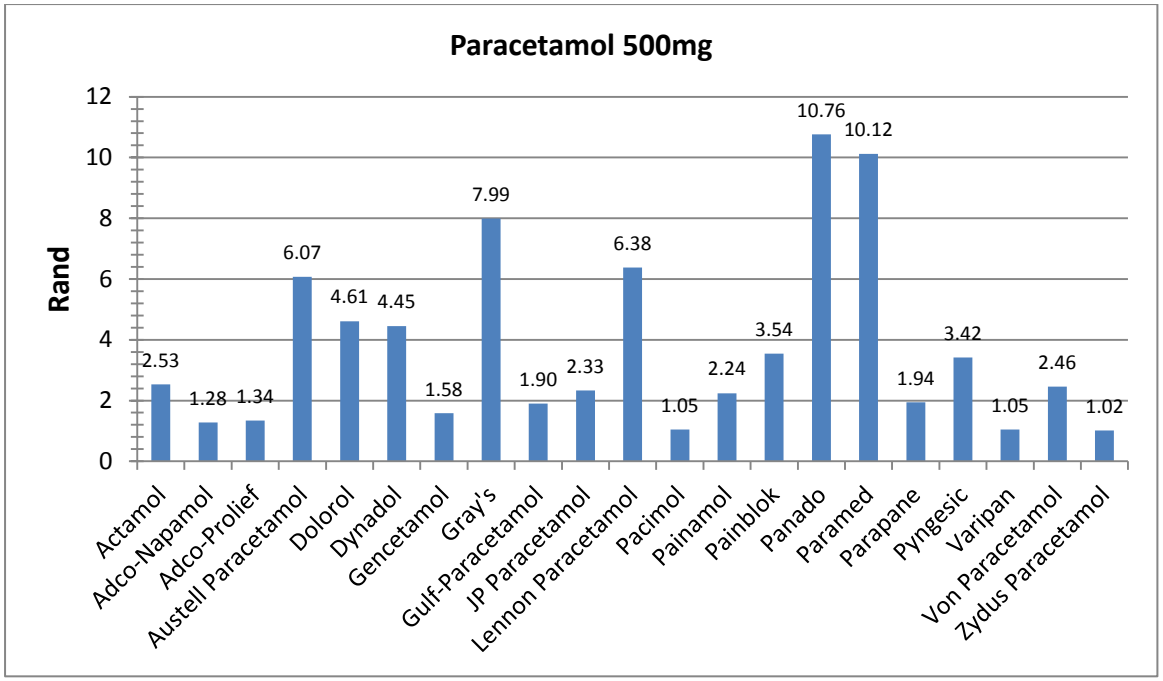
Appendix A – 35: Chloroquine brands in 2014



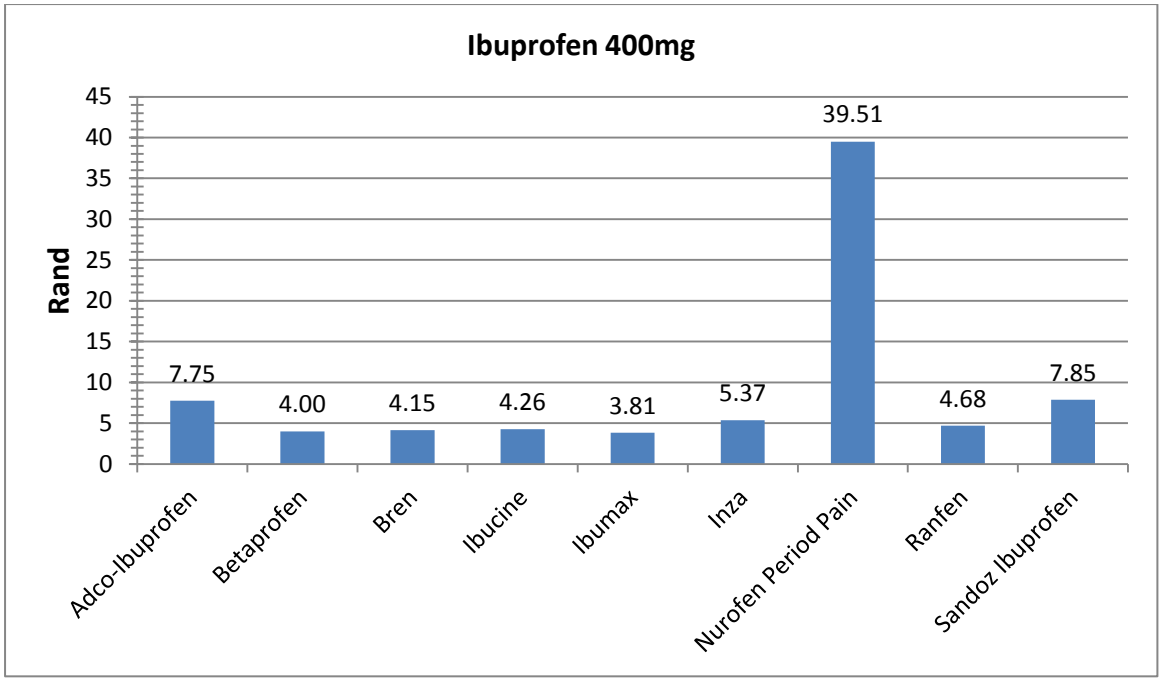
Appendix A – 36: Methotrexate brands in 2014



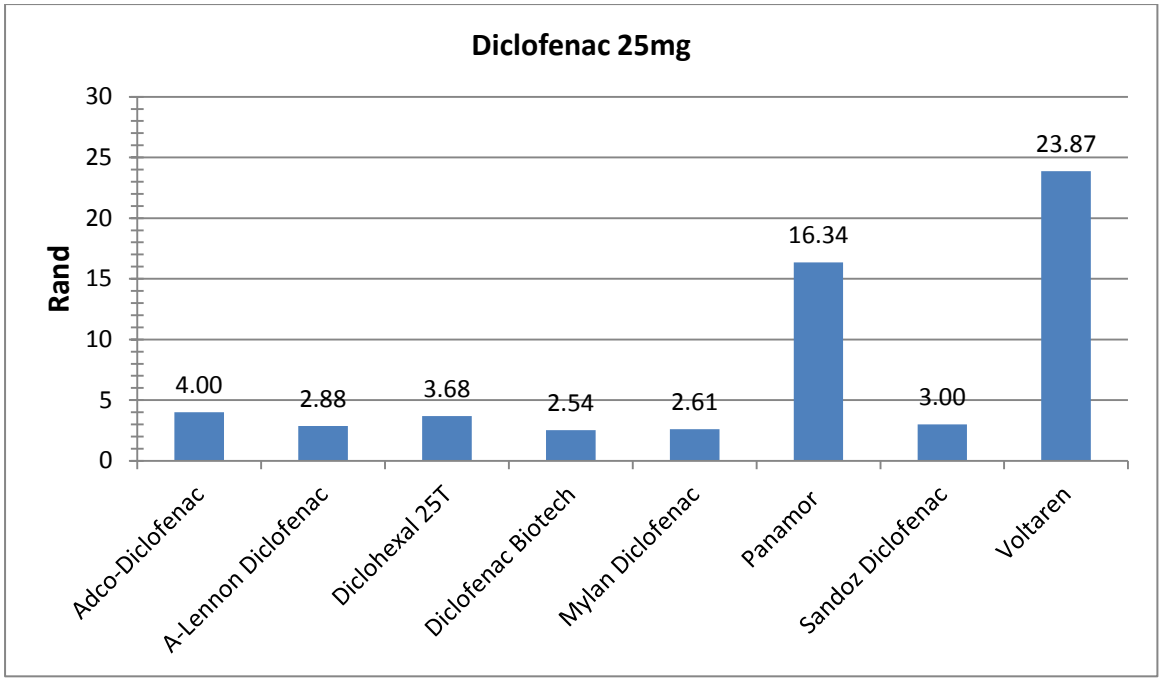
Appendix A – 37: Prednisone brands in 2014



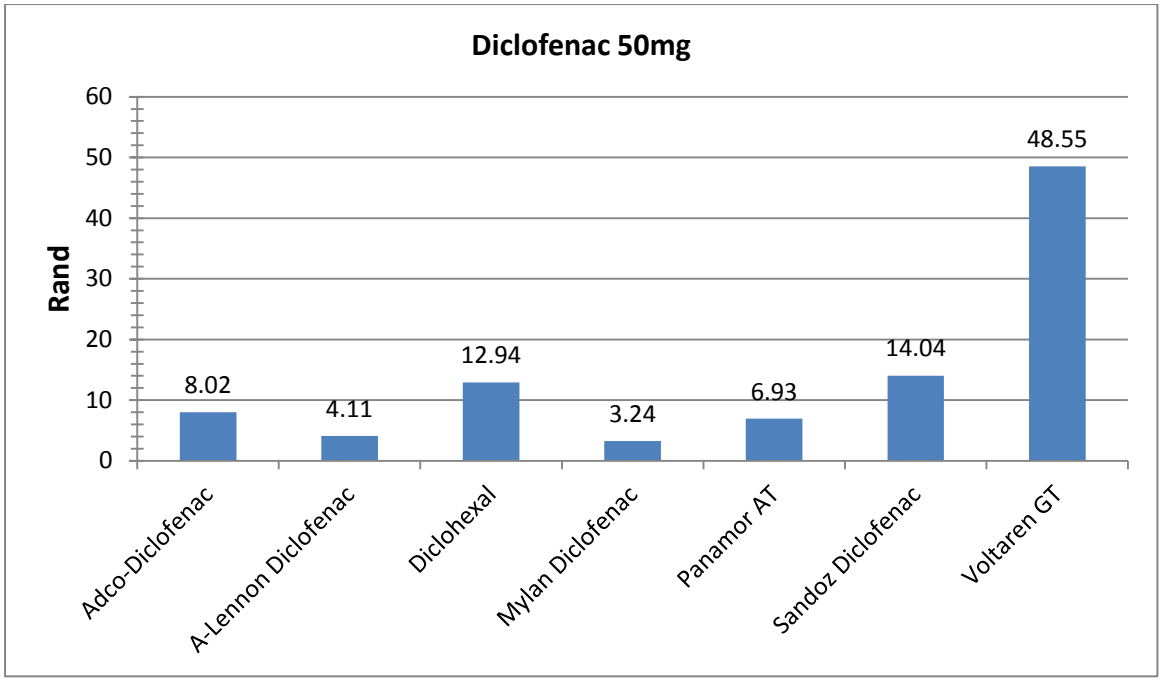
Appendix A – 38: Paracetamol brands in 2014



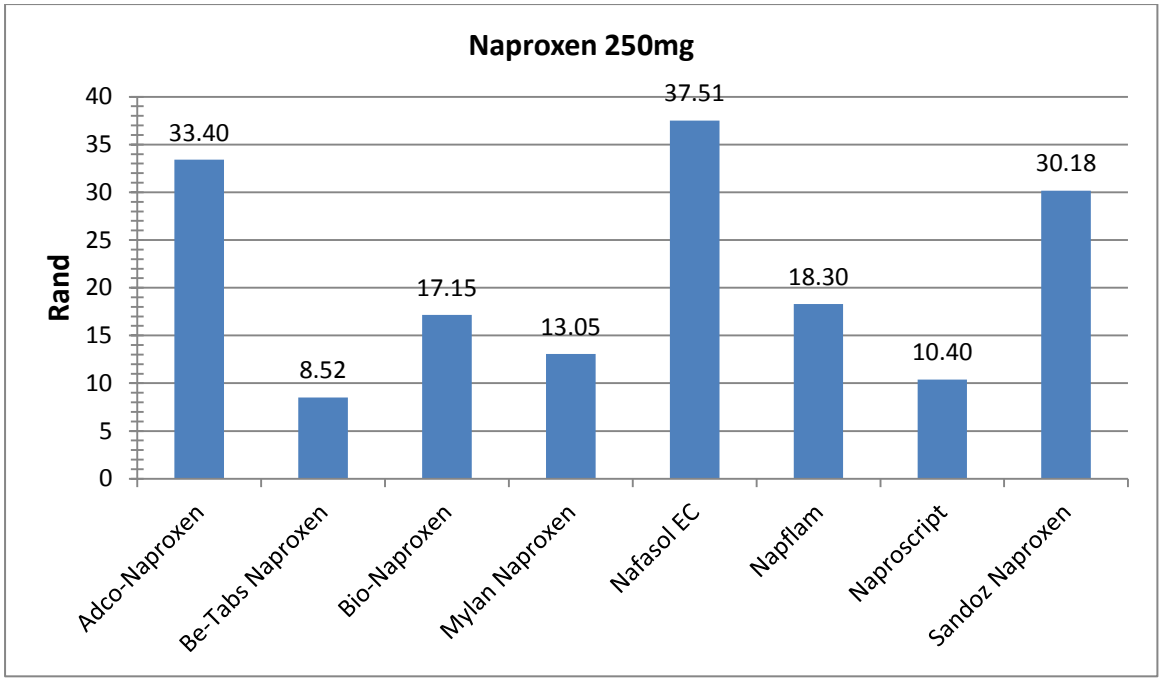
Appendix A – 39: Ibuprofen brands in 2014



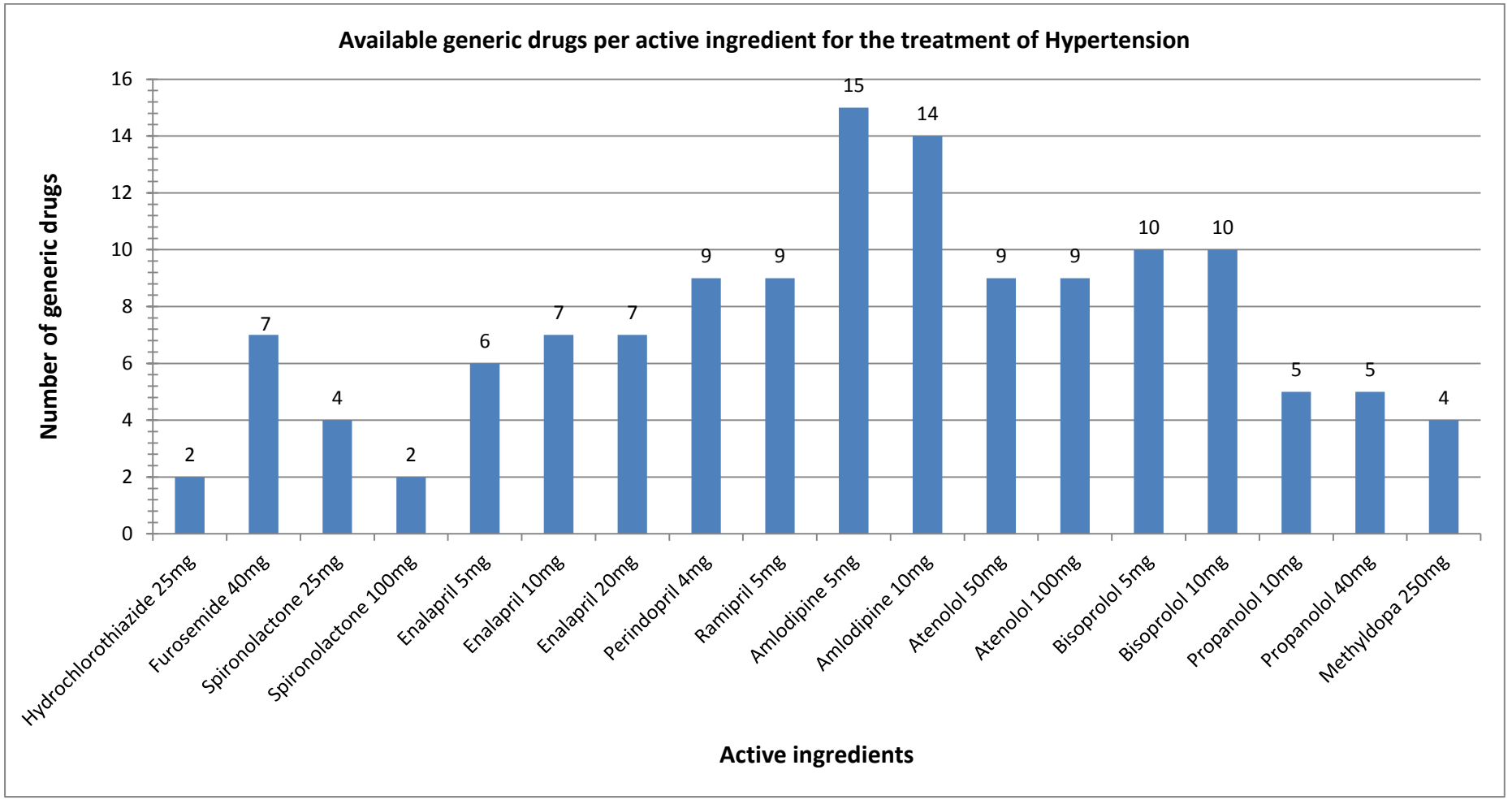
Appendix A – 40: Diclofenac 25mg brands in 2014



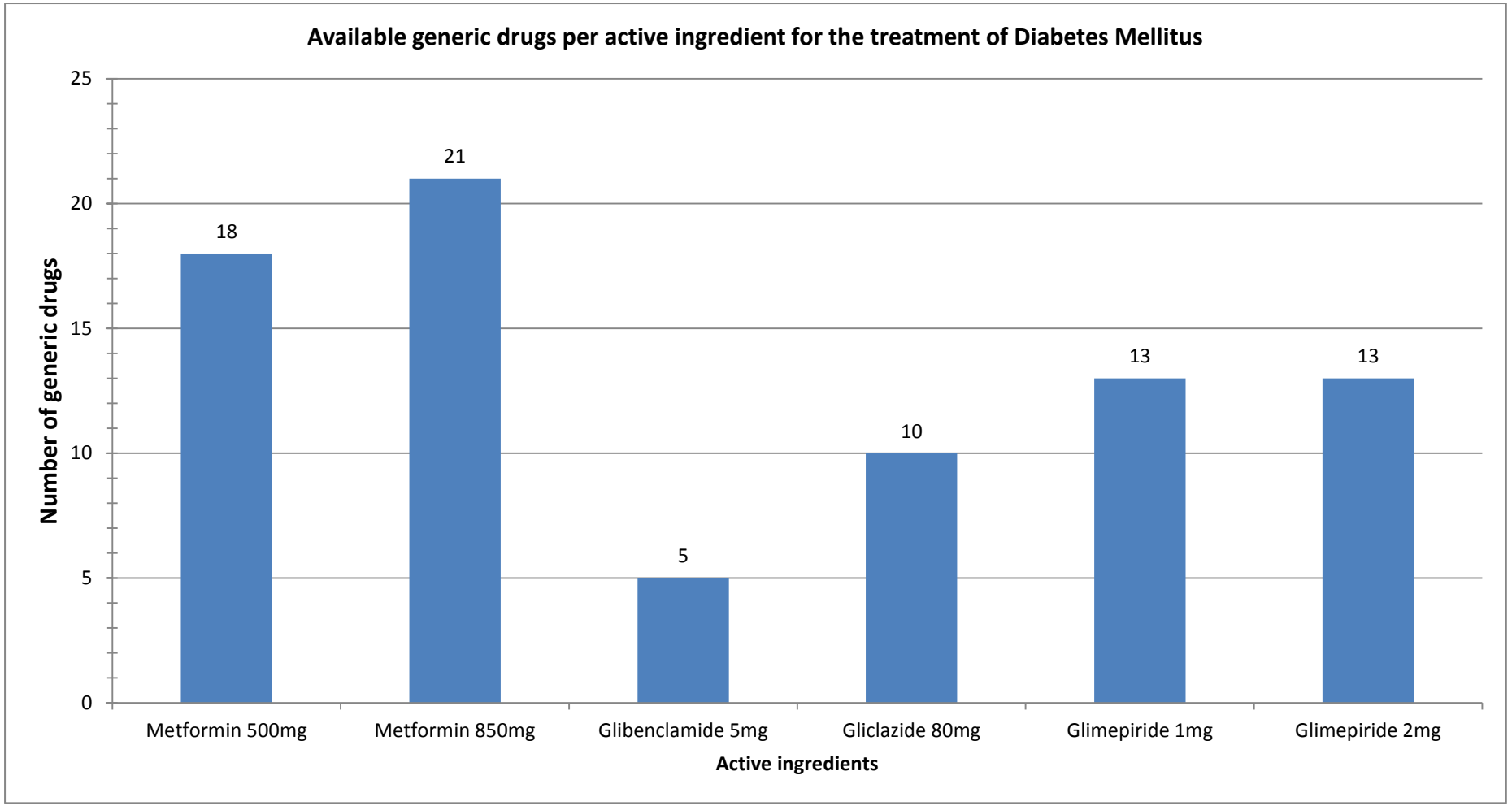
Appendix A – 41: Diclofenac 50mg brands in 2014



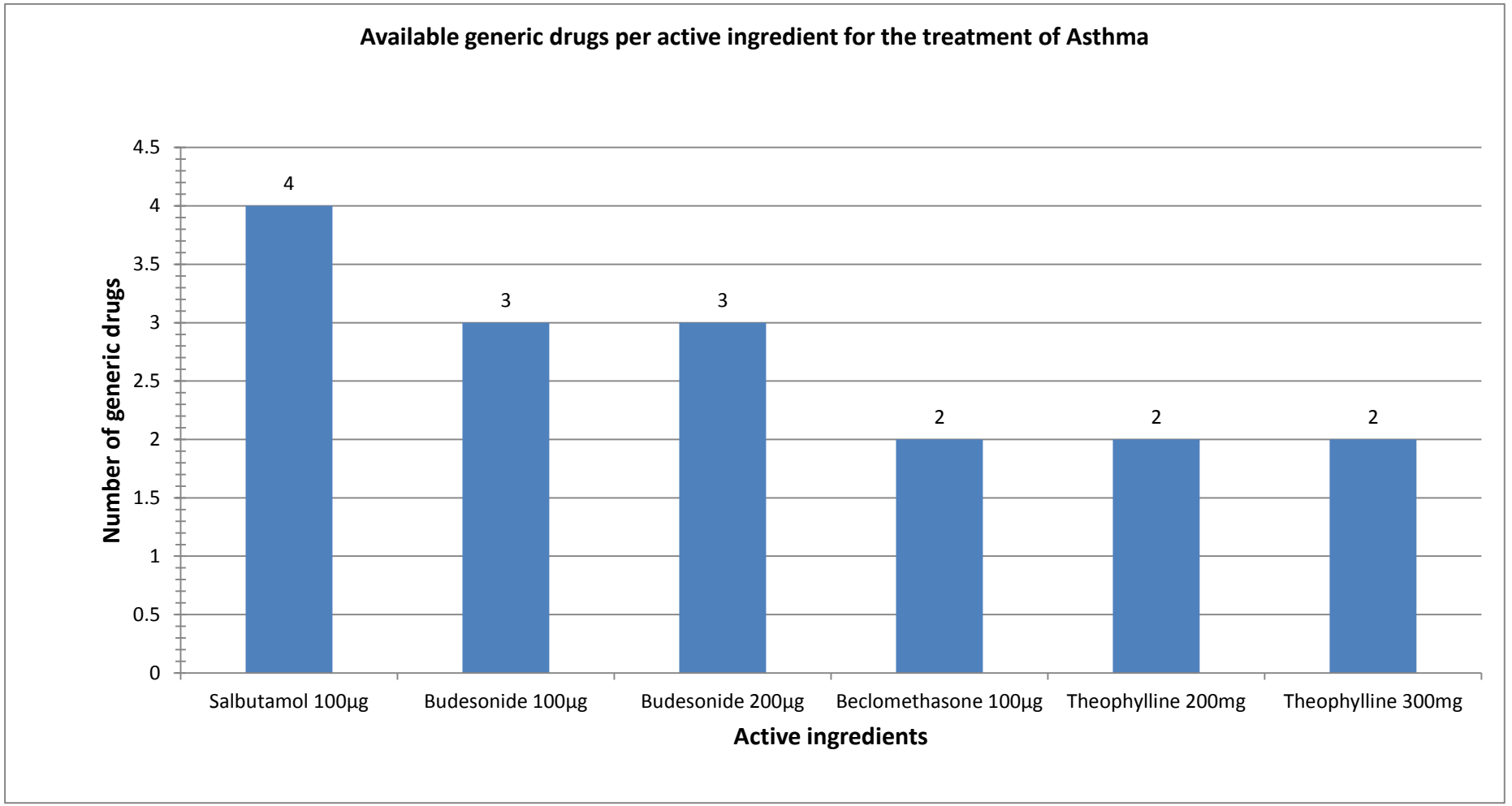
Appendix A – 42: Naproxen brands in 2014



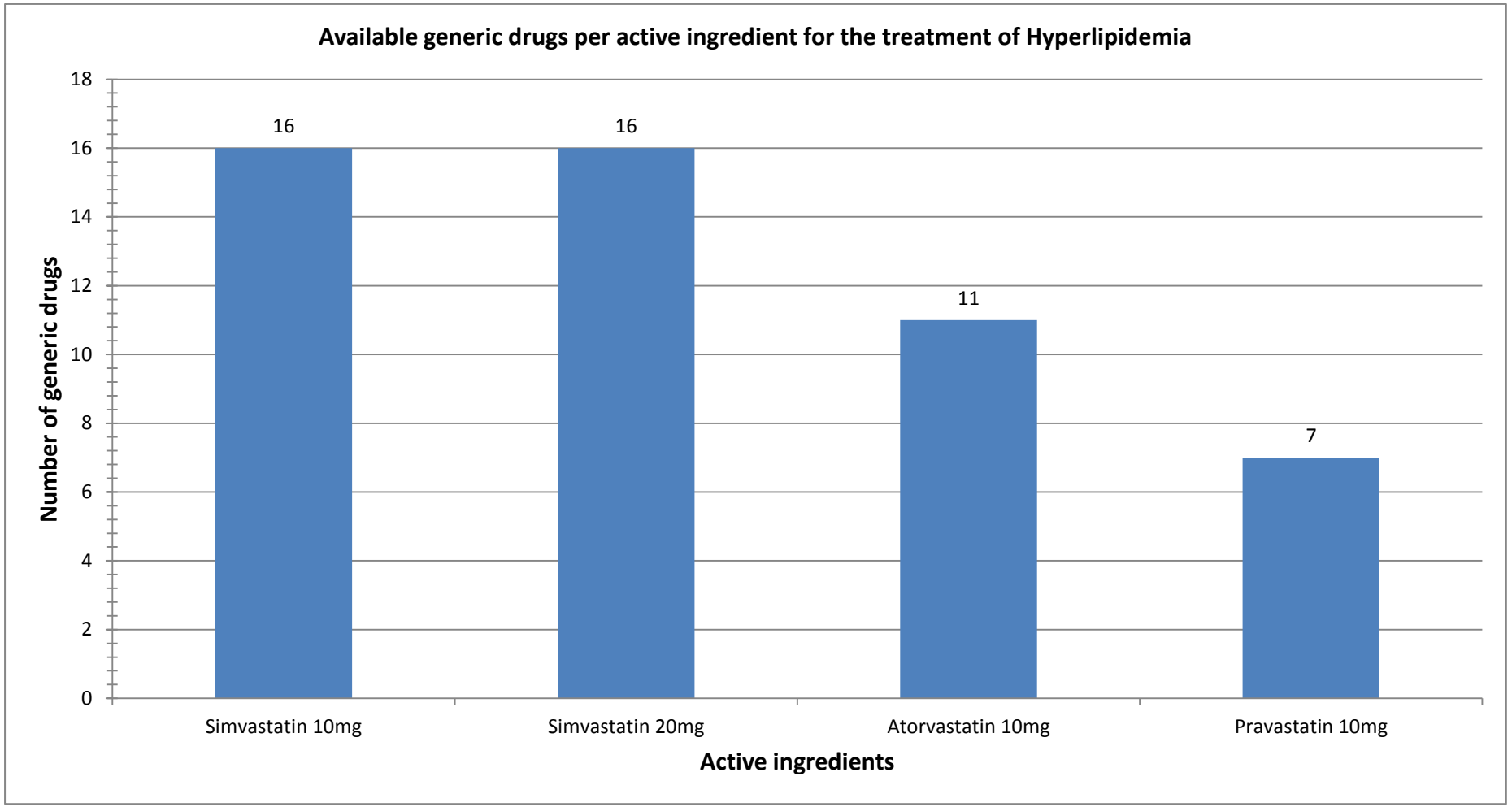
Appendix A – 43: Available generic drugs per active ingredient for the treatment of Hypertension in 2014



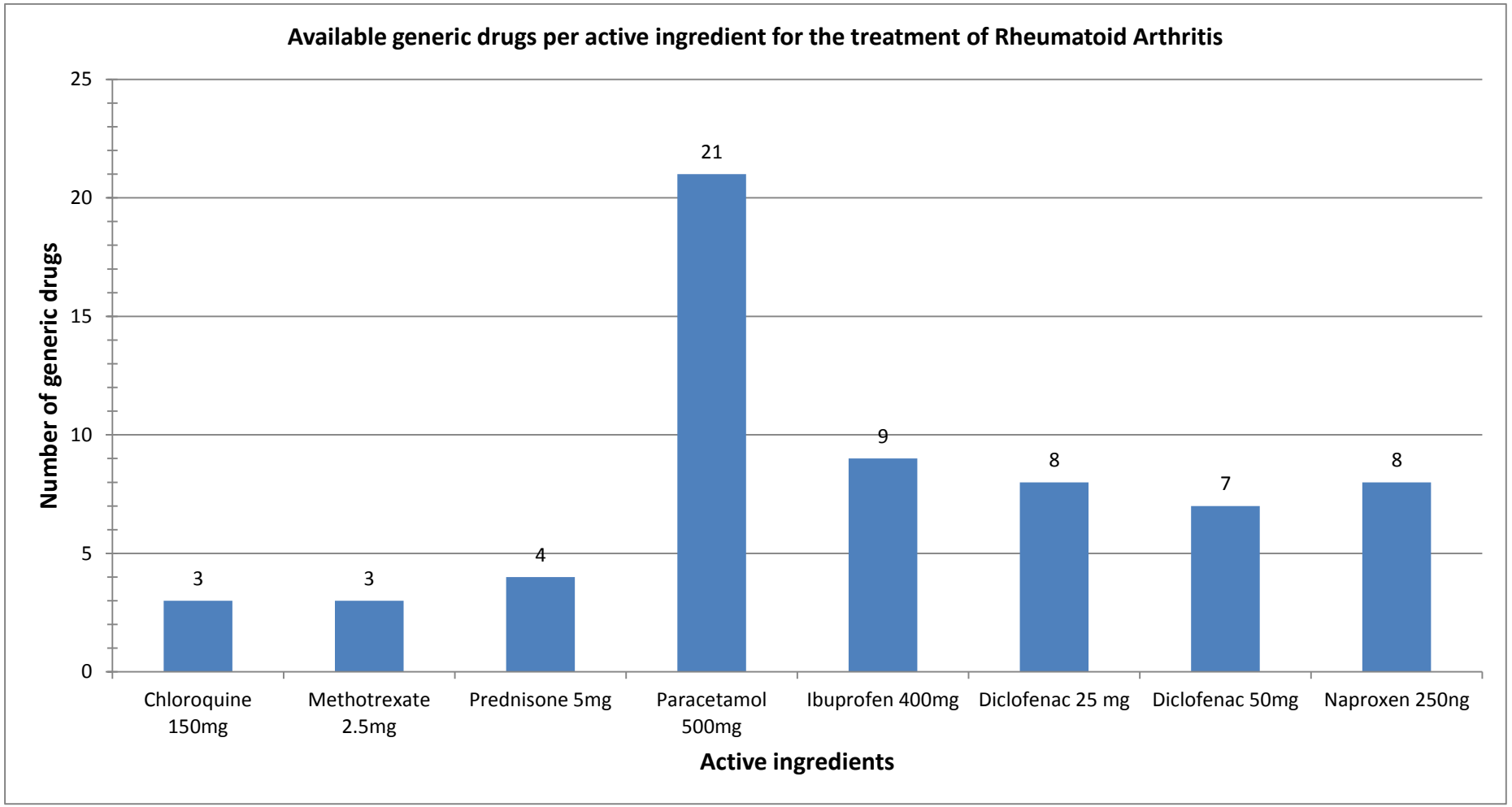
Appendix A – 44: Available generic drugs per active ingredient for the treatment of Diabetes Mellitus in 2014



Appendix A – 45: Available generic drugs per active ingredient for the treatment of Asthma in 2014



Appendix A – 46: Available generic drugs per active ingredient for the treatment of Hyperlipidemia in 2014



Appendix A – 47: Available generic drugs per active ingredient for the treatment of Rheumatoid Arthritis in 2014

Appendix A – 48: Data capture sheet - Hypertension						
Disease	**Class of drug**	**Active Ingredient**	**Brands**		**Cost (ZAR)**	
				Most Expensive (X)	**2nd Least Expensive (Y)**	**Least Expensive (Z)**
Hypertension	Diuretics	Hydrochlorothiazide 25mg	Ridaq	24.68		
			Hexazide			12.26
		Furosemide 40mg	Austell Furosemide	20.86		
			Beurises		4.53	
			Dino-Retic	5.18		
			Lasix	136.15		
			Mylan Furosemide			3.90
			Puresis	19.00		
			Sandoz Furosemide	15.93		
		Spironolactone 25mg	Aldactone		35.49	
			Aldazide		35.49	
			Sandoz Spironolactone			33.94
			Spiractin	35.52		
		Spironolactone 100mg	Aldactone	219.22		
			Spiractin	219.22		
	ACE Inhibitors	Enalapril 5mg	Alapren			18.76
			Ciplatec	29.65		
			Enap		29.50	
			HR-Enalapril	30.00		
			Pharmapress	29.54		
			Renitec	33.22		
		Enalapril 10mg	Adco-Enalapril	62.19		
			Alapren			32.25

			Ciplatec	43.78		
			Enap	42.20		
			HR-Enalapril		42.08	
			Pharmapress		42.08	
			Renitec	46.00		
		Enalapril 20mg	Adco-Enalapril	129.04		
			Alapren			32.25
			Ciplatec	74.21		
			Enap	74.11		
			HR-Enalapril		71.26	
			Pharmapress	74.76		
			Renitec	84.20		
		Perindopril 4mg	Auro-Perindopril	80.38		
			Ciplasyl	81.05		
			Coversyl	136.74		
			Pearinda	81.11		
			Prexum	103.32		
			Ran-perindopril			39.67
			Spec-Perindopril	80.01		
			Vectoryl	81.12		
			Zydus-Perindopril		76.60	
		Ramipril 5mg	Adco-Rilace			102.87
			Apex-Ramipril		131.11	
			Austell Ramipril	140.05		
			Ramace	224.14		
			Ramipril Hexal	143.06		
			Ramiwin	143.00		
			Rampil	141.70		

			Retace	143.06		
			Tritace	298.02		
	Calcium channel blockers	Amlodipine 5mg	Almadin	65.00		
			Amloc	77.17		
			Amlodac	61.59		
			Amlosyn	120.34		
			Austell Amlodipine	65.99		
			Calbloc	63.84		
			Ciplavasc	65.77		
			Indo Amlodipine		58.66	
			Gulf Amlodipine			35.34
			Keysal	69.30		
			Lomanor	61.50		
			Norcard	70.90		
			Norvasc	160.43		
			Pendine	65.16		
			Sandoz Amlodipine	74.29		
		Amlodipine 10mg	Almadin	101.21		
			Amloc	114.62		
			Amlodac	99.99		
			Amlosyn	168.94		
			Austell Amlodipine	100.00		
			Calbloc	96.44		
			Ciplavasc	106.46		
			Gulf Amlodipine			62.70
			Keysal	107.97		
			Lomanor		92.40	
			Norcard	103.46		

			Norvasc	225.20		
			Pendine	103.28		
			Sandoz Amlodipine	115.82		
	Beta-adrenergic blockers	Atenolol 50mg	Adco-Atenolol	35.85		
			Bio-Atenolol	16.50		
			Gulf Atenolol		16.47	
			Hexa-blok	24.50		
			Sandoz Atenolol	19.52		
			Ten-bloka	37.92		
			Tenopress	18.51		
			Tenormin	174.61		
			Zetenol			16.17
		Atenolol 100mg	Adco-Atenolol	52.47		
			Bio-Atenolol	28.68		
			Gulf Atenolol		28.01	
			Hexa-blok	49.01		
			Sandoz Atenolol	37.26		
			Ten-bloka	55.54		
			Tenopress	34.46		
			Tenormin	283.91		
			Zetenol			27.60
		Bisoprolol 5mg	Adco-Bisocor			45.08
			Betacor	50.78		
			Bilocor	50.79		
			Bislo	51.86		
			Bisoprolol Hexal	55.40		
			Bisoprolol Unicorn	50.94		

			Bisohexal	47.62		
			Cardicor	98.45		
			Concor	98.45		
			Ziapro		47.58	
		Bisoprolol 10mg	Adco-Bisocor			75.86
			Betacor	85.34		
			Bilocor	85.40		
			Bislo	87.84		
			Bisoprolol Hexal	93.47		
			Bisoprolol Unicorn	85.42		
			Bisohexal	80.31		
			Cardicor	155.68		
			Concor	155.68		
			Ziapro		80.28	
		Propranolol 10mg	Inderal	47.77		
			Indoblok			2.48
			Prodolol		3.22	
			Pur-Bloka	4.81		
			Sandoz Propranolol	3.61		
		Propranolol 40mg	Inderal	119.57		
			Indoblok			4.31
			Prodolol	5.86		
			Pur-Bloka	6.35		
			Sandoz Propranolol		4.79	
	Centrally acting agents	Methyldopa	Hy-Po-Tone	24.84		
			Mylan Methlydopa		22.99	
			Normopress	32.97		

			Sandoz-Methyldopa			18.81
		Captopril 25mg	Adco-Captomax	16.86		
			Adco-Captopril	18.13		
			Bio-Captopril	17.64		
			Capace	74.07		
			Capoten	169.42		
			Captohexal	32.68		
			Cardiace	94.62		
			Merck-Captopril			13.26
			Mylan Captopril		15.16	
			Sandoz Captopril	24.95		
			Zapto	25.21		

Appendix A – 49: Data capture sheet – Diabetes Mellitus Type 2				
Brands	**Cost (ZAR)**			
	Most Expensive (X)	**2nd Least Expensive (Y)**	**Least Expensive (Z)**	**Difference**
Accord Metformin	10.29			
Apex Metformin	11.82			
Arrow Metformin	11.39			
Austell Metformin	11.79			
Bigsens		10.20		6.33
Diamin	10.95			
Diaphage	16.53			
Gluconorm	11.22			
Glucophage	16.44			
Indo Metformin	10.72			
Mengen	11.42			
Metchek			9.92	6.61
Metaphage	11.09			
Metformin Alkem	10.75			
Metforal	11.02			
Metored FC	11.41			
Mylan Metformin	11.14			
Sandoz Metformin	11.54			
Accord Metformin	18.60			
Adco Metformin			18.13	11.81
Apex Metformin	21.57			
Arrow Metformin	21.28			
Austell Metformin	21.30			
Bigsens	18.37			

Diabetmin	25.32			
Diamin	20.21			
Diaphage		18.24		11.70
Forminal	25.23			
Gluconorm	21.25			
Glucophage	29.94			
Indo Metformin	19.78			
Mengen	20.82			
Metchek		18.24		11.70
Metforal	19.78			
Metformin Alkem	19.98			
Metored	20.81			
Metphage	20.16			
Mylan Metformin	19.85			
Sandoz Metformin	24.12			
Bio-Glibenclamide			6.88	153.02
Daonil	159.99			
Diacare	7.72			
Glycomin		7.05		152.94
Sandoz-Glibenclamide	7.38			
Adco Glucomed		23.95		20.32
Alembic Gliclazide	26.51			
Arrow Gliclazide	25.03			
Diaglucide	25.34			
Diamicron	44.27			
Glycobeta	28.06			
Glycron	25.53			

Glygard	25.39			
Mylan Gliclazide	26.72			
Sandoz Gliclazine			18.62	25.65
Accord Glimepiride			43.49	50.62
Amaryl	94.11			
Aspen Glimepiride	54.89			
Austell Glimepiride	47.77			
Diaglim	65.68			
Glamaryl	70.55			
Euglim	50.79			
Glimehexal	61.58			
Mylan Glimepiride	54.48			
Glimehexal	61.58			
Sandoz Glimepiride	53.20			
Sulphonor		46.27		47.84
Zydus Glimepiride	63.85			
Accord Glimepiride			86.05	92.75
Amaryl	178.80			
Aspen Glimepiride	107.49			
Austell Glimepiride	93.66			
Diaglim	128.07			
Euglim	100.50			
Glamaryl	134.10			
Glimehexal	120.02			
Mylan Glimepiride	103.56			
Glimehexal	120.02			
Sandoz Glimepiride	106.42			

Sulphonor		92.55		86.25
Zydus Glimepiride	124.41			

Appendix A – 50: Data capture sheet - Asthma				
Active Ingredient	**Brands**	**Cost (ZAR)**		
		Most Expensive (X)	**2nd Least Expensive (Y)**	**Least Expensive (Z)**
Salbutamol 100µg	Asthavent 200 Dose			22.56
	Airomir 200 Dose	65.19		
	Venteze 200 Dose		24.74	
	Ventolin	59.87		
Budesonide 100µg	Budeflam			145.75
	Inflammide		170.56	
innovator	Pulmicort	191.26		
Budesonide 200µg	Budeflam		208.02	
	Inflammide	240.30		
innovator	Pulmicort			191.26
Beclomethasone 100µg	Beclate		127.21	
	Becotide			79.21
	Qvar	205.70		
Theophyllin 200mg	Sandoz Theophyllin			43.96
	Theoplus	151.34		
Theophyllin 300mg	Sandoz Theophyllin			64.33
	Theoplus	175.56		

Appendix A – 51: Data capture sheet – Hyperlipidemia				
Active Ingredient	**Brands**	**Cost (ZAR)**		
		Most Expensive (X)	**2nd Least Expensive (Y)**	**Least Expensive (Z)**
Simvastatin 10mg	Adco-Simvastatin	32.38		
	Arrow Simvastatin		28.29	
	Aspen Simvastatin	36.82		
	Austell Simvastatin			21.72
	Biovac Simvastatin	30.30		
	Cipla Simvastatin	29.91		
	Michol	36.87		
	Redicor	32.40		
	Simayla Simvastatin	34.31		
	Simcard	85.92		
	Simvacor	34.25		
	Simvotin	34.37		
	Simzor	32.40		
	Upidex	97.41		
	Zocor	76.92		
	Zysim	28.59		
Simvastatin 20mg	Adco-Simvastatin	32.38		
	Arrow Simvastatin	31.75		
	Aspen Simvastatin	36.82		
	Austell Simvastatin			22.53
	Biovac Simvastatin	35.98		
	Cipla Simvastatin	32.38		
	Michol	51.64		
	Redicor	32.40		
	Simayla Simvastatin	34.31		

	Simcard	110.94		
	Simvacor	34.25		
	Simvotin	34.37		
	Simzor	32.40		
	Upidex	111.33		
	Zocor	76.92		
	Zysim		28.59	
Atorvastatin 10mg	Adco-Atorvastatin	32.10		
	Aspavor	32.10		
	Atolip	33.97		
	Atorvastatin Winthrop	70.44		
	Atorvastatin Unicorn	31.92		
	Dynator		30.80	
	Lestavor	33.97		
	Lipitor	197.88		
	Lipogen	67.99		
	Ran-Atorvastatin	71.95		
	Vastor			29.10
Pravastatin 10mg	Aspen Pravastatin	157.14		
	Austell Pravastatin		131.15	
	Colite	140.48		
	Pixeta	132.22		
	Pranalip			128.46
	Prava	229.24		
	Sandoz Pravastatin	148.99		

Appendix A – 52: Data capture sheet – Rheumatoid Arthritis				
Active Ingredient	**Brands**	**Cost (ZAR)**		
		Most Expensive (X)	**2nd Least Expensive (Y)**	**Least Expensive (Z)**
Chloroquine 150mg	Daramal			32.07
	Nivaquine	70.65		
	Plasmaquine		41.48	
Methotrexate 2.5mg	Abitrexate		39.18	
	Emthexate			37.03
	Methotrexate Pfizer	50.03		
Prednisone 5mg	Be-Tabs Prednisone		3.53	
	Meticorten	115.71		
	Panafcort			3.34
	Trolic			3.34
Paracetamol 500mg	Actamol	2.53		
	Adco-Napamol	1.28		
	Adco-Prolief	1.34		
	Austell Paracetamol	6.07		
	Dolorol	4.61		
	Dynadol	4.45		
	Gencetamol	1.58		
	Gray's	7.99		
	Gulf-Paracetamol	1.90		
	JP Paracetamol	2.33		
	Lennon Paracetamol	6.38		
	Pacimol		1.05	

	Painamol	2.24		
	Painblok	3.54		
	Panado	10.76		
	Paramed	10.12		
	Parapane	1.94		
	Pyngesic	3.42		
	Varipan		1.05	
	Von Paracetamol	2.46		
	Zydus Paracetamol			1.02
Ibuprofen 400mg	Adco-Ibuprofen	7.75		
	Betaprofen		4.00	
	Bren	4.15		
	Ibucine	4.26		
	Ibumax			3.81
	Inza	5.37		
	Nurofen Period Pain	39.51		
	Ranfen	4.68		
	Sandoz Ibuprofen	7.85		
Diclofenac 25 mg	Adco-Diclofenac	4.00		
	A-Lennon Diclofenac		2.88	
	Diclohexal 25T	3.68		
	Diclofenac Biotech			2.54
	Mylan Diclofenac	2.61		
	Panamor	16.34		
	Sandoz Diclofenac	3.00		
	Voltaren	23.87		

Diclofenac 50mg	Adco-Diclofenac	8.02		
	A-Lennon Diclofenac		4.11	
	Diclohexal	12.94		
	Mylan Diclofenac			3.24
	Panamor AT	6.93		
	Sandoz Diclofenac	14.04		
	Voltaren GT	48.55		
Naproxen 250ng	Adco-Naproxen	33.40		
	Be-Tabs Naproxen			8.52
	Bio-Naproxen	17.15		
	Mylan Naproxen	13.05		
	Nafasol EC	37.51		
	Napflam	18.30		
	Naproscript		10.40	
	Sandoz Naproxen	30.18		

APPENDIX B - ETHICAL CLEARANCE

UNIVERSITY OF
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18 June 2014

Mr D Gyanasivan Redhi (Student No. 213550705)
c/o Revd LJ Mathibe
Discipline of Pharmaceutical Sciences
Medical School Campus
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mathibel@ukzn.ac.za

Dear Mr Gyanasivan Redhi

Study Title: "Cost saving from the use for Generic Medicines for the treatment of the most common Chronic conditions in S.A." BREC REF No.: EXM295/14.

I refer to your application to BREC received on 28 May 2014 and wish to advise that exemption is granted for this study because all data is already in the public domain.

This exemption will be noted at the next Biomedical Research Ethics Committee meeting to be held on **08 July 2014.**

Yours sincerely

Prof D Wassenaar
Chair: Biomedical Research Ethics Committee

cc: Nenep1@ukzn.ac.za