

Prescribing patterns of methylphenidate and atomoxetine containing products in a section of the private health care sector of South Africa.

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Potchefstroom

2009

Acknowledgements

I wish to express my gratitude to the Lord, my Saviour, for giving me the strength and faith throughout this dissertation. I would like to thank the following people and institutions that have contributed to and guided me through this dissertation.

- *Prof. M.S. Lubbe, as supervisor and Prof L.Brand, as assistant-supervisor of this dissertation, for their guidance, support and expert advice throughout this study.*
- *Mr. G. John, Prof J.J. Gerber and Prof. J.H.P. Serfontein for their guidance and moral support throughout this study.*
- *The Pharmacy Benefit Management company for providing the data for this study.*
- *Ms. A. Bekker, for her assistance with regard to the analysis of this study and support with regard to some sections.*
- *Mrs. H. Steyn, for her support with regard to language corrections to this dissertation.*
- *The National Research Foundation (NRF) for the financial support.*
- *The personnel of Pharmacy Practice of the North-West University for their kindness and support.*
- *Mrs. M. Terblance, for her assistance with the language editing.*
- *My Brother, L. Rothmann, for his support and encouragement.*
- *My parents, for their devoted love and constant support.*
- *Mr. C. van Zyl, for his support, assistance and friendship and constant support.*
- *Mr. R. Reay, for his friendship and support.*

ABSTRACT

Title: Prescribing patterns of methylphenidate and atomoxetine containing products in a section of the private health care sector of South Africa

Key words: methylphenidate, atomoxetine, prevalence, medicine costs of treatment, attention deficit hyperactivity disorder (ADHD), private health care sector, drug utilisation review

The general aim of this study was to investigate the prescribing patterns of products that contain methylphenidate or atomoxetine in a section of the private health care sector of South Africa. A quantitative, retrospective drug utilisation review was performed according to data obtained from the database of a South African medicine claims pharmacy benefit management company's for three consecutive study years (i.e. 2005 to 2007).

The results indicated that a total of 7,990 patients had been prescribed products that contained methylphenidate or atomoxetine in 2005. The total for 2006 was 8,575 and it decreased to a total of 7,828 in 2007. Of all the patients who received the mentioned products, the percentage for females increased from 27.75% (N = 7,990) in 2005 to 29.06% (N = 7,828) in 2007. With regard to the same products the percentage for males decreased from 72.03% (N = 7,990) in 2005 to 70,89% (N = 7,828) in 2007. The ratio for the gender-related prescribing patterns of medicine items that contained methylphenidate or atomoxetine in this section of the private health care sector of South Africa was $\pm 2.55:1$ for males to females in comparison with the international male:female ratio of 3:1.

According to the medicine claims on the database for 2005 the total number of prescriptions that indicated products containing methylphenidate or atomoxetine was calculated as 8,522,798 (i.e. N = 8, 522,798) or as a percentage of 0.32% prescriptions. The percentage showed an increase to 0.41% in 2007 (N = 8,015,538). Of all the medicine items containing methylphenidate or atomoxetine those products that contained atomoxetine represented 4,69% and those that contained methylphenidate represented 95.31%. In 2005 the average cost per prescription that indicated items containing methylphenidate or atomoxetine amounted to R318.29 \pm R162.09. In 2007 the amount increased to R358.91 \pm R208.10.

The percentage of children younger than five years of age, and who had been prescribed products containing methylphenidate or atomoxetine, increased from 0.91% in 2005 (N = 7,990) to 1.11% in 2007 (N = 7,828). The percentage for children aged 5 to 12 years

decreased from 53.62% in 2005 to 49,23% in 2007. For adolescents the percentage increased from 26.32% in 2005 to 27.35% in 2007. The same pattern repeated itself in the case of adults (age 18+ years).

Among the top trade name products prescribed were Ritalin LA 20mg®, Ritalin 20mg®, Concerta 36mg®, Ritalin LA 30mg® and Concerta 18mg®.

Possible drug-drug interactions were found between products containing methylphenidate or atomoxetine and products containing imipramine, amitriptyline and carbamazepine.

Findings indicated that the number of products containing methylphenidate or atomoxetine increased from 2005 to 2007, while also revealing that those products containing methylphenidate remained in the majority. The average costs of products containing methylphenidate or atomoxetine increased from 2005 to 2007.

Opsomming

Titel: Voorskryfpatrone van metielfenidaat- en atomoksetienbevattende produkte in 'n deel van die private gesondheidsorgsektor van Suid-Afrika.

Sleutelwoorde: Metielfenidaat, atomoksetien, voorkoms, medisynekoste van behandeling, aandagafleibaarheidhiperaktiwiteitsindroom (AAHS), private gesondheidsorgsektor, medisyneverbruikevaluering

Die algemene doel van hierdie studie was om die voorskryfpatrone van metielfenidaat- en atomoksetienbevattende produkte te ondersoek in 'n gedeelte van die private gesondheidsorgsektor van Suid-Afrika. 'n Kwantitatiewe, retrospektiewe medisyneverbruikevalueringstudie is uitgevoer op medisyne-eise data van drie agtereenvolgende studiejare (d.i. 2005 tot 2007) wat verkry is vanaf 'n Suid-Afrikaanse apteekvoordelebestuursmaatskappy.

Die resultate het getoon dat 'n totaal van 7,990 pasiënte metielfenidaat- of atomoksetienbevattende medikasie in 2005 ontvang het, met 8,575 in 2006 en 'n dalende getal van 7,828 in 2007. Die persentasie vrouens wat metielfenidaat- of atomoksetienbevattende produkte ontvang, het vermeerder van 27.75% (N = 7,990) in 2005 tot 29.06% (N = 7,828) in 2007. Die persentasie mans het verminder van 72.03% (N = 7,990) van die totale aantal pasiënte wat metielfenidaat- en atomoksetienbevattende produkte in 2005 ontvang het, tot 70.89% in 2007 (N = 7,828). Die verhouding van die geslagsverwante voorskryfpatrone van metielfenidaat- of atomoksetienbevattende produkte in hierdie gedeelte van die private gesondheidsorgsektor van Suid-Afrika was $\pm 2.55:1$ vir mans:vrouens in vergelyking met die internasionale man:vrou verhouding van 3:1.

Metielfenidaat- of atomoksetienbevattende voorskrifte verteenwoordig 0.32% van al die voorskrifte wat gedurende 2005 ge-eis is. Die persentasie het gestyg tot 0.41% in 2007 (N = 8,015,538). Atomoksetienbevattende produkte verteenwoordig 4.69% terwyl metielfenidaatbevattende produkte 95.31% verteenwoordig van alle metielfenidaat- en atomoksetienbevattende produkte. Die gemiddelde koste per metielfenidaat- en atomoksetienbevattende voorskrifte was $R318.29 \pm R162.09$ in 2005 en het verhoog tot $R358.91 \pm R208.10$ in 2007.

Die persentasie kinders jonger as 5 jaar wat metielfenidaat- of atomoksetienbevattende produkte ontvang, het vermeerder van 0.91% in 2005 (N = 7,990) tot 1.11% in 2007 (N = 7,828). Die getal kinders 5 tot 12 jaar het verminder van 53.62% in 2005 tot 49.23% in 2007. Die getal adolessente wat metielfenidaat- of atomoksetienbevattende produkte ontvang, het vermeerder van 26.32% in 2005 tot 27.35% in 2007. Dieselfde patroon is gevind by volwassenes (18 jaar en ouer).

Die top handelsnaamprodukte wat voorgeskryf is, was Ritalin LA 20mg®, Ritalin 10mg®, Concerta 36mg®, Ritalin LA 30mg® en Concerta 18mg®.

Moontlike geneesmiddel-geneesmiddelinteraksies op voorskrifte is hoofsaaklik gevind tussen metielfenidaat- of atomoksetienbevattende produkte en produkte wat imipramien, amitriptilien en karbamasepien bevat.

Opsommend is gevind dat die getal metielfenidaat- of atomoksetienbevattende voorskrifte vanaf 2005 tot 2007 vermeerder het, met voorskrifte vir metielfenidaatbevattende produkte steeds in die meerderheid. Die gemiddelde koste van metielfenidaat- of atomoksetienbevattende produkte het gestyg vanaf 2005 tot 2007.

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1 CHAPTER 1

Introduction

1.1 INTRODUCTION

The general objective of this study was to investigate the prescribing patterns of products containing methylphenidate or atomoxetine in a section of the private health care sector in South Africa. A retrospective drug utilisation study was conducted on medicine claims data from a pharmacy benefit management company (PBM) in South Africa.

1.2 PROBLEM STATEMENT

Atomoxetine is a non-stimulant, selective noradrenergic reuptake inhibitor effective in the treatment of attention deficit/hyperactivity disorder (ADHD) in adults (Wilens *et al.*, 2008:146) while methylphenidate is effective in the treatment of children with ADHD (Tripp & Wickens., 2009:582).

Attention deficit hyperactivity disorder (ADHD) is a behavioural manifestation that includes features such as inattention, impulsivity and hyperactivity generally first apparent in childhood (Marcetti *et al.*, 2001:23; Markowitz *et al.*, 2003:394).

Karande (2005:59) and Spencer (2009:S4) categorised ADHD into three subtypes:

- ADHD primarily of the inattentive type (ADHD/I).
- ADHD primarily of the hyperactive-impulsive type (ADHD/HI).
- ADHD combined type (ADHD/C).

ADHD is a condition that can be found among children of all nations, with prevalence ranging from 3% to 19% in children (Leibson *et al.*, 2003:1240). The reported prevalence of ADHD in 2001 based on gender in the United States of America was 9.2% (varying from 5.8% to 13.6%) in male populations and 2.9% (varying from 1.9% to 4.5%) in female populations. Prevalence in school populations was 6.9% (varying from 5.5% to 8.5%) and in a community setting 10.3% (varying from 8.2% to 12.7%) (Marcetti *et al.*, 2001:1905).

Little is known about the global usage and cost of medication for ADHD (Scheffler *et al.*, 2007:450). Truter (2005:61) conducted a study on the prescribing patterns of

methylphenidate in the private health care sector and found that the majority of patients (75.6%) were males. The researcher also indicated that the average age for males was 10.8 (standard deviation of 3.7) years and for females 9.8 (standard deviation of 4.6) years. Although adult ADHD epidemiological studies have not been generally conducted, Perwien *et al.* (2004:122) indicated adult ADHD has been occurring in approximately 4% of adults in the United States. A study conducted by Kessler *et al.* (2006:720) estimated a prevalence of 4.4% for adult ADHD which correlated with Perwien's estimation. A study by Secnik *et al.* (2005:96) on the prevalence of ADHD in various adult age groups in the south, north and north-east regions of the United States revealed that 43.95% of the individuals were between the age of 18 years to 25 years, 12.52% were between the age of 25 years to 35 years, 22.56% were between the age of 35 years to 45 years, 17.41% were between the age of 45 years to 55 years and 3.55% were between 55 years to 65 years.

It is important that guidelines for proper diagnoses of ADHD be followed, so that disorders with similar symptoms, such as bipolar disorder (refer to Chapter 2, Section 2.10.2), do not receive inappropriate stimulant treatment. In the United States about half of the children and adolescents that had been diagnosed with ADHD received stimulant medication (e.g. Ritalin[®] 10mg) or related agents (Scheffler *et al.*, 2007:450). Statistics show that individuals with ADHD are more likely (significantly so) to be diagnosed with bipolar disorder (4.48%) or with depression (17.10%) and other mental illnesses (Secnik *et al.*, 2005:97). There is a likelihood of an individual being diagnosed with either asthma (4.71%) or drug or alcohol abuse (5.11%) (Secnik *et al.*, 2005:97).

Products containing methylphenidate or modafinil (Provigil[®]) that are available on the South African market are also used for narcolepsy or excessive daytime sleepiness, which can be defined by the uncontrollable urge to sleep and intermittent manifestations of Rapid Eye Movement (REM) (Littner *et al.*, 2001:451). According to Littner *et al.* (2001:451) health care providers are cautious in the treatment of narcolepsy, due to the use of stimulant medication, which is the basic treatment of narcolepsy. This precaution is being taken to prevent possible abuse of the methylphenidate containing products.

According to Perwien *et al.* (2004:125), depression occurred frequently in ADHD individuals in nearly one third of children (31.6%) and two thirds of adults (63%). They also found anxiety in more than one third of adults (36.4%) and 10.3% of children with ADHD. This study further revealed that 53% had an anxiety disorder and 34% had alcohol abuse or dependence (Perwien *et al.*, 2004:125).

Bipolar disorder is characterised by periods of excitability (mania) alternating with periods of depression. The changes between depression and the mania phases can be sudden and

unexpected (ANON, 2007b). Symptoms of the mania stadium of bipolar disorder that may overlap with ADHD include: hyperactivity, increased energy, racing thoughts, little need for sleep and poor temper control (Ballas, 2006).

Although it is not possible to differentiate in the empirical study between the different diagnoses, the correlation of ADHD, bipolar disorder and depression is a significant part of the literature study, due to the possibility of misdiagnoses with ADHD and the other mental illnesses, or disorders mentioned.

A recent study (Silver, 2007) in New York identified the most common mistakes in diagnosing ADHD as being the following:

- Misdiagnosis – the condition is not ADHD.
- Relying on inconclusive evidence, e.g. not taking history.
- Failing to consider coexisting conditions, e.g. anxiety, learning disability and bipolar disorder.

Statistics have shown that there is no difference in socio-demographic and cost disparities in children taking short-acting and long-acting stimulants, which include gender, age and even ethnicity/race (Stevens *et al.*, 2005:32).

According to Cohen-Zion and Ancoli-Israel (2004:380) the first treatment studies examined the effectiveness of traditional immediate release (IR; short-acting) stimulants, that are absorbed within 30 minutes, peak after 1-3 hours and completely dissolve within 6 hours (e.g. methylphenidate (Ritalin®) and therefore would require children to take medication either twice or three times a day. According to Schwartz and Rushton (2004:676) “OROS” methylphenidate (Concerta®) is the first second-generation, long-acting stimulant medication to become FDA-approved for prescription use for ADHD in children older than 6 years. The uniquely coated layered tablet provides an immediate dose of methylphenidate within 1 hour, increasing and peaking over the next 4 to 5 hours, followed by slowly decreasing blood levels during the next 6 hours, for 12 hours of average effectiveness.

Atomoxetine is marketed as a non-stimulant alternative for the treatment of ADHD (Wilens *et al.*, 2008:146). According to Kashani and Ruha (2007:177) atomoxetine is rapidly absorbed from the gastrointestinal tract in therapeutic doses. It has a half-life of 5 hours, and reaches peak plasma levels within 2 hours after ingestion. This statement is supported by Caballero and Nahata (2003:3068).

The norepinephrine reuptake inhibitor atomoxetine, which is the only non-stimulant medication approved for the treatment of ADHD carries little risk of abuse (Spencer, (2009a:S1) and Spencer (2009b:S8)). According to Spencer (2009b:S10), clinical trials indicate that methylphenidate treatment for ADHD symptoms is effective. In comparison both methylphenidate and atomoxetine have the same physiological effects. However, atomoxetine may be described as a safe medicine as it does not induce the same subjective effects as methylphenidate such as insomnia and growth retardation (Gibbon, 2005:448). Atomoxetine can safely be prescribed to patients with a history of substance abuse (Paul, 2003:1).

1.3 RESEARCH QUESTIONS

The following research questions can be formulated based on the literature that has been reviewed:

- What does ADHD as a disease entail?
- What is the prevalence of ADHD on an international level and in South Africa?
- What are the available treatment options for addressing the problem of ADHD?
- What does drug utilisation entail?
- What do pharmacoeconomics entail?
- What is the prevalence of the usage of methylphenidate and atomoxetine containing products in the private health care sector of South Africa?
- Are there differences in the prescribing patterns of methylphenidate and atomoxetine containing products in different age and gender groups?
- Are there differences in the prescribed daily dosage (PDD) of general practitioners and specialists with regard to methylphenidate and atomoxetine containing products?
- What is the cost implication of these medications on medical schemes?
- What is the prevalence of possible drug-drug interactions between products containing methylphenidate or atomoxetine with other central nervous system (CNS) products?
- Which other CNS products are prescribed together with methylphenidate and atomoxetine containing products?

- Is there a potential cost saving generated by generic substitution of methylphenidate products?

1.4 RESEARCH OBJECTIVES

1.4.1 General research objective

The general research objective of the study was to investigate the prescribing patterns of methylphenidate and atomoxetine containing products in a section of the private health care sector of South Africa by making use of a medicine claims database.

1.4.2 Specific research objectives

The specific objectives from the literature and empirical study were to conceptualise the following:

1.4.2.1 Literature study

The specific research objectives of the literature included the following:

- To conceptualise ADHD as a disease from available literature.
- To determine from the literature the prevalence of ADHD on an international level as well as in South Africa.
- To determine from the literature the comorbid diseases with regard to ADHD.
- To establish from available literature the medicine treatment for ADHD.
- To determine from the literature possible drug-drug interactions between atomoxetine or methylphenidate containing products and other drugs.
- To investigate from the literature the cost associated with ADHD treatment.
- To establish from the literature the importance of disease management, drug utilisation review, pharmacoeconomics, evidence-based medicine, drug classification systems and prescribed minimum benefits (PMB).

1.4.2.2 Empirical study

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

- To determine the usage patterns and cost of drugs in general according to all medicine items and prescriptions in the total database for the study period 2005 to 2007.

- To analyse the prescribing patterns and cost of methylphenidate and atomoxetine containing products in a section of the private health care sector of South Africa.
- To determine the influence of age and gender on the prescribing patterns of all medicine items with special reference to methylphenidate and atomoxetine containing products in a section of the private health care sector
- To determine the total cost, medical scheme and patient cost contribution of all medication and methylphenidate and atomoxetine containing products specifically in a section of the private health sector of South Africa.
- To determine the prescribed daily dosages (PDD) of methylphenidate and atomoxetine containing products in patients of different age groups, gender, and prescribed by different types of prescribers (e.g. general practitioners, specialist etc.).
- To determine the potential cost savings that can be generated by practising generic prescribing/substitution with methylphenidate containing products.
- To investigate the prevalence of possible drug-drug interactions between methylphenidate or atomoxetine containing products and other CNS medication on prescriptions.
- To identify which other CNS medications were prescribed together with methylphenidate or atomoxetine containing products.

1.5 RESEARCH METHODOLOGY

A retrospective, quantitative drug utilisation study was conducted on medicine claims database of a pharmacy benefit management (PBM) company in South Africa. Data from 1 January 2005 to 31 December 2007 were sub-divided into three study years. The data were analysed by using the Statistical Analysis System® for Windows 9.1® (SAS institute Inc., 2002-2003). The study population included all prescriptions which contained methylphenidate and atomoxetine containing products. Ethical considerations were performed and the following number of permission was awarded: NWU-0046-08-S5.

1.6 CHAPTER DIVISION

The chapters of the study will be divided as follows:

Chapter 1 Introduction

- Chapter 2 Treatment of ADHD with methylphenidate and atomoxetine containing products.
- Chapter 3 Research methodology
- Chapter 4 Results and discussion
- Chapter 5 Conclusion & recommendations

1.7 CHAPTER SUMMARY

In this chapter the problem statement, research questions, research objectives that were divided into general and specific objectives, research methodology, the literature and empirical review, as well as the chapter division have been discussed.

The following chapter will entail the nature of ADHD and an overview of drug utilisation review and pharmacoeconomics and other related aspects.

2 CHAPTER 2

Treatment of ADHD with methylphenidate and atomoxetine containing products

In this chapter the focus is on the nature of attention deficit/hyperactivity disorder (ADHD). This includes the history of ADHD; treatment with methylphenidate and/or atomoxetine containing products which are associated with ADHD; different types of ADHD; misdiagnoses and co-existing disorders of ADHD in relation to other psychiatric or mental illnesses. ADHD is described in-depth in accordance with gender, age, ethnicity, the nature and the extent of ADHD.

2.1 DEFINITION OF ADHD

There are several views on the nature of ADHD highlighting essential aspects of the disease. ADHD can be described as

- a very misunderstood psychological condition (Hawkins, 2009);
- an ongoing, chronic condition (Van Cleave & Leslie, 2008:1);
- a neurobehavioural condition (Furman, 2005:994);
- and a biologically based disorder (Pavuluri *et al.*, 2006:936).

ADHD can be characterised by a combination of inattentiveness, distractibility, impulsivity, physical restlessness or hyperactive behaviour (Phillips & Mersch, 2007). The core symptoms of ADHD include over-emotionality or over-reactivity, academic underachievement, low self-esteem and interpersonal difficulties (Mercugliano, 1999:841).

According to Leibson and Long (2003:1239) this is one of the most common psychiatric disorders in children. Children with ADHD are characterised by a lack of attention and impulse control as well as by signs of restlessness, impulsivity and distractibility which can carry on into adolescents and even adulthood.

Karande (2005:59) and Spencer (2009b:S4) categorised ADHD into three subtypes:

- ADHD primarily of the inattentive type (ADHD/I).
- ADHD primarily of the hyperactive-impulsive type (ADHD/HI).

- ADHD combined type (ADHD/C).

2.2 POSSIBLE CAUSES OF ADHD

According to Attention Deficit and Hyperactivity Support Group of South Africa (ADHASA) (ADHASA, 2008), the exact cause of ADHD is unknown and the substantiated causes could be characterised as belonging to a neurological realm – where there is a biological imbalance of certain neurotransmitters (especially dopamine) which is characterised by the deficiency in Prostaglandin's E1, E3 (PE1, PE3) and through a genetics realm.

2.2.1 Neurological causes

Neurological causes of ADHD, involves abnormal levels of certain brain chemicals called neurotransmitters such as dopamine, nor-epinephrine and serotonin (Gleason *et al.*, 2008). These transmitters make it possible for nerve impulses to travel from one nerve cell to another and therefore play an essential role in the functioning of the brain. According to Swierzewski (2001), dopamine is involved in emotions, reactions, concentration and reasoning. According to Tripp and Wickens (2009:582) dopamine plays a central role in the learning mechanisms. Therefore, if the brain does not produce enough dopamine, it may lead to impulsive symptoms and a lack of self-control (Gleason *et al.*, 2008). Lower levels of released dopamine will lead to the reduction of available transporters due to the body's attempt to compensate. Therefore, if the number of transporter proteins rises, the body will reduce the amount of released dopamine which will eventually cause the decline in attention (ANON, 2006a).

A reduced production of nor-epinephrine by the brain can lead to the development of hyperactivity, which is consistent with ADHD symptoms (Gleason *et al.*, 2008). Van der Walt (2007) confirms that a nor-epinephrine imbalance is involved in some cases of ADHD which leads to hyperactivity in patients. Information published by Hunt (2006:1) verified that nor-epinephrine plays a role in some essential processes such as: (1) maintaining and increasing overall arousal, (2) contributing to affect regulation related to excitability and response to danger or opportunity, and (3) contributing to memory storage and retrieval, especially after affect-related or emotionally intense events. NE also assists in maintaining basal or tonic alertness. At quieter moments (e.g. reading a book), the effort required to remain on task is partially mediated by NE. Signs of aggression may appear when there is an over-production in serotonin (Gleason *et al.*, 2008).

2.2.2 Environmental causes

According to Swierzewski (2001) a correlation exists between environmental agents such as smoking and the use of alcohol during pregnancy which can contribute to the development of ADHD in children. If these environmental agents are induced during pregnancy, the intake can cause poor motor and muscular development as well as sensory impairment. Other problems that appear are problems related to learning, memory, attention; as well as problems with mental health and social interactions (Swierzewski., 2001). Gleason *et al.* (2008) and Juhn *et al.* (2007) support the statement that the use of alcohol and drugs (including nicotine) are risk factors during pregnancy for the development of ADHD in children.

Other risk factors that should be considered include environmental toxins such as lead (Gleason *et al.*, 2008) found in old buildings, where lead still exists in the plumbing systems and the remainders of old paint (ANON., 2009). This can cause irritability, poor concentration, and distractedness (Swierzewski., 2001).

2.2.3 Biological causes

According to Gleason *et al.* (2008) and Swierzewski (2001) a child who experiences brain trauma during pregnancy, delivery or immediately after birth may show signs of behaviour similar to that of ADHD. However, Zappitelli *et al.* (2001:542) stated that stressors such as pregnancy and delivery complications have been found to increase the risk of ADHD. Another risk factor that may present signs of ADHD is illnesses in or around the time of birth such as viral or bacterial infections, meningitis or seizures caused by high fevers (Gleason *et al.*, 2008). According to Swierzewski (2001) about 50% of children with paediatric autoimmune neuropsychiatry disorder infection related with streptococcal infections have ADHD.

2.2.4 Genetic causes

According to ADHASA (2008), ADHD is a genetic condition in 80% of cases and often runs in families. According to Bulut *et al.* (2007:437) several studies have suggested that genetics and other factors might have an effect on children with ADHD. In a case of identical twins, if one twin has ADHD there is a 100% chance that the other twin will also show symptoms of ADHD (Van der Walt, 2007:1). To fully understand the genetic inheritance a closer investigation on the molecular genetics has to be done. Polymorphisms¹ of the dopamine 4

¹ Polymorphisms: In Greek *Polus* means *many* while *morphe* means *form*, therefore multiple forms (Brink. 2001)

receptor (DRD4) affect receptor binding, allele² containing seven tandem repeats in exon³ 3 (DRD4*7R) that has been associated with ADHD (Castellanos *et al.*, 1998:431).

A study on the DRD4*7R gene reported by Faraone *et al.* (2001:1052) shows that this gene can be associated with ADHD. The DRD4*7R gene can also be associated with novelty seeking behaviours e.g. Tourette syndrome (TS); pathological gambling and substance abuse (Comings *et al.*, 1999). Although ADHD is a highly hereditary psychiatric condition (Holmes *et al.*, 2000), much more research is needed to fully clarify the genetic architecture of this disorder (Anon, 2000).

2.3 HISTORY

According to Londrie (2006), ADHD has been around for decades but was not known as Attention Deficit Disorder (ADD). Previously, the disorder had undertaken various names over the years such as “*defect of moral control*”, “*post encephalitic behaviour disorder*” and “*minimal brain dysfunction*”. In 1980 the disorder was named ADD which later changed in 1987 to ADHD.

2.3.1 Identifying ADHD

According to Londrie (2006) in 1902, Sir George Frederic Still, a British paediatrician, diagnosed the impulsive disorder named “Defect of moral control”, which was supported by (MacMartin, 2000). Sir George reported his observations in a series of lectures to the Royal College of Physicians in England. Prior to Sir George’s work, the only “treatment” for the disorder was physical punishment (Gamache, 2008).

Follow-up documentation in 1922 presented similar symptoms to the “*Defect of moral control*”. The ADHD associated symptoms were named “*Post-Encephalitic Behaviour Disorder*” due to the encephalitis epidemic in 1917-1918 (Londrie, 2006).

During this time doctors noted that many children showed the symptoms that Sir George Still had previously described (de Arams, 2001). The following event was documented in 1937, where Dr. Charles Bradley introduced stimulants in children who were hyperactive and the stimulants had a reducing effect (Londrie, 2006). In the 1940s, even as far back as 1937, ADHD behaviour was defined as “minimal brain damage” due to the fact that the doctors

² Allele: In which is an alternative form of a gene (one member of a pair) that is located at a specific position on a specific chromosome (Bailey, 2008)

³ Exon: e.g. in bacteria the coding sequences are continuous, but in higher organisms these coding sequences (exons) are interrupted by intervening sequences that are non-coding (interons) at various positions (KUMAR, 2002)

realised that the children were too intelligent according to tests done, to be classified as having brain damage (de Armas, 2001).

A disorder called "hyperkinetic reaction of children", resembling the ADHD disorder, appeared in the Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (DSM-III-R) in 1987 (APA, 1987). It is now defined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) as attention deficit hyperactivity disorder (ADHD) (Gamache, 2008). The American Psychiatric Association noted that the disorder was a medical diagnosis, and not purely a psychological diagnosis as once believed (Londrie, 2006).

Thus it can be observed that regardless of the terms by which ADHD had been named, the fact remains that the term ADHD evolved over time to this currently known condition.

2.4 NEUROLOGICAL RELATIONSHIP WITH ADHD.

2.4.1 Brain sizes

There is consistent evidence that the brain volumes in all regions throughout childhood and adolescent years in ADHD individuals are significantly smaller in the test group than the healthy, controlled individuals (Castellanos *et al.*, 2002:1740; Durston *et al.*, 2001:1012; Durston *et al.*, 2004:332). When brain magnetic resonance imaging scans from 30 boys with ADHD were compared and matched to their unaffected, healthy control siblings (n=30), the boys in the ADHD group in comparison to their unaffected siblings displayed a reduction in right prefrontal grey matter and left occipital grey and white matter by up to 9.1% (Durston *et al.*, 2004:332). The right cerebella volume reduced by 4.9% in individuals with ADHD but not in unaffected siblings. A further 4.0% reduction in intracranial volume was found in individuals with ADHD, while this trend was not observed in unaffected siblings (Durston *et al.*, 2004:332).

Individuals with ADHD showed 3% to 4% smaller brain volumes in all of the following brain regions namely the frontal lobes, the temporal grey matter, the caudate nucleus and cerebellum (Castellanos *et al.*, 2002:1740). Results of anatomical imaging studies indicated subtle reductions in the total brain and cerebella volumes in children with ADHD (Sowell *et al.*, 2003:1699; Castellanos *et al.*, 2002:1740). According to Sowell *et al.* (2003:1704) the extent of brain surface is reduced in most regions up to 4mm bilaterally in the lateral aspects of the anterior temporal cortices and in the inferior portion of the dorsolateral prefrontal cortices and even brain size reduction in the right parietal cortex.

Although white matter increases with age (Durstun *et al.*, 2001:1012), “it is often described that children with ADHD are less mature than their peers and many relate to the delays in white matter maturation” explained Castellanos *et al.* (2002:1741).

Volumetric reductions in cortical grey and white matter in individuals with ADHD as well as their unaffected siblings; showed a relation to an increased risk to families for the disorder (Durstun *et al.*, 2004:332; Filipek *et al.*, 1997:589; Kates *et al.*, 2002:63). Some studies have shown that the caudate nucleus located in the Basal ganglia, indicated a decrease in volume in children with ADHD (Castellanos *et al.*, 2002:1740; Hill *et al.*, 2003:496), and some have not (Bussing *et al.*, 2002:216; Pineda *et al.*, 2002:97). It is still unclear whether the caudate nucleus is asymmetric, but if it was found, it often indicated greater left than right volumes (Pineda *et al.*, 2002:97; Filipek *et al.*, 1997:589).

In contrast to these studies; Sowell *et al.* (2003:1699) used high-resolution MRI and surface based; computational image analytic techniques to map brain sizes and grey matter abnormalities at the cortical surface in a group of 27 children and adolescents with ADHD and 46 controls, where groups were matched by age and sex. Findings of this study indicated grey matter density to be increased by 15 to 30% in the posterior temporal lobes and inferior parietal lobes in ADHD individuals (Sowell *et al.*, 2003:1705). Like white matter, ADHD group demonstrated smaller, total Corpus Collosum area than in the control group (Hill *et al.*, 2003:496). With these high resolutions, three dimensional maps of ADHD brains, an indication of anatomical differences within areas of the brain thought to control attention and inhibitory control systems, compared to control groups (Rosack, 2004:26).

There is an apparent higher prevalence of ADHD in boys – two to three times as many boys as girls have ADHD (Marcetti *et al.*, 2001:1905. A recent anatomical MRI study indicated that male and female individuals with ADHD were comparable on all measures (Castellanos *et al.*, 2002:1740).

The above sections of the brain are illustrated in figures 1 and 2 below.

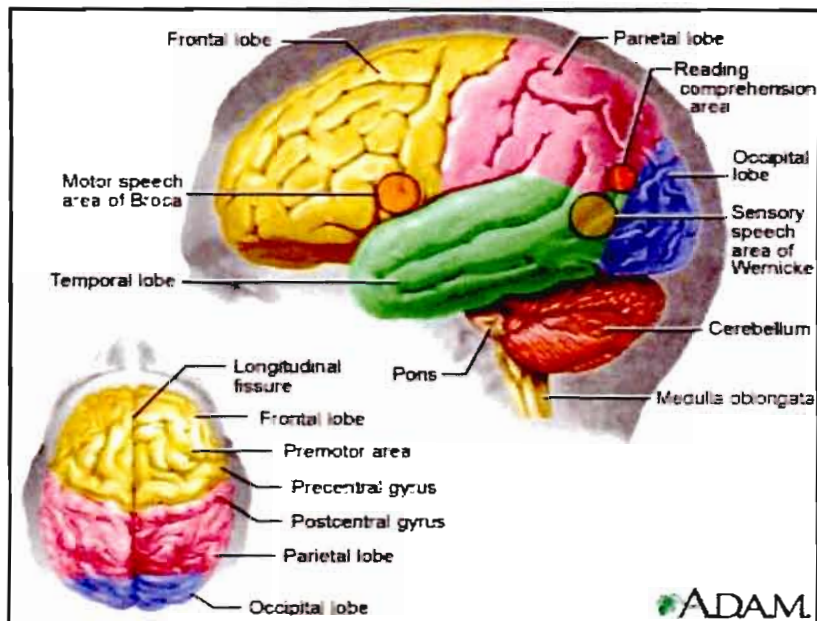


Figure 2.1: Physiology of the human brain (Adopted from A.D.A.M accredited by U.R.A.C also known as the American Accreditation HealthCare Commission (2008).

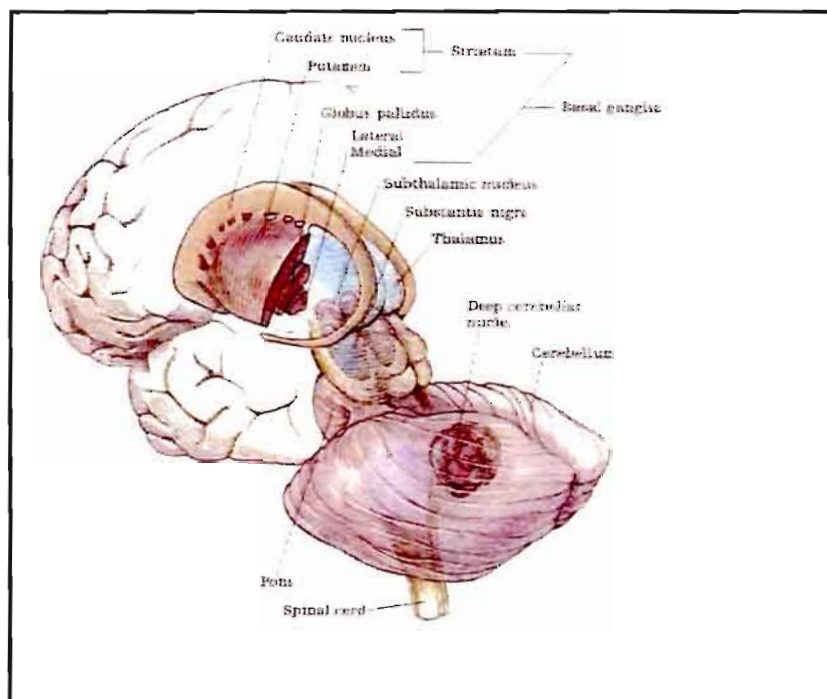


Figure 2.2: Physiology of the basal ganglia (Adopted from St. Clair et al., 2009)

A study conducted by Hesslinger *et al.* (2002:319), found that eight male patients who never had received medication for ADHD had a significant smaller left orbital-frontal cortex than the

17 patients in the healthy control group. In a sample of 12 boys with ADHD and 12 matched healthy controls, a decreased size of the frontal lobe in ADHD children indicated to account for 48 % of total cerebral volume reduction (Mostofsky *et al.*, 2002:785). The prefrontal cortex (PFC) has shown to be smaller in ADHD children than in the control group (Durstun *et al.*, 2004;332; Kates *et al.*, 2002:63). Furthermore the results of a comprehensive report, suggest that stimulant drugs like methylphenidate do not contribute to group differences in brain morphology in patients with ADHD (Sowell *et al.*, 2003:1705).

2.5 DIAGNOSIS

According to the APA (2000) a practitioner needs to carry out a detailed interview regarding the DSM-IV symptoms (Table 2.1). ADHD rating scales can be found at <http://www.neurotransmitter.net/adhdscales.html>

Table 2.1: Symptoms and signs of attention deficit/hyperactivity disorder (American Psychiatric Association, 2000):

Presented requirements:

- Symptoms present for at least six months to an extent that is disruptive and inappropriate for developmental level.
- Some symptoms that caused impairment were present before the age of seven.
- Some impairment from the symptoms is present in two or more settings (e.g. at school – or at work – and at home).
- Existence of clear evidence of significant impairment in social, academic, or occupational functioning.

Table 2.1 Inattention: (requires 6 or more requirements)

- Fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities.
- Often has trouble sustaining attention on tasks or play activities.
- Often fails to listen when spoken to directly.
- Often does not follow instructions and fails to finish schoolwork, chores, or duties in the workplace (not because of oppositional behaviour or failure to understand instructions).
- Often has difficulty in organising activities.
- Often avoids, dislikes, or does not want to engage in tasks or activities that require prolonged mental effort (such as schoolwork or homework).
- Often loses things required for tasks and activities (e.g. toys, school assignments, pencils, books, or tools).
- Often distracted easily.
- Often forgetful in daily activities.

B. Hyperactivity and Impulsivity

- Often fidgets with hands or feet or squirms in seat.
- Often leaves seat in classroom when it is expected to remain seated.
- Often runs about or climbs when and where it is not appropriate (adolescents or adults may feel very restless).
- Often has difficulty playing or enjoying leisure activities quietly.
- Is often “on the go” or often acts as if “driven by a motor”.
- Often talks excessively.
- Often blurts out answers before questions have been completed.
- Often has difficulty waiting his/her turn.
- Often interrupts or intrudes on others (e.g. butts into conversation or games).

Extracted from American Psychiatric Association (APA): Diagnostic and Statistical Manual of Mental Disorders. 4th ed, text revision. Washington, DC: American Psychiatric Association, 2000.

According to the APA (2000) three types of ADHD comes to light, based on the criteria.

- ADHD, Combined type: if both criteria 1A and 1B have been met for the past six months (DSM-IV: 314.01).
- ADHD, Predominantly Inattentive Type: if criterion 1A have been met but criterion 1B has not been met for the past six months (DSM-IV: 314.00).
- ADHD, Predominantly Hyperactive-Impulsive Type: if criterion 1B has been met but criterion 1A has not been met for the past six months (DSM-IV: 314.01).

ADHD is frequently co-morbid with other psychological impairments (e.g. depression, mania, anxiety, tic disorders, substance abuse, and learning disability) (Pliszka, 2007).

2.5.1 Several problems that may be experienced in diagnosing ADHD

A recent study in New York released the following published data containing information on the three most common mistakes in diagnosing ADHD.

The **first error** is the undiagnosed prescribing of medication. This will surely state that the paediatrician misdiagnosed the child's case for ADHD rather than a simple learning disability. Taken the description of the teacher and the parents in account, a diagnosis was made and treated without checking the diagnostic criteria for ADHD (Silver, 2007:1).

The **second error** is to rely on inconclusive evidence. In this case the psychologist made his diagnosis based upon raking scales of an ADHD test as well as the results of a computerised test. He did not include a detailed history of the child (Silver, 2007:1):

The **third error** is failing to consider coexisting conditions. A forty-year-old woman that had a history of hyperactivity, inattention and impulsivity was studied. Her situation had an early onset since elementary school. When someone has ADHD, there is a possibility of about 50% that the person might have a learning disability, anxiety, depression and Obsessive Compulsive Disorder (OCD). Through further analysis and including detailed information of her history, a diagnosis was made that she had ADHD, but she also had dyslexia and suffered from anxiety and OCD (Silver, 2007:2).

2.6 DIAGNOSES AND MISDIAGNOSES

It is well known that ADHD is commonly associated with one or more psychiatric disorders. These co-morbidities include the following:

- Oppositional defiant disorder (ODD) (Adewuya & Famuyiwa, 2007:10).
- Conduct disorder (CD) (Adewuya & Famuyiwa, 2007:10).
- Bipolar Disorder (Gillberg *et al.*, 2004).
- Tic disorders including Tourette syndrome (Gillberg *et al.*, 2004).
- Obsessive compulsive disorder (OCD) (Den Braber *et al.*, 2008).
- Depression and anxiety disorder (Adewuya & Famuyiwa, 2007:10).
- Autistic features (Gillberg *et al.*, 2004:80).
- Learning disabilities (Adi-Japha *et al.*, 2007).
- Developmental co-ordination disorder (DCD) (Querne *et al.*, 2008).

Although these are co-morbidities, the above stated disorders need to be considered in any child diagnosed with ADHD. (McGough *et al.*, 2005:1621; Gillberg *et al.*, 2004: 81;

Banaschewski *et al.*, 2007:5). ODD and CD are the most common of co-morbid disorders (Kadesjo & Gillberg, 2001:487) and according to Gillberg *et al.* (2004:81), 16% to 26% of children meeting the criteria for ADHD also meet the criteria for a “depressive syndrome”, 12% meet the criteria for “*emotional disorder*” (corresponding to anxiety disorder) and bipolar disorder has been found in a number of ADHD children (Kent & Craddock, 2003), learning disabilities are also included in the co morbidities of ADHD, including central auditory processing disorder and reading disorder (Gomez & Condon, 1999; Luca *et al.*, 2007). An overall prevalence of ADHD and co-existing disorders, is that 87% cases meeting the diagnostic criteria for ADHD also meet the criteria for at least one more DSM-III-R diagnosis and 67 % of cases meet the criteria for at least two DSM-III-R diagnoses (Kadesjo & Gillberg, 2001:490)

According to Gillberg *et al.* (2004:88), all individuals who receive treatment for ADHD, need to be fully assessed for the occurrence of co-existing disorders, which will be discussed below.

2.6.1 Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD)

ODD and CD are rated as the most common co-morbid disorders of ADHD, where approximately 50% to 60% of ADHD children meet the criteria for ODD (Gillberg *et al.*, 2004:81). Children with ADHD without the presence of early signs of ODD will be co morbid with anxiety and learning problems rather than the occurrence of CD in adolescents (Gillberg *et al.*, 2004:81).

According to Loeber *et al.* (2000:1469), it is believed that a proportion of ODD children, in the future develop CD, and a proportion of those with CD in the future meet the criteria for Antisocial Personality Disorder (ASP).

Oppositional Defiant Disorder is characterised by an improper pattern of negative, disobedient, defiant, and hostile behaviour toward authority figures that continues for at least six months, which will lead to impairment in social, educational, or occupational (work-related) functioning. DSM-IV classifies ODD as a disruptive behaviour disorder (McKinney & Renk, 2006:39).

In conjunction with the above, children with ODD may refuse to do things they dislike and even the things that they do like and deliberately do things to annoy those around them, especially adults. With this said, it seems possible that an individual may exhibit hostile behaviour towards authority figures. What can be seen from the above stated symptoms, it

seems that an individual is touchy, spiteful, argues and misbehaves, only to mention a few (McKinney & Renk, 2006:39).

Conduct disorder is characterised by a recurring and constant pattern of behaviour in which basic rights or rules are violated (rule-breaking) e.g. aggressive toward people and animals, destruction of property, deceitfulness or theft and serious violations of rules. (Scholte & Van der Ploeg, 2008:283; Gelhorn *et al.*, 2007:529).

According to Scholte and Van der Ploeg (2008:283), symptoms like bullying, physical fighting, use of a weapon, lighting fires, cruelty, destruction of property, harmful conduct to others, stealing, breaking an entry, telling lies, cheating to obtain goods, shoplifting, staying out late, running away and playing truant were included. Aggressive behaviour is predominantly measured by the first seven items, as violations of social norms (denoted as antisocial behaviour) is predominantly measured by the remaining items.

In conjunction with the above, the following can be stated. CD is a disorder that requires attention due to the fact that it is a worrisome disorder. Individuals show symptoms of tantrums, destructiveness, lying, stealing, truanting, fighting and even cruelty towards others and animals (McArdle *et al.*, 2000:92).

2.6.2 Bipolar Disorder

Bipolar disorder should be considered when there is a family history of the disorder. It should be considered when hyperactivity is correlated with mood swings, irritability, grandiosity, crying, racing thoughts and hyper sexuality. Due to the fact it has not yet been accepted that bipolar disorder can have an onset in the first years of life, bipolar is the most likely misdiagnosed disorder in ADHD (Gillberg *et al.*, 2004:81).

In conjunction with the above it is obvious from the leading symptoms of bipolar disorder why ADHD can be misdiagnosed with bipolar disorder. If we highlight a few bipolar disorder symptoms, it is noticeable that there is correlating symptoms with ADHD (e.g. irritability and racing thoughts).

2.6.3 Tic disorders including Tourette syndrome

Symptoms of tic disorders make it possible to divide into two categories – motor and vocal tics (Gillberg *et al.*, 2004:82). Tourette syndrome shows associated symptoms of multiple motor tics which include one or more vocal tics. Approximately half of the cases reported chronic tics or Tourette syndrome meeting the criteria for ADHD which ranges from 25% to 85% (Gillberg *et al.*, 2004:82). Furthermore children with Tourette syndrome and ADHD

indicate lower social adaptation than the children with pure Tourette syndrome. Therefore early ADHD is a risk factor for other related psychiatric problems (e.g. tic disorder). (Gillberg *et al.*, 2004:82)

Tourette syndrome is a neuropsychiatry disorder which is characterised by motor and vocal tics (Ackermans *et al.*, 2008:339). Motor tics may involve individuals or small groups of muscle with isolated contractions (simple tics) such as eye blinking, throat clearing, while complex tics include head shaking, scratching, throwing, touching, and uttering phrases, or uttering obscene words, which is one of the most distressing and predominant symptoms that is recognised in only 10% of patients (Ackermans *et al.*, 2008:339). These symptoms are the involuntary movements of the body and face (Ivarsson & Melin, 2008:971).

2.6.4 Obsessive-compulsive disorder

Obsessive compulsive disorder is characterised by recurring, persistent, and invasive anxiety-provoking thought or images (obsessions) and successive repetitive behaviours (compulsions) performed to reduce anxiety and/or distress caused by the obsessions (Den Braber *et al.*, 2008:91). Known obsessions include fear of contamination, pathological doubt, need for symmetry as well as somatic, sexual and aggressive obsessions. While the compulsions aspect includes checking, washing, counting, symmetry/precision and hoarding behaviour (Den Braber *et al.*, 2008:91)

2.6.5 Depression and anxiety disorder

Anxiety is a distressing, unpleasant emotional state of nervousness and uneasiness. It is often accompanied by physical changes and behaviours similar to those caused by fear.

In conjunction with the above, the following statements can be made. Symptoms associated with anxiety include palpitations, sweating, trembling or shaking, nausea, light headedness, motoric restlessness, muscle tension (Wilhelm & Roth, 2001:107).

Depression is a common mental disorder that presents with a depressed mood, loss of interest and pleasure, feelings of guilt and low self-worth, disturbed sleep and appetite, low energy and poor concentration (Hamer *et al.*, 2007:20). Furthermore according to Bosch *et al.* (2009:40) depression can be associated with inflexible responses to social demands, a reduction in social engagement, a constricted range of self-reported emotions and a diminished display of facial expressions.

The treatment of depression and anxiety in ADHD usually does not respond to the use of stimulants. This is probably due to the fact that the depressive features become more

predominant and perhaps because the child becomes more focused on his/her own feelings and needs. This may lead to a feeling of sadness and even loss (Gillberg *et al.*, 2004:81). Therefore it is important that anxiety and depressive disorders be recognised at onset to overcome this problem and to treat it effectively.

2.6.6 Autistic features

According to Gillberg *et al.* (2004:84), autism is a rare disorder in ADHD. Nevertheless, between 65% and 80% of all clinic children with ADHD match the criteria for DSM-IV autistic disorder. Furthermore social deficits, peer relationships and empathy problems are common in ADHD individuals. This been said, problems exist in determining whether one is dealing with a combined subtype of ADHD or autistic behaviour (or both). Autism should be well thought-out in a hyperactive child when the individual shows little or no interest in other individuals, restricted or strict selection of behaviours, dominated by motor stereotypes or constricted interest patterns (Gillberg *et al.*, 2004:84).

2.6.7 Learning disabilities

It is known that children with ADHD illustrate more spelling errors than their peers, but indicate a unique pattern in letter substitutions, transpositions and omissions (Adi-Japha *et al.*, 2007:700). Disorders of written expression is a combination of difficulties in an individual's capability to create written text that is manifested by unreadable handwriting, letter shape distortion, diffluent writing, spelling errors and difficulty in written expression of ideas that cannot be recognised as disabilities in reading or oral expression (Adi-Japha *et al.*, 2007:700). According to Gillberg *et al.* (2004:85), an impairment exists in writing grammatically correct sentences and organised paragraphs, and this is often associated with dysgraphia (extremes of poor handwriting), which refers to illegible handwriting and spelling errors, as handwriting is one of the basic skills, which is impaired in children with ADHD where spelling errors are also common (Adi-Japha *et al.*, 2007:700).

In conjunction with the above, visual perceptual problems and auditory perceptual problems are dominant in learning disabilities. Visual perceptual problems can be interpreted as the recognition of shapes (e.g. letters) and the ability to arrange those shapes (letters or words) on the page which is necessary to learning to read (Novartis, 2008). An example is the following sentence:

“Skills that is required for reading is taken for granted”

In the eyes of a visual perceptual impaired individual, it might look like this:

“5kii5 ahtt 5i repkuird ofr rcobing 5i tokcin ofr grontcb”

Visual perception impaired individuals typically mix up letters and numbers with the same shape: e.g. **p** and **q**; **b** and **d**; **s** and **5** only to name a few (Novartis, 2008).

Auditory perceptual problems can be interpreted as a child that is unable to interpret or remember that he or she has heard. These children are unable to follow complex instructions and will probably complete the first step only. It stands to reason that this could be a problem for them due to the fact that in the classroom a number of facts or instructions may be given at the same time. (Novartis, 2008)

Motor kinematics production was tested for writing efficiency and consistency, writing practice and graphic accuracy (Adi-Japha *et al.*, 2007:700). In conjunction with this statement, a probability could arise that a child could find it difficult to colour in, draw and write. Due to this a child would be reluctant to take part in these activities and could be seen as untidy and careless (Novartis, 2008).

In conjunction with all the above statements, it can be clearly seen why it is possible for an individual to become angry, upset, irritated and reluctant to read or write and draw when a co-morbid disorder is present in ADHD patients.

2.6.8 Developmental co-ordination disorder (DCD)

Developmental co-ordination disorder (DCD) include a diverse spectrum of difficulties that affect a child's ability to learn and carry out co-ordinated motor skills, especially when these cannot be recognised to be a mental retardation or general medical condition (e.g. muscular dystrophy). Furthermore, the motor difficulties must have a negative impact on academic achievement or daily life activities (Querne *et al.*, 2008:89)

2.6.9 Possible co-existing disorders

The following disorders need to be considered at all times as likely co-existing disorders in individuals diagnosed with ADHD, DCD, ODD, depression and anxiety disorders. The female gender has a higher tendency for co-existing disorders due to the fact that fewer “external” ADHD symptoms are present. In ADHD individuals, where tic syndromes and bipolar disorder are considered, possible learning problems and autistic symptoms need to be assessed, (Gillberg *et al.*, 2004:81). Thus it is important for all individuals who are treated for ADHD to be assessed for the presence of co-existing disorders (Gillberg *et al.*, 2004:81).

According to Kessler *et al.* (2005:1442) co-morbid DSM-IV disorders are associated with ADHD with symptoms of mood disorders (i.e. major depressive disorder), anxiety disorders

(i.e. generalised anxiety disorder), impulse-control disorders (i.e. conduct disorder) and substance use disorder (i.e. drug abuse or dependence).

The following figure shows the different co-morbid diseases which can be associated with attention deficit hyperactivity disorder.

Co-morbidities of ADHD

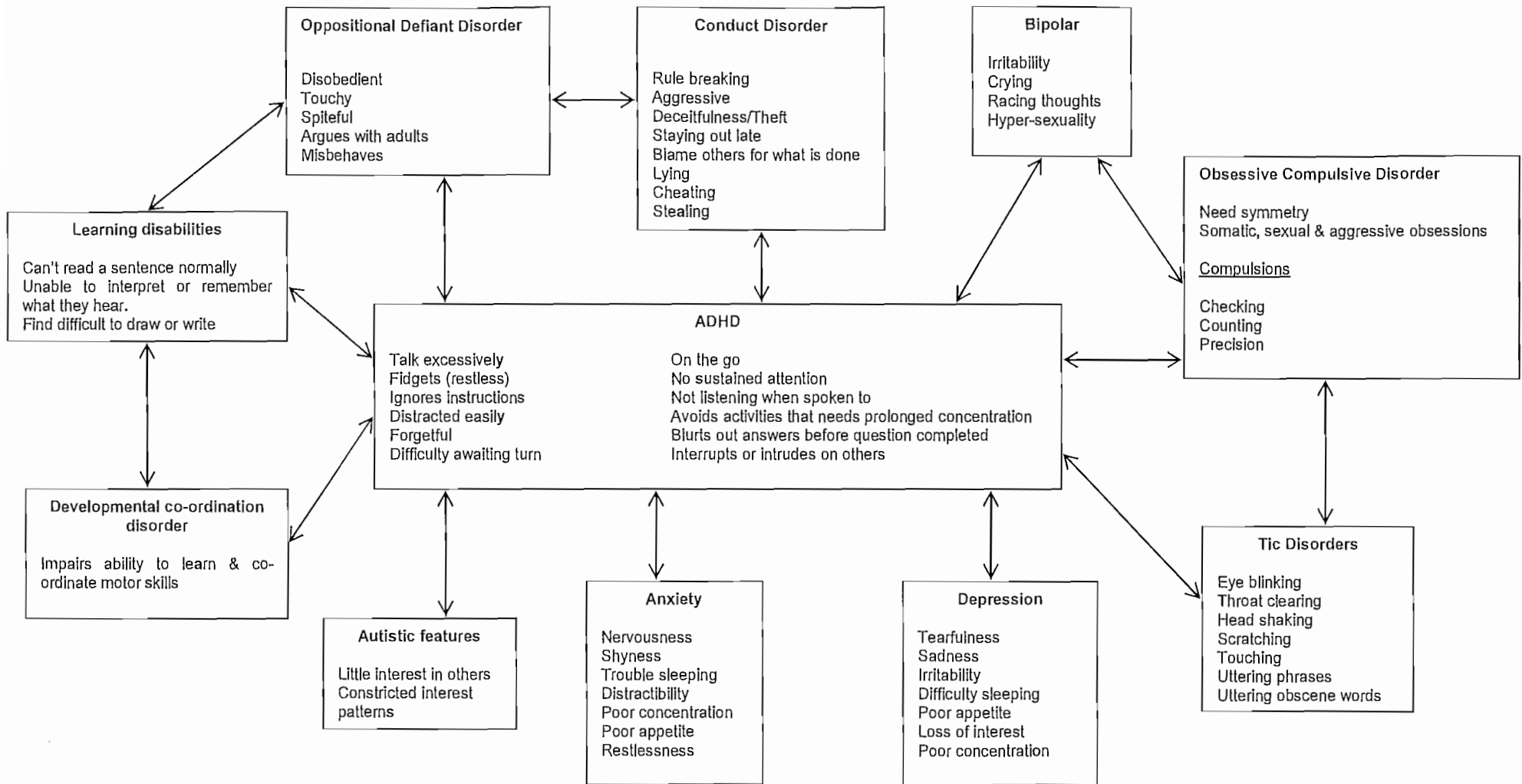


Figure 2.3: Co-morbid disorders associated with ADHD

2.7 DRUG TREATMENT

According to Volkow and Swanson (2003:1909), methylphenidate, a psychostimulant (Brandon & Steiner, 2003:1584), is the most commonly prescribed drug for attention deficit/hyperactivity disorder (ADHD). Furthermore, atomoxetine, which is a selective noradrenaline reuptake inhibitor, shows efficacy in the treatment of ADHD. It is a licensed nonstimulant treatment for ADHD (Chamberlain *et al.*, 2007:977).

Methylphenidate has a short half-life and thus produces a dosage problem during school and after-school hours. Therefore an extended-release methylphenidate (MPH) preparation has been designed to last at least 12 hours which is equivalent to a 3-times-daily dosing (Pelham *et al.*, 2001:1). Table 2.11 provides the information for switching patients to the recommended dose Ritalin LA® from the standard formulation or SR (Slow-Release) formulation (Theodora, 2005).

Table 2.2 Recommended dose of Ritalin LA from standard formulation or SR formulation

Previous methylphenidate dose	Recommended Ritalin LA dose
5mg b.i.d	10mg once daily
10mg b.i.d or 20mg SR	20mg once daily
15mg b.i.d	30mg once daily
20mg b.i.d or 40mg SR	40mg once daily
30mg b.i.d or 60mg SR	60mg once daily

Table 2.3 is supported by the research figures for the extended release formulations.

b.i.d = Twice daily.

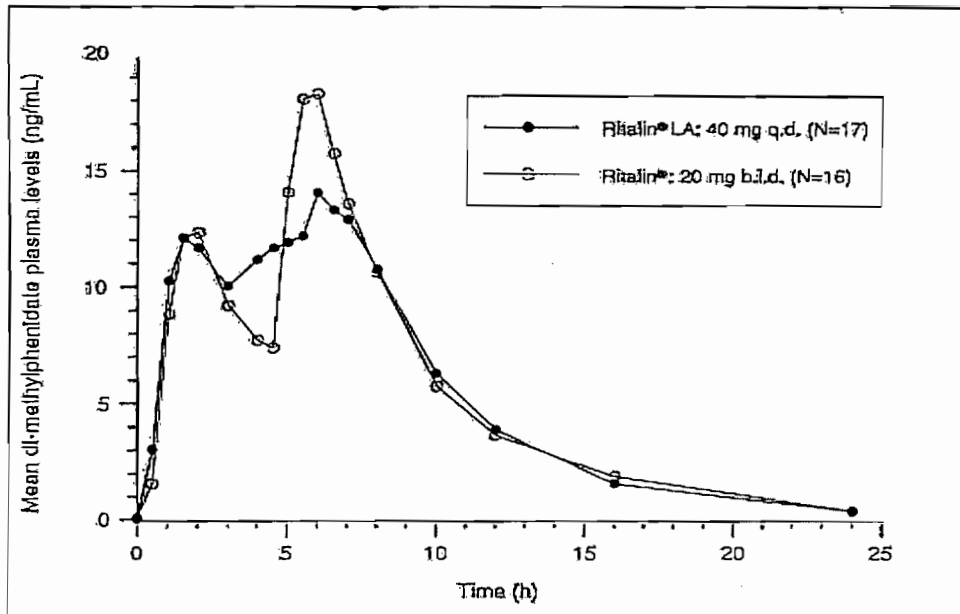


Figure 2.4: Extracted from http://www.theodora.com/drugs/ritalin_la_capsules_novartis.html

Figure 2.4 illustrates the mean plasma of the methylphenidate concentration after a single dose of Ritalin LA® 40mg once daily and Ritalin® 20mg had been given in two doses four hours apart.

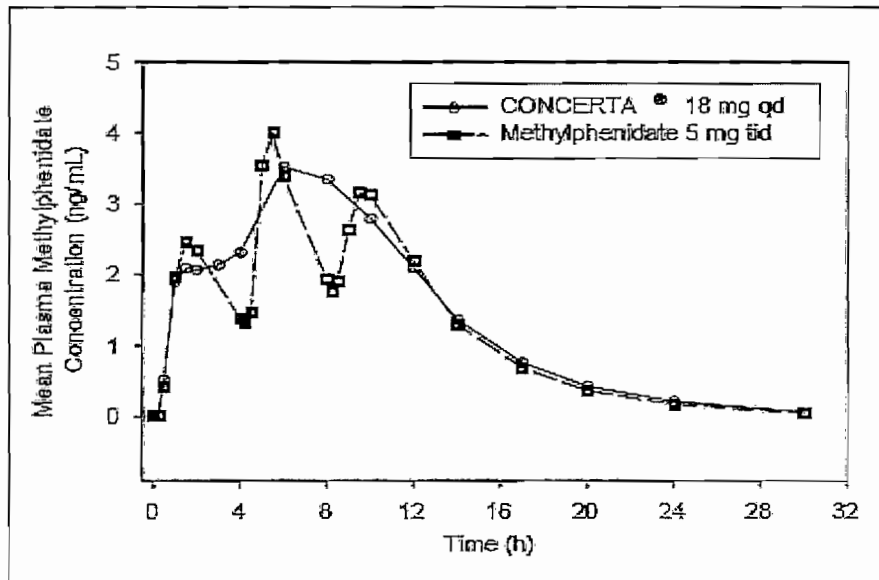


Figure 2.5: Extracted from <http://www.rxlist.com/concerta-drug.htm>

Figure 2.5 illustrates the mean plasma of the methylphenidate concentration of 18mg Concerta® to be given once daily (qd) to the immediate release methylphenidate 5mg to be provided three times per day (tid).

2.7.1 Possible drug-drug interactions

Methylphenidate may inhibit the metabolism of barbiturates, primidone, phenytoin, tricyclic antidepressants and warfarin and therefore increase their effects. Monoamine oxidase inhibitors (e.g. tranylcypromine) may potentiate the clinical effects of methylphenidate by increasing the amount of catecholamine in the sympathetic neurons. Other suppressing agents should also be used with caution (Gibbon, 2005:447). Plasma levels of drugs metabolised by CYP3A4 e.g. midazolam, will increase if co-administered with atomoxetine (Gibbon, 2005:448). Monoamine oxidase inhibitors should not be taken concurrently or within a two week washout period (Gibbon, 2005:448).

According to Gibbon (2005), drug interactions of atomoxetine with other medication do present. Atomoxetine with beta2 agonists (e.g. salbutamol), presser agents and drugs that affect noradrenalin should be used with caution as action on the cardiovascular system can be potentiated. The atomoxetine levels will be affected, necessitating slow upward titration of dose with the usage of drugs that induce or inhibit CYP2D6.

According to Tatro (2009) there are a few factors that are brought into account in the significance of each drug (precipitant) interaction with methylphenidate and atomoxetine containing products. The severity of the effect ranged from 1 to 5 with 1 being a major effect and 5 being a minor effect. Effects with methylphenidate containing products are illustrated in table 2.3. Effects with atomoxetine containing products are illustrated in table 2.4.

Table 2.3: Significance of drug-drug interactions with methylphenidate containing products

Methylphenidate containing product	
Significance	Precipitant
1	Phenelzine
	Tranylcypromine
4	Carbamazepine
	Cyclosporine
	Phenytoin
	*Guanethidine
5	Amitriptyline
	Clomipramine
	Imipramine
	*Nortriptyline
	Trimipramine
	*Amoxapine
	*Desipramine
	*Dicumarol
	*Doxepin
	*Protriptyline
	*Isocarboxazid

***These products are not included in the South African Medicine Formulary.**

Table 2.4: Significance of drug interactions with atomoxetine containing products

Atomoxetine containing product	
Significance	Precipitant
1	*Isocarboxazid
	Phenelzine
	Tranylcypromine
4	Fluoxetine
	Paroxetine

***These products are not included in the South African Medicine Formulary.**

2.7.1.1 Interaction with: Carbamazepine

Carbamazepine (Degranol®) is a first-line agent for the management of generalised tonic-clonic epilepsy (Gibbon, 2008). The significance of the interaction is not rated high but still has to be considered (Tatro, 2009). A possibility is that carbamazepine will reduce the effect of the methylphenidate blood concentrations which will lead to a *decrease* in pharmacological effects which must be stated. The onset of the effect is *delayed* as the

severity is *moderate* (Tatro, 2009). Monitoring the clinical response when starting, stopping or changing patient on carbamazepine is needed (Tatro, 2009).

2.7.1.2 Interaction with: Phenytoin

Phenytoin (Epanutin®) is an agent used for all forms of epilepsy except absence (petit mal) and myoclonic seizures (Gibbon, 2008). There is a possibility of phenytoin level *increase* which will result in an increase in the pharmacologic and toxic effects of phenytoin (Tatro, 2009). The onset of the effect is *delayed* as the severity is *moderate*. Management is to monitor serum phenytoin levels for toxicity or decrease in activity if methylphenidate is discontinued from the treatment regimen (Tatro, 2009).

2.7.1.3 Interaction with: Cyclosporine

Cyclosporine (Sandimmun Neoral®) is an agent used in the prevention and treatment of graft rejection following organ and tissue transplantation (Gibbon, 2008). Cyclosporine has an interaction due to the fact that the Cyclosporine concentrations may be elevated, which will *increase* the risk of toxicity. The onset of the effect is *delayed* as the severity is *major* (Tatro, 2009). Management is to monitor cyclosporine blood levels and serum creatinine to observe toxicity, where an adjustment in the cyclosporine dose may be needed (Tatro, 2009).

2.7.1.4 Interaction with antidepressants

2.7.1.4.1 Monoamine Oxidase (MAO) inhibitors

Tranylcypromine (e.g. Parnate®), an antidepressant, is a Monoamine Oxidase (MAO) inhibitor (Gibbon, 2008). In combination there is a suspected increased risk of serious or fatal reactions, including hyperthermia, automatic instability with possible rapid fluctuations of vital signs, and mental status changes (Tatro, 2009). Management states that co-administration is contraindicated. Dexamethylphenidate is contraindicated due to suspected hypertensive crisis (Tatro, 2009). The onset may be *delayed* as the severity of the effect is *major*. The monitoring of blood pressure during combination of MAO inhibitor and methylphenidate is needed. After discontinuing an MAO inhibitor, allow at least 2 weeks before administering atomoxetine (Tatro, 2009). Allow at least 2 weeks after discontinuing atomoxetine before giving an MOA inhibitor (Tatro, 2009).

Phenelzine, an antidepressant, is a Monoamine Oxidase (MAO) inhibitor (Gibbon, 2008). In combination there is a suspected increased risk of serious or fatal reactions, including hyperthermia, automatic instability with possible rapid fluctuations of vital signs, and mental status changes (Tatro, 2009). Phenelzine in combination with dexamethylphenidate (a more pharmacological active enantiomer of methylphenidate) is contraindicated due to a

suspected hypertensive crisis effect. The onset of the effect may be *delayed* but the severity of the effect is *major*. The monitoring of blood pressure during combination of MAO inhibitor and methylphenidate is needed. (Tatro, 2009) Management states that the co-administration is contraindicated. After discontinuing an MAO inhibitor, allow at least 2 weeks before administering atomoxetine. Allow at least 2 weeks after discontinuing atomoxetine before giving an MOA inhibitor (Tatro, 2009).

2.7.1.4.2 Tricyclic antidepressants

Amitriptyline (Trepiline®) is an agent used to manage depressive illnesses (Gibbon, 2008). There is a possibility of an **increased** serum *concentration* of tricyclic antidepressants through the inhibition of tricyclic antidepressants metabolism. The onset is *delayed* as the severity is *minor*. Management states that clinical symptoms should be monitored with a decrease or discontinuation of one of the drugs when side-effects are noted.

Clomipramine (Anafranil®) is a tricyclic antidepressant used to manage depressive illness (Gibbon, 2008). There is a possibility of an increased serum concentration of the tricyclic antidepressants through the inhibition of tricyclic antidepressants metabolism. The onset is delayed as the severity of the effect is minor. Management states that clinical symptoms should be monitored with a decrease or discontinuation of one of the drugs when side-effects are noted.

Imipramine (Tofranil®) is a tricyclic antidepressant used to manage depressive illness (Gibbon, 2008). There is a possibility of an increased serum concentration of the tricyclic antidepressants through the inhibition of the tricyclic antidepressants' metabolism. The onset is delayed as the severity of the effect is minor. Management states that clinical symptoms should be monitored with a decrease or discontinuation of one of the drugs when side-effects are noted.

Trimipramine (Surmontil®) is a tricyclic antidepressant used to manage depressive illness (Gibbon, 2008). There is a possibility of an increased serum concentration of the tricyclic antidepressants through the inhibition of tricyclic antidepressants' metabolism. The onset is delayed as the severity of the effect is minor. Management states that clinical symptoms should be monitored with a decrease or discontinuation of either one of the drugs when side effects are noted.

2.7.1.4.3 Selective serotonin re-uptake inhibitors (SSRIs)

Fluoxetine (e.g. Nuzak®), a selective serotonin re-uptake inhibitor (SSRI), used in depressive disorders, bulimia nervosa, obsessive-compulsive disorder and also used off-label for anxiety

disorders. Atomoxetine in combination with fluoxetine causes a possibility that the atomoxetine plasma concentrations may be elevated, increasing the pharmacologic and adverse effects. The onset is delayed as the severity is moderate. Management suggested that patients receiving atomoxetine should be closely monitored when starting, stopping, or changing the dose of certain serotonin re-uptake inhibitors. The dose of atomoxetine should be adjusted as needed.

Paroxetine (e.g. Aropax®) selective serotonin re-uptake inhibitor (SSRI), is used in major depressive disorders, especially where sedation is undesirable, panic disorder, obsessive-compulsive disorder and social anxiety disorder. In combination with atomoxetine there is a possibility that the plasma concentrations may be elevated, increasing the pharmacologic and adverse effects. The onset is delayed as the severity is moderate. Management suggested that the patients receiving atomoxetine should be monitored closely when starting, stopping, or changing the dose of certain serotonin re-uptake inhibitors. Adjust the dose of atomoxetine as needed.

2.7.2 Possible side effects

According to Papakostas *et al.* (2006:372) the most common side-effects were insomnia, increased anxiety, nausea and dry mouth. Common side-effects of methylphenidate include insomnia, loss of appetite, stomach-aches, headaches, dizziness (Thompson & Thompson, 2007:3; Vance *et al.*, 1999:400).

Rapport and Moffitt (2002:1124) suggested potential side-effects such as weight gain, reduction in height with the treatment of psychostimulants. Some patients undergoing methylphenidate treatment indicated an elevated heart rate in the range of 3 to 10 beats per minute (bpm).

2.8 AN OVERVIEW OF PHARMACOECONOMICS, DRUG UTILISATION REVIEW AND MANAGED CARE

Drug utilisation review, pharmacoconomics, evidence-based medicine and pharmaco-epidemiology are information systems which can be used in disease management programmes of specific medical conditions.

2.8.1 Disease management

2.8.1.1 Definition

The term 'disease management' has been widely used in the recent past, with a variety of definitions (Norris *et al.*, 2003:478). The definition may also vary with the writer's perspective

(economic, research, or clinical) and the delivery system to which the term is being applied (Norris *et al.*, 2003:478).

The *definition* of chronic disease management according to Norris *et al.* (2003:480), is an organised, proactive, multi-component, patient-centred approach to health care delivery that involves all members of a defined population who have a specific disease entity or a subpopulation with specific risk factors (Norris *et al.*, 2003:480).

According to Holdford (1998:258), the *definition* of disease management is an integrated, systems approach to health care designed to influence the progression of disease within selected patient populations.

Furthermore, disease management is *defined* by the Disease Management Association of America as a system of coordinated health care interventions and communications for populations with conditions in which patient self-care efforts are significant (Coughlin *et al.*, 2006:198). Disease management according to Coughlin *et al.* (2006:198) include the following:

- Supports the physician-patient or practitioner-patient relationship and plan of care
- Emphasises prevention of exacerbations and complications utilising evidence-based practice guidelines and patient empowerment strategies
- Evaluates clinical, humanistic, and economic outcomes on an ongoing basis with the goal of improving overall health.

Ideally, disease management is meant to follow and treat patients through the course of their disease and coordinate care that crosses organisational and professional boundaries (Holdford, 1998:258). The goal of disease management is to maximise the impact of health care on clinical and economic outcomes by focusing on patient populations with diseases that use significant resources within the health care system (Holdford, 1998:258).

According to Curtiss (2004:166) the ultimate measures for effective managing of ADHD is to assist with social performances, scholastic performance (such as parents spending time with children on homework assignments or use of tutors) or work performance. Secondline therapy might involve the assistance of professional educators, counsellors, psychologists, school personnel, community mental health therapists, or primary care clinician (Curtiss, 2004:166).

2.8.1.2 What is disease management?

According to Hunter and Fairfield (1997:50), disease management views patients as entities experiencing the clinical course of a disease, rather than viewing their care as a series of discrete episodes or as fragmentary encounters with different parts of the health care system. Disease management consists of the following three parts:

- A knowledge base that quantifies the economic structure of a disease and includes guidelines covering the care to be provided, by whom, and in what setting for each part of the process.
- A care delivery system without traditional boundaries between medical specialities and institutions.
- A continuous improvement process which develops and refines the knowledge base, guidelines and delivery system.

2.8.1.3 Steps in ideal disease management programme

The ideal disease management programme would be produced by following these steps:

- Step 1: select the disease of interest
- Step 2: develop or adapt a guideline for treating it
- Step 3: choose a small number of outcome measures of interest and address the most pressing ones in the disease management programme
- Step 4: streamline the guideline to address the most important outcomes
- Step 5: implement the intervention strategy (Goetzel & Ozminkowski, 2000:124).

2.8.1.4 Features of successful disease management process

Hunter and Fairfield (1997:51), listed the features of successful disease management as follows:

- Patient centred and outcome focused.
- Objective and evidence-based, to ensure credibility and acceptance.
- Flexible and pragmatic, to account for normal variations and uncertainties in medical practice at patient level.

- Dynamic, to enable evolution and durability.
- Based on what happens in the real world and not on what ought to be happening.
- Designed to minimise difficulties and maximise benefits.

2.8.1.5 Framework for assessing in disease management

- Patient issues – patients' interests should be paramount.
- Ethical issues – there should be no conflict with ethical requirements of practitioners to provide whatever treatment they consider clinically necessary for an individual patient.
- Protection and use of patient information.
- Legal issues – all parties should satisfy themselves as to the legality of any proposed venture.
- Transparency and accountability – services specified in a joint venture should be published.
- Finance issues – joint ventures should represent value for money.
- Evaluation – joint venture schemes should include arrangements for monitoring and evaluation (Hunter & Fairfield, 1997:51).

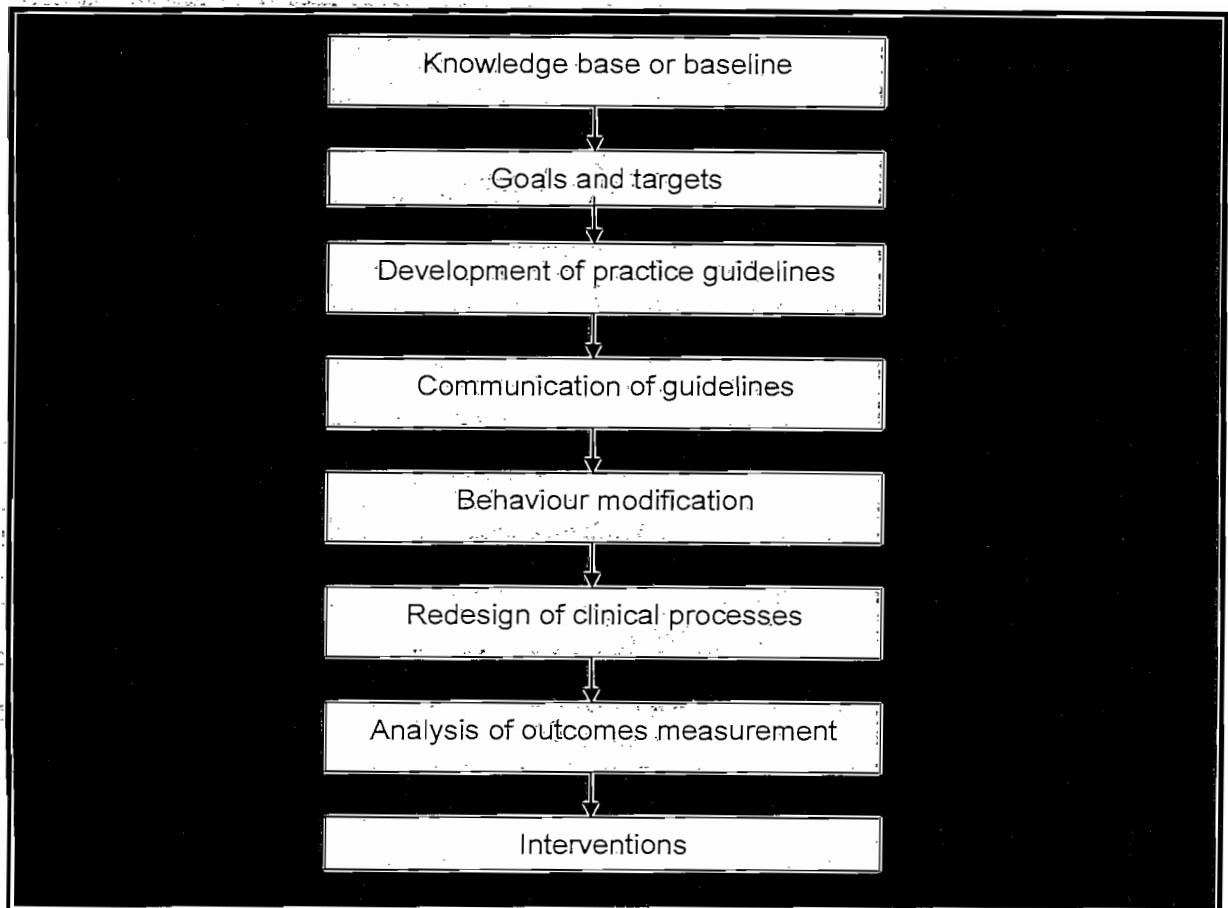


Figure 2.6: The disease management process (Adopted from Hunter and Fairfield, 1997:53)

2.8.2 Drug Utilisation Review (DUR)

2.8.2.1 Introduction

The mission of state of *drug utilisation review (DUR)* programmes involves identifying suboptimal drug therapy and providing educational materials to improve therapy in these patients (Owens *et al.*, 2008:267). Guo *et al.* (1995:1175) support the above stated. The main purpose of a DUR programme is to control inappropriate prescribing and reduce drug costs through prospective, concurrent, and retrospective review processes (Guo *et al.*, 1995:1175). It is apparent that a DUR programme is absolutely necessary.

2.8.2.2 Definition

Guo *et al.* (1995:1175) defined *drug utilisation review (DUR)* as “an authorized, structured, and continuing program that reviews, analyzes, and interprets patterns (rates and costs) of drug usage in a given health care delivery system against predetermined standards”. In 1977 the World Health Organization (WHO) defined DUR as “the marketing, distribution,

prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences" (WHO, 2003:8).

2.8.2.3 Classification of drug utilisation review

The principal aim of *drug utilisation research (DUR)* is to facilitate the rational use of drugs in populations (WHO, 2003:9). This view is supported by Sjöqvist and Birkett (2003:78). According to Fulda *et al.* (2004:434), DUR can be performed *retrospectively or prospectively* (also known as concurrent) where the approaches and focus of each is different.

2.8.2.3.1 Retrospective drug utilisation review (rDUR)

Retrospective drug utilisation review programmes are structured ongoing initiatives that interpret patterns of drug use in relation to predetermined criteria and attempt to minimise inappropriate prescribing (Hennessy *et al.*, 2003:1494). According to Fulda *et al.* (2004:434) a "*retrospective DUR occurs after the prescriptions have been dispensed and uses practice pattern analysis to identify the use of high-cost drugs, to compare particular classes of drug use by different facilities or providers, or to monitor adherence to pharmacotherapy recommendations from practice pattern guidelines for the treatment of particular diseases*".

A *retrospective DUR* process involves screening (computerised) of medicine claims each month to detect "exceptions" that appear to violate predetermined criteria for appropriate prescribing (Hennessy & Strom, 2003:1494). If the criteria are valid, then exceptions represent prescribing errors (Hennessy & Strom, 2003:1494). *Retrospective DUR* evaluates patient use patterns of prescriptions that have already been dispensed and focuses on the patient's drug profile (Radloff & Jones, 2007:33). Patterns that suggest potentially inappropriate prescription drug utilisation prompt communications to prescribers, patients or pharmacists detailing the identified issue, relevant supporting literature and recommended actions (Radloff & Jones, 2007:33). Further according to Radloff and Jones (2007:33) *retrospective DUR* addresses the excessive or unnecessary use of prescription medications that lead to adverse drug actions.

2.8.2.3.2 Prospective/concurrent drug utilisation review (pDUR)

Prospective DUR involves reviewing each prescription for an individual patient before it is dispensed in order to identify drug-related problems such as drug-drug interactions (DDI) or drug-disease contraindications (when disease information is available or using surrogate indicators), therapeutic duplication, or other potential adverse drug events (Fulda *et al.*, 2004:434). *Prospective DUR* can help determine improper drug selection, which includes prescribing drugs that are inappropriate with respect to the patient's diagnosis or age,

inconsistent with accepted prescribing guidelines or prescribed at an improper dose (Radloff & Jones, 2007:33).

Reviews are typically conducted electronically during the claims adjudication process before the product is dispensed and are designed to identify potential problems such as drug-drug interactions, therapeutic duplication, inappropriate dosage, or duration of therapy (Fulda *et al.*, 2004:434). Most pharmacy practice computer systems include *pDUR* software that checks all drug history and selected medical information (allergies, adverse effects, etc.) that may be available (Fulda *et al.*, 2004:434). This computerised *pDUR* has access to the patient's entire history of pharmacy (and sometimes medical) claims, thereby allowing for more comprehensive review (Fulda *et al.*, 2004:434).

Concurrent DUR uses an electronic claim-adjudication process to subject pharmacy-processed prescriptions to a series of tests designed to detect potentially inappropriate prescribing and refers to evaluation of appropriateness at the time the medication is dispensed (Radloff & Jones, 2007:33).

2.8.3 Pharmacoeconomics

Pharmacoeconomics can be defined as the evaluation of the economic, humanistic and clinical outcomes which are connected to pharmaceutical services and products (Vogenberg, 2001:4). Furthermore, according to Cantor (2002:S29), pharmacoeconomics is an interdisciplinary science that incorporates elements from pharmacies, clinical medicine, clinical epidemiology, statistics, psychology, economics, and ethics.

2.8.3.1 Quantitative tools

The quantitative tools of pharmacoeconomics include: cost-minimisation analysis (CMA), cost-effective analysis (CEA), cost-utility analysis (CUA), cost-benefit analysis (CBA) (Walley *et al.*, 2004:108 and Bootman *et al.*, 1996:9). The quantitative tools will be discussed in table 2.5.

Table 2.5: Different methodologies of the economic evaluation (Walley et al., 2004:108 and Bootman et al., 1996:9).

Methodology	Measurements of outcome (health benefits)	Cost measurement unit
Cost-minimisation analysis (CMA)	Assumed to be equivalent in comparative groups	Monetary (Rand value)
Cost-effectiveness analysis (CEA)	Health benefits are measured in natural units (e.g. life years gained)	Monetary (Rand value)
Cost-utility analysis (CUA)	Quality-adjusted life year (QALY) or other utilities.	Monetary (Rand value)
Cost-benefit analysis (CBA)	Always evaluated in monetary units (e.g. amount willing to pay to prevent a death)	Monetary (Rand value)

2.8.3.1.1 Cost-minimisation analysis (CMA)

According to Newby and Hill (2003:145), cost-minimisation is the appropriate form of economic analysis to carry out whenever two drugs have the same clinical effect and to determine equal-effective doses.

2.8.3.1.2 Cost-effectiveness analysis (CEA)

Cost-effectiveness analysis (CEA) is a technique which is designed to assist a decision maker in identifying a preferred choice among the possible alternatives. Cost-effectiveness is defined as a series of analytical and mathematical procedures which will help in selecting the course of action from alternatives (Bootman et al., 1996:11). Furthermore CEA relies on the accurate selection of appropriate outcome measures expressed as cost-effective ratios, including cost per case cured, cost per life saved to allocate comparison of alternative therapies (Lee et al., 2003:133).

The effectiveness is measured in terms of "quality-adjusted life years" (QALY's). Results of three modelling analyses indicate that methylphenidate is a cost-effective treatment option for children with ADHD. A study by Norvartis reviewed by Matza et al. (2005) indicated that the cost per QALY gained was \$27,766.

In a study by De Ridder and De Graeve (2006:75-90), it was indicated that 87.2% of ADHD children were boys. Therefore in correlation with the findings, indicated a higher prevalence for ADHD in boys than in girls, whereas the mean age of ADHD children was 11.1 years. A majority of ADHD children (90.8%) took medication continuously, whereas 89.8% of those took methylphenidate and 4.1% took combination therapy of methylphenidate and another drug. ADHD children, according to the results, presented with more emergency department

visits and hospitalisations as a result of accidents (as opposed to an illness). Results also indicated higher usage of non-ADHD-related medication (e.g. anti-bacterial and cold medication). As can be seen from this study by De Ridder and De Graeve (2006:75-90) a heavy burden is being placed on the parents of ADHD individuals.

To validate the currency on a South African basis, a conversion table was used (interbank rate). The average of the South African Rand (R) over the Euro (€) value over 365 days was R8.53141 for 2006 (Oanda, 2008). It was found that a number of parents reduced their working hours (44.5%), or had to take a more flexible job (mothers: 22.4%; fathers: 12.4%). Therefore plenty of time and money is being spent by parents to gather information about the disorder. Out-of-Pocket expenses included the cost of one methylphenidate tablet €0.13 (one packet costs €2.6 and contains 20 tablets). However in 2003, the price of methylphenidate increased by a factor of 2.5 (one packet costs €6.5 and still contains 20 tablets, where a single tablet costs €0.33).

A study by De Ridder and De Graeve (2006:75-90) investigated parents' out-of-pocket annual costs (€) per medicine item for ADHD children and siblings. It has to be taken into account that some children do not take their medication over weekends and during school holidays and therefore the number of days children take their medication amounts to 324 days per year. Some of the out-of-pocket cost to be taken into account is medication, therapy, extra lessons, visits to the general practitioner and/or specialist, visits to the emergency department and hospitalisation.

2.8.3.1.3 Cost-utility analysis (CUA)

Cost-utility analysis (CUA) is an economic evaluation that assimilates the cost and penalties of health programmes within the utility framework and can be perceived as a smaller fragment of CEA. CEA focuses on the utility for the individual patient, or serves to analyse how the patient is feeling about and as a result of the treatment (Francic *et al.*, 2003:146).

Due to the nature of the data of this study, it would not be possible to use this method.

CUA is measured in monetary terms while the units are not natural (e.g. life-years). Quality-adjusted life-years are determined by multiplying extra years of life by quality-of-life (QOL) expressed as a utility measure (Struwig, 1997:127).

Calculation: If the patient lives an extra two years and the patient's quality of life (QOL) or utility is valued at 0.5 due to health difficulties, then the Quality-adjusted life-years (QALY) is 1,0. Therefore an indication of a healthy person's utility (QALY = 1,0).

2.8.3.1.4 Cost-benefit analysis (CBA)

According to Bootman *et al.* (1991:5) CBA is a tool which can be used to improve the decision making process in the allocation of funds to health care and other programmes. If the benefits are positive, it is an indication that the treatment has worked and if the benefits are negative, it shows that the treatment has not worked (Barner & Rascati, 2003:115).

Barner and Rascati (2003:120) showed that CBA consists of five essential steps in order to determine the cost benefit ratio of an intervention. These steps include identifying the programme of intervention, identifying the alternatives, identifying the cost and benefits, measuring cost and benefits and calculating the results of cost and benefits.

2.8.4 Drug classification systems

Each of the classification systems will have its advantages and limitations which depend on the purpose. Of all the various systems only two have a principal position in drug utilisation research worldwide. They are the Anatomical Therapeutic (AT) and Anatomical Therapeutic Chemical (ATC) system (WHO, 2003:33).

2.8.4.1 The ATC classification system

The ATC classification system divides the drugs into different groups according to the organ or system on which they act and according to their chemical, pharmacological and therapeutic properties (WHO, 2003:34). The drugs can be classified in groups at five different levels. The drugs are divided into 14 main groups at first level with two therapeutic/pharmacological subgroups (second and third levels). The fourth level is a therapeutic/pharmacological/chemical subgroup and the fifth level is the chemical substance. The second, third and fourth levels are often used to identify pharmacological subgroups (WHO, 2003:34).

For the purpose of this study the ATC classification of methylphenidate and atomoxetine is N06BA04 (Billiard *et al.* 2006:1038) and N06BA09 (Billiard *et al.*, 2006:1042) respectively.

2.8.5 Prescribed minimum benefits (PMB)

According to the Medical Schemes Act (131/1998) the PMB is a feature by which medical schemes have to cover the costs related to the diagnosis, treatment and cost of treatment at all times. The specifications include the following:

- Any emergency medical condition.

- A limited set of 270 medical conditions (defined in the Diagnosis Treatment Pairs or DTP).
- 27 chronic conditions (defined in the Chronic Disease List or CDL).

2.8.5.1 Objectives of Prescribed Minimum Benefits (PBM) objectives

According to the Medical Schemes Act (131/1998) the introduction of Prescribed Minimum Benefits aim to:

- Provide treatment access even where members do not have normal medical scheme cover due to their plan benefits or limits having been exceeded/depleted.
- Avoid excess pressure on the limited resources of the state-owned public hospitals.
- Encourage more efficient use of the limited health care resources of the public and private sectors.

PMB should be managed under an insured benefit pool and must be covered, even if there are specified scheme exclusions and waiting periods applicable, or a limit for a specific benefit has been depleted.

2.8.6 Drug utilisation metrics and their applications

In this section below the tools of drug utilisation will be discussed according to defined daily dose (DDD), prescribed daily dose (PDD) and volume.

2.8.6.1 Defined daily dose (DDD)

According to Sjöqvist and Birkett (2003:83) the DDD is the assumed average maintenance dose per day of a drug used for its main indication in adults. This statement is supported by the WHO (2003:38). According to the WHO (2003:38) the DDD is a unit of measurement and does not necessarily correspond to the recommended or prescribed daily dose (PDD). Doses for individual patient groups will often differ from the DDD as they must be based on individual characteristics (e.g. age and weight) and pharmacokinetic considerations.

The DDD is often a compromise based on a review of the available information about doses used in various countries. The DDD may even be a dose that is seldom prescribed, due to the fact that it is an average of two or more commonly used dose sizes (WHO, 2003:38).

Drug utilisation figures should ideally be presented as numbers of DDDs per 1000 inhabitants per day or, when drug use by inpatients is considered, as DDDs per 1000 bed-

days. For anti-infective (or other drugs normally used for short periods), it is often considered to be most appropriate to present the figures as numbers of DDDs per inhabitant per year (WHO, 2003:38).

2.8.6.1.1 DDDs per 1000 inhabitants per day

Sales or prescription data presented in DDDs per 1000 inhabitants per day may provide a rough estimate of the proportion of the study population treated daily with a certain drug or group of drugs. If a figure of 10 DDDs/1000 inhabitants/day it indicates that 1% of the population on average might receive a certain drug or group of drugs daily. It may be important to consider the size of the population as the denominator. General utilisation is calculated for all age groups, but some drug groups have very limited use among people below the age of 45 years (WHO, 2003:38).

2.8.6.1.2 DDDs per 100 bed-days

This section may be applied in hospitals where drug use by inpatients is considered and may differ between hospitals and countries, i.e. 70 DDDs per 100 bed-days of hypnotics provide an estimate of the therapeutic intensity and suggests that 70% of the inpatients might receive a DDD of a hypnotic every day. This unit is quite useful for benchmarking in hospitals (WHO, 2003:38).

2.8.6.1.3 DDDs per inhabitant per year

This term may give an estimate of the average number of days for which each inhabitant is treated annually, i.e. an estimate of five DDDs per inhabitant per year indicates that the utilisation is equivalent to the treatment of every inhabitant with a five-day course during a certain year (WHO, 2003:38).

2.8.6.2 Prescribed daily dose/Consumed daily dose

According to the WHO (2003:39) the prescribed daily dose (PDD) is defined as the average dose prescribed according to a representative sample of prescriptions. It is important to relate the PDD to the diagnosis on which the dosage is based. The PDD can vary according to both the illness treated and national therapeutic traditions and it should be noted that PDD does not necessarily reflect actual drug utilisation (WHO, 2003:39).

2.8.6.3 Volume

Common physical units (e.g. grams, kilograms and litres), numbers of packages or tablets and numbers of prescriptions are also used for quantifying drug utilisation, but have certain

disadvantages. These units can be applied only when the use of a single drug or of well-defined products are evaluated (WHO, 2003:39).

2.8.7 Evidence-based medicine (EBM)

Over the past few years the concepts and ideas attributed to and labelled collectively as EBM have become a part of daily clinical lives, and clinicians increasingly hear about evidence-based guidelines, evidence-based care paths, evidence-based questions and solutions (Bhandari & Giannoudis. 2006:302).

2.8.7.1 The definition of evidence-based medicine

According to Masic and Miokovic (2008:219) evidence-based medicine represents the integration of clinical expertise, patient's values and best available evidence in process of decision making related to patients' health care. Abalos *et al.* (2005:15) simplified the answer of what evidence-based medicine entails, namely that it is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. Figure 2.7 below illustrates the different steps that can be applied with regard to evidence-based medicine.

2.8.7.2 The steps in evidence-based medicine (Abalos *et al.*, 2005:16)

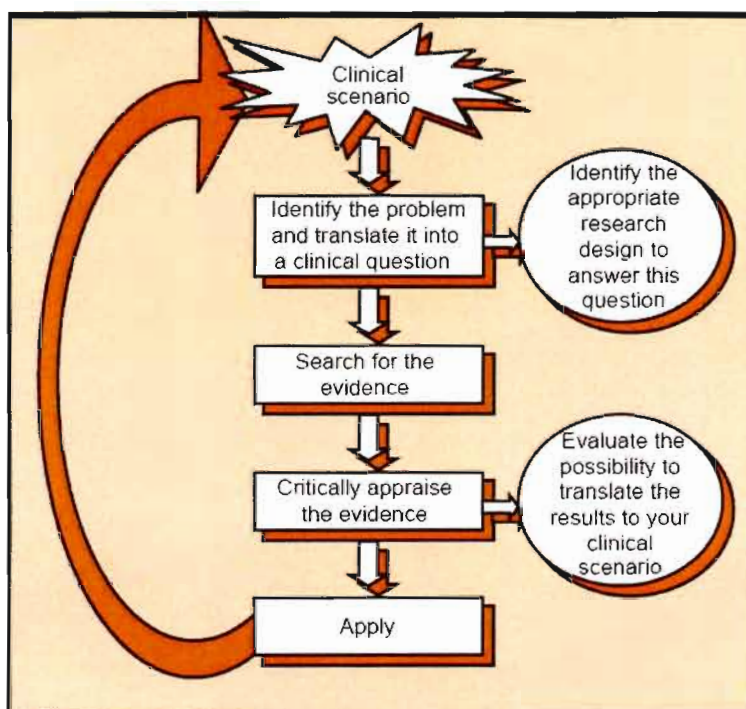


Figure 2.7 How to use/practice evidence-based medicine (extracted from Abalos et al., 2005:16)

According to Bhandari and Giannoudis (2006:303) the evidence cycle incorporates the facet of evidence-based medicine as including relevant questions, acquiring the information, appraising its quality, applying the results, and ultimately acting on the patient.

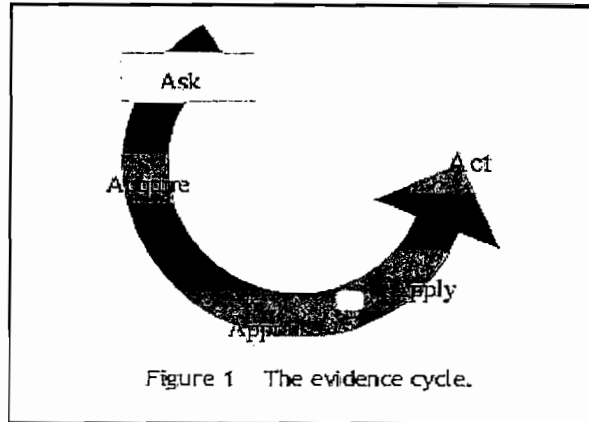


Figure 2.8: Illustrating the evidence cycle (Extracted from Bhandari and Giannoudis., 2006:303).

According to Masic and Miokovic (2008:221) a group for evidence-based medicine resource from McMaster University identified an approach in 5 steps that each physician in the application of this approach must follow. The steps include the following

- Defining the problem is the first step for the approach to evidence based medicine. A good clinical question must be clear, directly focused on the problem, and answerable by searching the medical literature. A good clinical question should have four essential structured components (patient or problem, intervention, comparison, outcome).
- Search for wanted sources of information: This step aims to gather the most relevant information to provide the answer to the question. The sources to gather the information include medical journals (which treat certain problems in the field of Family Medicine), search of electronic database and communication with colleagues. The ideal information source is valid (contains high quality data), relevant (clinically applicable), comprehensive (has data on all benefits and harms of all possible interventions) and is user friendly (is quick and easy to access and use).
- Critical evaluation of information: This step is important to ensure that the evidence obtained is valid for clinical use because not all the published information is of equal importance and value.
- The application of information of the patient: This is the crucial step if not the most complex step in this process. It is necessary to decide whether there is something in

relation to our patient as a result of which it would be necessary to discard the acquired information.

- Efficacy evaluation of evidence-based medicine application on a patient: During this process it is important to assess whether certain evidence, which is applied to the patient, caused changes to the better and to the extent that is confirmed by research. In this way the process will be updated and improved throughout.

Mahtomedi *et al.* (2007:93-98), conducted a study at Eersterus and Weskoppies Clinics, and the primary objectives included determining the prevalence of child ADHD (CADHD) and the persistence into adulthood. Secondary objectives included determining of occupational and marital histories as well as co-morbid conditions in individuals with ADHD and those without ADHD. Results of these studies are as follows:

- Fifty nine (n=59) children had been identified as having ADHD at the Eersterus and Weskoppies Clinics where only thirty four (n=34) could be included in the study, i.e. potentially sixty eight (68) parents, but only 58 parents completed the questionnaire (85.3%).
- Of these 58 respondents, only 5 (8.6%) had been diagnosed with ADHD as children, of which 2 (40%) were male and 3 (60%) female. Furthermore 17 (29.3%) parents were found to meet the criteria for CADHD through the DSM-IV criteria. Of these parents, 8 (47.1%) were male and 9 (52.9%) were female.

In a study done by Mahomedy *et al.* (2007:93), individuals were divided into a group with no ADHD (n=36) and one suggestive of adult ADHD (AADHD) (n=8). Mahomedy *et al.* (2007:93) indicated that ADHD adults were more likely to have multiple marriages than individuals without ADHD. The study by Mahomedy *et al.* (2007:93) indicated that in 62.5% of ADHD patients were in a first marriage and 25% had been divorced whereas in the no ADHD group 50% were in first marriage and 25% divorced. The sample size and range of the study, could accounted for discordance with literature. According to this study by Mahomedy *et al.* (2007:93), ADHD individuals as compared to their peers indicated higher grade retention (42% vs. 13%), suspension (60% vs. 19%), drop-out (32% vs. 0%) respectively and were less likely to graduate high school. The ADHD group in comparison with the control group indicated (62.5% vs. 33.3%) had Grade 12c, (11.1% vs. 12.5%) had degrees and (25% vs. 0%) had diplomas respectively. Mahomedy *et al.* (2007:93 mentioned that the sample size and that the participants had been recruited from public facilities (low

socio-economic status) and this could also be a reflection of the educational level of these participants.

2.8.8 Employment status

In a study by Mahomedy *et al.* (2007:93-98) it was indicated that there was a higher rate of unemployment in the adult ADHD group (50.0%) versus the 36.1% adults without ADHD respectively. An important factor that emerges from these results is that 50% of the ADHD group had held more than three (3) jobs within the previous 5 years versus 11.1% of the ADHD-free group. One of the individuals noted in the ADHD group held 25 jobs within the previous 5 years. (Mahomedy *et al.* 2007:93-98).

2.8.9 Substance abuse

Furthermore results from Eersterus and Weskoppies Clinics indicated substance abuse. The paragraph below summarised some of the findings.

Of the 58 individuals in this study 26 (44.8%) were using alcohol on a daily, weekly or monthly basis. According to gender, 14 (56.0%) of males and 12 (36.4%) of females used alcohol. A total of 9 (15.5%) females had used marijuana in the past, whereas 6 (66.7%) were male. In the ADHD group 37.5 % of individuals used marijuana in the past vs. 11.1% of the control group. From the ADHD group one that is (1.7%) admitted having used cocaine monthly. Fifteen that is 25.9% of the individuals admitted using antidepressants.

Furthermore according to Marchetti *et al.* (2001:1904-1921), an increase in stimulant use (methylphenidate) in children has been cited as evidence of over-diagnosis of ADHD. The increase in stimulant prescriptions is most likely due to an improved understanding of the disorder and the subtypes; therefore, more children are receiving appropriate diagnosis and treatment. Children with ADHD are being treated with pharmacotherapy (~12% of ADHD children). It is estimated that between 18 and 4.9 million children in the United States have ADHD and may require pharmacotherapy. By applying these numbers to the total expected cost of medication in this study, the results are the estimated incremental costs of methylphenidate immediate release (MPH IR) (\$ 259 million) and Metadate controlled dose (\$ 706 million) respectively.

According to Marchetti *et al.*, (2001:1904), pharmacotherapy for ADHD not only implicated the administration of the drug, but included finding the child in the school, taking inventory of the drugs, keeping the drugs secured as required for class II substance, notifying parents about refills, and completion of formalities. In a report by the US General Accounting Office it was indicated that 60% of schools use a school nurse to administer ADHD medications and

40% used an office staff member. If the proportion of schools using a nurse is >12%, then the contribution of the nurses' higher salaries to the total cost of ADHD treatment would increase (Marchetti *et al.*, 2001:1904). When the total per-patient expected annual costs are applied to ADHD prevalence data, the conclusion is that the total expected cost for all paediatric patients in the United States ranges from ~\$2 billion to ~\$11 billion (Table VII). It must be kept in mind that the lack of compliance in the usage of the medication may result in higher total expected costs.

2.8.10 Cost associated with ADHD

Direct costs are defined as the monetary valuation of the resources used to detect and treat medical problems (Hakkaart-van Roijen *et al.*, 2007:318). Furthermore indirect costs also include the productivity lost due to absenteeism and reduced efficiency at work. (Hakkaart-van Roijen, 2007). In this study the total direct medical costs included the total number of medical contacts (outpatient visits, hospital length of stay, use of medication, etc.) multiplied by the 2004 reference unit prices of the corresponding health care service.

2.8.10.1 Direct costs

A study by Hakkaart-van Roijen *et al.* (2007:320), concluded the mean direct medical cost per year for children with ADHD. To validate the currency on a South African basis, a conversion table was used (interbank rate). The average of the South African Rand (R) to the Euro (€) value over 365 days was R9.67099 for 2007 (Oanda, 2008).

From these results, the mean direct medical costs per child per year were over € 2000, compared to behaviour problems (€ 288) and the comparison group (€ 177) respectively. A patient reported in this study had an 84-day admission period to a psychiatric hospital and if this patient is to be left out, the mean direct medical cost drops to € 1173. Out-of-pocket costs per year for children with ADHD were on average virtually € 20 (SD €130). Mean direct medical costs per year for children who had psychiatric co-morbidities were € 5908, compared to € 974 for children with ADHD alone (Hakkaart-van Roijen *et al.*, 2007). If the above stated patient is left out, the mean cost of co-morbidity individuals would be reduced to € 1946. Also to be noted is that the total means annual direct medical costs for mothers of individuals with behaviour problems were € 202, and the same costs for mothers of individuals with no behaviour problems were € 154. According to Hakkaart-van Roijen *et al.* (2007), the annual mean direct medical costs for mothers of ADHD individuals with psychiatric co-morbidity were € 839, compared to mean direct medical costs of € 755 for mothers of children with ADHD only.

A research article by Schlander (2007), indicated in a base case scenario, which is believed to reflect the most probable course of future events, implied an increase of drug spending for children and adolescents with ADHD for year 2012 by a factor of 12 by German Statutory Health Insurance (SHI, GKV which covers approximately 90% of the German population) or factor 10 by National Health Service (NHS) in England over 2002. An annual growth rate of 5% for drug expenditures between 2005 and 2012 (except for ADHD in children and adolescents), projected ADHD treatment costs (from NHS perspective, £78 million) would make up 3.8% of NHS spending for CNS drugs in 2012, compared to only 0.77% in 2002 Schlander (2007). This increase is the effect of increasing awareness and recognition of ADHD, growing rates of pharmacotherapy, somewhat increased intensity (dose and duration) of treatment, and the shift to novel, more expensive products. A plausible range of spending estimates from 259 to 380 million in Germany and from £63 to £101 million in England in 2012 were recorded (Schlander, 2007).

2.8.10.2 Indirect costs

According to Hakkaart-van Roijen *et al.* (2007) it was found that from a group of mothers of ADHD individuals, 16% were absent from work due to health-related problems. This been said, only one mother indicated that she had been absent for longer than two weeks. The corresponding mean indirect costs per year due to absenteeism from work were € 1691 per mother. Reduced efficiency at work had a mean annual associated cost of nearly € 552. The mean number of days lost due to reduced efficiency was low, i.e. approximately half a working day per year.

A third of mothers of ADHD individuals with a paid occupation experienced difficulties at work due to health-related problems at baseline. Approximately one third (36%) of mothers of ADHD individuals indicated that they needed to be alone; one fifth occasionally experienced problems with concentration, working pace and decision making. Six per cent of mothers of ADHD individuals indicated to have postponed work. Resulting efficiency scores were 13.0 for mothers of ADHD individuals, 6.31 for mothers of individuals with behaviour problems and 6.44 for mothers of individuals with no behaviour problems. Twenty per cent of mothers of ADHD individuals experienced problems in performing unpaid work, e.g. household work. .

Matzo *et al.*, (2005) did a review study on the economic burden of ADHD. To validate the currency on a South African basis, a conversion table was used (interbank rate). The average of the South African Rand (R) to the US Dollar (\$) value over 365 days was R6.38113 for 2005 (Oanda, 2008).

2.8.10.3 Direct medical costs in adult ADHD

According to prevalence data on adult ADHD, estimates of 30% to 70% of children with ADHD continue with symptoms into adulthood. Symptoms of children are somewhat different from symptoms of those in adults and would include an indication of less hyperactivity with continued problems with organisational tasks and distractibility. Negative outcomes for adults include high rates of criminality, poor job performance, lower occupational status, problems in social skills, poor driving records as well as co-morbid psychiatric disorders. In this review two studies have indicated that adults with ADHD have significantly higher annual medical costs (from \$ 4,929 to \$ 5,651) than controls (from \$ 1,473 to \$ 2,771). Excess ADHD-related treatment costs for women amounted to \$ 0.13 billion and \$ 0.40 billion for men. Excess overall health care costs for women amounted to \$ 4.79 billion and for men \$ 8.51 billion (Matza *et al.*, 2005).

2.8.10.4 Cost to families

Family members of ADHD individuals had 1.6 times more medical claims than the control group. Annual direct per-capita medical costs were twice as much for family members with ADHD (\$ 2,740) than family members of control group (\$ 1,365). Indirect costs which included disability and absenteeism amounted to \$ 888 for family members of ADHD individuals and \$ 551 for family members of control group. Excess health care costs were estimated as \$ 6.78 billion for family members of children with ADHD and \$ 12.10 billion for family members of adults with ADHD. Furthermore, mothers of ADHD children were 3.3 times more likely to state that the family could not afford prescription medication and 7.4 times as likely not to afford mental health care for the child. These findings demonstrate the economic burden of ADHD. Parents who perceived their child's ADHD to be a serious problem were 17.6 times more likely to say that their child's ADHD had a financial impact related to their work (Matza *et al.*, 2005).

2.8.10.5 Costs of criminality

According to Matza *et al.* (2005), a study conducted in Los Angeles indicated that children between the ages of 6 and 12 years with ADHD, had significantly higher juvenile (46% vs. 11%) and adult (21% vs. 1%) arrest than the controlled group. Furthermore a study in San Francisco indicated that the ADHD group had a higher prevalence of being on probation, in jail, or assigned to a social worker than the control group. In a review study by Matza *et al.* (2005), information was gathered from the Bureau of Justice Statistics, the Federal Bureau of Investigation, and the Criminal Justice Institute. In their comparison the control group with the ADHD group it was indicated that the ADHD group was twice as likely to have been arrested

as the control group (48% vs. 20%). The mean criminal costs for ADHD individuals in comparison with the control group individuals were \$ 12,868 vs. \$ 498 respectively.

2.8.10.6 Costs of co-morbidities

According to Matza *et al.* (2005) an estimated co-morbidity cost over the two years for depression increased by an average of \$ 358 per individual per year. Oppositional defiant disorder increased by \$ 258, bipolar by \$541, conduct disorder by \$488, anxiety by \$499, nondependent drug use by \$868, tics by \$198, and personality disorders by \$247. Non-psychiatric medical disorders included respiratory illness at \$630, acute sinusitis at \$670, general injuries at \$972, and allergies at \$507. In a sample, average annual treatment costs for children with ADHD and co-morbid epilepsy were \$ 5,194, compared to the \$ 4,246 with ADHD only.

2.8.10.7 Costs of accidents

Due to tendencies toward impulsivity and overactive behaviour, children with ADHD had shown to be more accident prone than other children. Injuries included broken bones, lacerations, head injuries, bruises, lost teeth, or accidental poisonings. ADHD individuals in all age groups (children under 12 years, adolescents aged 12 to 18 years and adults) had at least one accident claim more than their peers. Children, 28% vs. 18%; adolescents 32% vs. 23%; and adults, 38% vs. 18% (Matza *et al.*, 2005). Therefore accident-specific direct medical costs were higher for ADHD individuals than for the control group (\$ 642 vs. \$194) according to Matza *et al.* (2005).

Furthermore Swensen *et al.* (2004:346) compared the prevalence of accidents of ADHD patients to those of the control group. In their study it was found that ADHD patients had a statistically significant difference in internal injury (n=143), superficial injury (n=129), traumatic complications and unspecified injuries (n=100), open wounds (n=97), fractures (n=77), poisoning (n=22) and burns (n=12) of all accidents taken into account (N=415).

2.8.10.8 Costs of work loss

Work-related problems in adult ADHD individuals include poor job performance, lower occupational status, less job stability, and increased absence days in contrast with adults without ADHD. According to Matza *et al.* (2005), the indirect work loss costs were calculated by using employer payments for distractibility claims and imputed wages for medically-related work absence days. The estimated excess costs were \$ 1.20 billion for ADHD woman and \$ 2.26 billion for men with ADHD.

2.9 CHAPTER SUMMARY

In this chapter the focus was on the nature of attention deficit/hyperactivity disorder (ADHD). This includes the history of ADHD; treatment with methylphenidate and/or atomoxetine containing products which are associated with ADHD; different types of ADHD; misdiagnoses and co-existing disorders of ADHD in relation to other psychiatric or mental illnesses. ADHD is described in-depth in accordance with gender, age, ethnicity, the nature and the extent of ADHD. Further in this chapter, managed health care has been discussed with regard to pharmacoeconomics, drug utilisation review, evidence based medicine and prescribed minimum benefits.

In Chapter 3, the research methodology of this study will be discussed.

3 CHAPTER 3

Research methodology

3.1 INTRODUCTION

The contents of this chapter encompass the research objectives, empirical research methodology, study population, selection of research design, selection of measuring instruments, data analysis and classification systems.

3.2 RESEARCH OBJECTIVES

The research objectives of this study consisted of both general and specific research objectives.

3.2.1 General research objective

The general research objective was to investigate the prescribing patterns of products containing methylphenidate and atomoxetine in a section of the private health care in South Africa for the period of 2005 until 2007.

3.2.2 Specific research objectives

The specific research objectives included the following (refer to chapter 1).

3.2.2.1 Literature study

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

- To conceptualise ADHD as a disease from available literature.
- To determine from the literature the prevalence of ADHD on an international level as well as in South Africa.
- To determine from the literature the comorbid diseases with regard to ADHD.
- To establish from available literature the medicine treatment for ADHD.
- To determine from the literature possible drug-drug interactions between atomoxetine or methylphenidate containing products and other drugs.

- To investigate from the literature the cost associated with ADHD treatment.
- To establish from the literature the importance of disease management, drug utilisation review, pharmacoconomics, evidence-based medicine, drug classification systems and prescribed minimum benefits (PMB).

3.2.2.2 Empirical study

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

- To determine the usage patterns and cost of drugs in general according to all medicine items and prescriptions in the total database for the study period 2005 to 2007.
- To analyse the prescribing patterns and cost of methylphenidate and atomoxetine containing products in a section of the private health care sector of South Africa.
- To determine the influence of age and gender on the prescribing patterns of all medicine items on the database with special reference to methylphenidate and atomoxetine containing products in a section of the private health care sector.
- To determine the total cost, medical scheme and patient cost contribution for all medication and methylphenidate and atomoxetine containing products specifically in a section of the private health sector of South Africa.
- To determine the prescribed daily dosages (PDD) of methylphenidate and atomoxetine containing products in patients of different age groups, gender, and prescribed by different types of prescribers (e.g. general practitioners, specialists, etc.).
- To determine the potential cost savings that can be generated by practising generic prescribing/substitution with methylphenidate containing products.
- To investigate the prevalence of possible drug-drug interactions between methylphenidate or atomoxetine containing products and other CNS medication on prescriptions.
- To identify which other CNS medications were prescribed together with methylphenidate or atomoxetine containing products.

3.3 RESEARCH METHODOLOGY

3.3.1 Research design

A retrospective quantitative drug utilisation study (refer to chapter 2) was conducted on medicine claims data of a PBM company in South Africa for the years 2005 to 2007. A drug utilisation study was defined in 1977 by the World Health Organization (WHO, 2003:8), as the marketing, distribution, prescription, and use of medication in a society, emphasising the resulting medical, social and economic consequences. Retrospective drug utilisation study is discussed in Section 2.12.2.3.1.

A PBM organisation is a type of managed care specialty service organisation that seeks to contain the costs of prescription drugs or pharmaceuticals while promoting more efficient and safer drug use. Such an organisation may also be known as a prescription benefit management plan (Pam Pohly's net guide, 2006). In this study the PBM is an independent and specialist PBM organisation that provides effective and innovative medicine management solutions to its clients. The solutions are delivered through real-time electronic processing of medicine claims and the authorisation of chronic medication applications (Bester & Badenhorst, 2008:29).

3.3.2 Data source

The data were extracted from the medicine claims database of the PBM. The data from 1 January 2005 to 31 December 2007 were divided into three study periods. Period 1 was from 1 January 2005 to 31 December 2005. Period 2 was from 1 January 2006 to 31 December 2006, and Period 3 was from 1 January 2007 to 31 December 2007.

The following fields of the database were used in this study:

- Date of dispensing of the prescription
- Birth date of the patient (was used to calculate the age of the patient on the day of treatment)
- NAPPI codes
- NAPPI code description – Trade name
- Generic indicator of the medicine
- Day's supply

- Quantity of medicine items dispensed
- Final amount paid by medical aid (Total scheme contribution)
- Final amount paid by patients (Total patient contribution)
- Total cost of dispensed prescriptions
- Gender of the patient
- Prescriber type

3.3.2.1 Target population

The target population included all medicine items claimed through the South African PBM for the years 2005, 2006 and 2007 (refer to section 2.11.4).

The following table indicates the number of all prescriptions claimed through the PBM according to the study year.

Table 3.1: The number of all prescriptions claimed in the total database for 2005, 2006 and 2007

Period	Number of all prescriptions
2005	8,522,798
2006	9,048,541
2007	8,015,538

3.3.2.2 Study population

The study population included all prescriptions that contained methylphenidate and atomoxetine containing products (MIMS classification 1.1.3) for the study period 2005 to 2007.

The following table indicates the number of prescriptions indicating methylphenidate and atomoxetine containing products that were claimed through the PBM according to the study year.

Table 3.2: The number of prescriptions indicating methylphenidate and atomoxetine containing products for 2005, 2006 and 2007.

Period	Number of prescriptions
2005	27,680
2006	31,577
2007	32,647

3.3.3 Ethical considerations

The research study was conducted from the perception that all data obtained from the database were correct and accurate. To ensure the confidentiality of the patients, ethical approval was obtained from the NWU ethical committee as part of the main project entitled **“Investigation of medicine usage patterns in a section of the private health care sector utilising data from a Pharmaceutical Benefit Management (PBM) Company in South Africa”** (Ethical number: NWU-0046-08-S5).

3.4 CLASSIFICATION SYSTEMS FOR THE RESEARCH PROJECT

For the purpose of this study, different classification systems were used.

3.4.1 Medication

3.4.1.1 NAPPI code

The NAPPI code (National Pharmaceutical Product Interface), is a 9 digit code and contains the following information: the product description, strength, pack size and manufacturer (Healthwebsa, 2009).

- The first 6 digits describe the product e.g. Brufen® tablets.
- The last three digits describe the pack size.

To summarise it means that if the medicine item had different pack sizes, the first 6 digits would be the same but the last three digits would differ. (Healthwebsa, 2009). Therefore individual medicine products are identified by using the NAPPI code.

3.4.1.2 MIMS classification

The MIMS® classification group 1 was used for central nervous system medicine items, group 1.1 for central nervous system stimulant items, group 1.1.3 for other items.

Methylphenidate (both short-acting and long-acting) and atomoxetine containing products are classified under section 1.1.3 (MIMS®, 2007:2). Both methylphenidate and atomoxetine containing products are used for ADHD. In addition the methylphenidate containing products (Ritalin 10mg®, Ritalin SR 20mg®, Adaphen® and Methylphenidate HCl-Douglas®) are also used for the treatment of narcolepsy.

Medicine information in the MIMS® (Monthly Index of Medical Specialties) is updated monthly and is compiled from package inserts supplied by pharmaceutical companies and should be read in conjunction with *Standard Editorial Notes* as well as *Information for Prescribers* which would include information on the active ingredients (MIMS, 2007:6a).

3.4.2 Age

The age of the patient on the day that the prescription was dispensed was calculated by subtracting the member's date of birth from the treatment date minus the member date of birth divided by 365.25. Toddlers, children, adolescents and adults have been divided into different age groups to observe the prescription frequency of products containing methylphenidate and atomoxetine in these age groups. The age categories used in this study were selected with advice of a paediatrician (Bocking, 2008). He recommended that patients should be divided into the following age groups as illustrated in Table 3.3.

Table 3.3. Age category classification

Group	Age category (years)	Description
1	≤ 5 years	All patients older than 0 years and younger than or equal to 5 years were included in this category – mostly young children.
2	5 < and ≤ 12 years	All patients older than 5 years and younger than or equal to 12 years were included in this category – most of the children included in this category were attending school
3	12 < and ≤ 18 years	All patients older than 12 years and younger than or equal to 18 years were included in this category – most of them were adolescents and young adults.
4	> 18 years	All patients older than 18 years were included in this category.

3.4.3 Gender

According to reports conducted by Castellanos *et al.* (2002) the prevalence of stimulant (methylphenidate) and non-stimulant (atomoxetine) usage for the treatment of ADHD differs according to gender. Data on the database were categorised into the following gender groups.

- Gender group M: Male
- Gender group F: Female
- Gender group U: Unspecified

The unspecified group included those patients whose gender was not indicated in the database. This could be the result of the medical practitioner/pharmacist not entering the gender on the patient's profile (complete profile).

3.4.4 Prescriber

PMB data was divided into the following four categories according to the prescriber type (i.e. the person who prescribed the medicine):

- General medical practitioner: a medical practitioner or physician who treats acute and chronic illnesses and provides health education to all ages and to both genders.
- Paediatrician: a medical practitioner or physician who specialises in the medical care of infants, children and adolescents.
- Psychiatrists: a medical practitioner or physician who specialises in the treatment of mental disorders.
- Neurologists: a medical practitioner or physician who specialises in the medical care of patients with neurological difficulties.
- Other: This group include, inter alia, the following prescribers:

Anaesthesiology, cardiology, clinical haematology, dermatology, gastroenterology, homeopaths, maxillo-facial and oral surgery, nuclear medicine, obstetrics and gynaecology, oncology, ophthalmology, oral pathology, orthodontics, orthopaedics, otorhinolaryngology, periodontics and urology.

3.5 DESCRIPTIVE MEASURES

The following descriptive measures were selected to obtain the specific objectives set out in this study.

3.5.1 Prevalence

Prevalence (P) is defined as the number of existing cases of a disease (or any outcome, e.g., adverse drug reaction, drug use) in a population at a particular point in time (Waning & Montagne, 2001:108).

$$P = \frac{\text{Number of existing cases in a population}}{\text{Total number of people in that population}}$$

In this study the prevalence of each individual trade name product according to active ingredient (products containing methylphenidate and atomoxetine) over the three years was discussed.

This was done to describe the prevalence of products containing methylphenidate and atomoxetine according gender, age as well as prescriber type over the three years.

3.5.2 Age

Age is usually derived from the time that has elapsed since the date of birth of the patient (Refer to section 3.5.2) (Stedman Medical Dictionary, 2009). For this project, the age will refer to the number of days/months/years lived by the patient, on the day of treatment.

3.5.3 Gender

The World Health Organization (2009a) defines gender as the socially *constructed roles*, behaviours, activities, and attributes that a given society *considers appropriate* for men and women. In other words *male* and *female* are sex categories, while *masculine* and *feminine* are gender categories (WHO, 2009b). It is important that gender be included in this study to establish susceptibility to ADHD in each gender group.

3.5.4 Cost analysis

To calculate the economic burden of methylphenidate and atomoxetine containing products on the patient and medical scheme, cost was selected as criterion for this part of the study. In this study the total medicine treatment cost, medical scheme contribution as well as patient contribution were investigated. The average cost per prescription and item was investigated and discussed (Refer to chapter 4).

3.5.5 Drug interactions

According to Gibbon (2005), the drug interactions of methylphenidate with other medication are the following: barbiturates*, phenytoin*, tricyclic antidepressants* and warfarin*, monoamine oxidase inhibitors*.

Precipitant interactions with methylphenidate are phenelzine*, tranylcypromine*, carbamazepine*, cyclosporine*, guanethidine, phenytoin*, amitriptyline*, amoxapine, clomipramine*, desipramine, dicumarol, doxepin, imipramine*, nortriptyline, protriptyline, trimipramine* and isocarboxazid (Tatro, 2008).

Precipitant interactions with atomoxetine are isocarboxazid, phenelzine*, tranylcypromine*, fluoxetine* and paroxetine* (Tatro, 2008).

**Note that the items marked with (*) were available on the South African Medicine database.

3.6 DATA ANALYSIS

The data were analysed by using the Statistical Analysis System® for Windows 9.1® (SAS for Windows 9.1). Microsoft (MS) Excel® and Microsoft (MS) Word® were used for the illustration of the results through tables and graphs.

3.6.1 Descriptive statistics

3.6.1.1 Arithmetic mean (average)

Brase and Brase (1999:94) indicated that the *mean* (also known as *arithmetic mean*), is an average that uses the exact value of each entry. To compute the mean, the values of all the entries (x-values) are added together and then divided by the number of entries (n).

The *mean* can be calculated by using the following formula (Kirkwood, 1988:12).

$$\text{Mean, } \bar{X} = \frac{\sum X_i}{n}$$

Where:

X_i = values of the variable.

Σ = the sum of.

n = number of observations.

For the purpose of this study, the arithmetic mean (average) was used to determine:

- The average number of prescriptions claimed per year.
- The average number of medicine items per prescription.
- The average cost per prescription.
- The average cost per medicine item.

3.6.1.2 Standard deviation

As stated by Barlo (2009), the standard deviation value represents the average distance of a set of scores from the mean. According to Steyn *et al.* (2004), standard deviation is the *square root* of the variance. Standard deviation can be calculated by using the following formula (Steyn *et al.*, 2004:131).

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

Where:

$\sigma = S$ = standard deviation.

Σ = the sum of.

X = values of the variable.

n = number of observations.

3.6.1.3 Cost saving

In this research project the cost was expressed in Rand-value. The total cost of prescriptions or items can be divided into the following cost components: total cost (a+b), total patient contribution (a) and total medical scheme contribution (b). The potential cost saving is the Rand-value that could have been saved if all medicine items had been substituted for generic items. Calculations for this section were done by multiplying the number of innovator products containing methylphenidate ("O" indicated) with the average cost per item for generic products containing methylphenidate ("Y" indicated) where the dosage of the active ingredient corresponded with each other. Ritalin 10mg[®] could be substituted for Adaphen 10mg[®] and Methylphenidate HCl-Douglas[®]. Ritalin SR 20mg[®] could be substituted for Adaphen XL 20mg[®]. Cost saving can be calculated by using the following formula:

Calculation: $X - (Y * Z)$

Where:

X = total cost of Ritalin 10mg[®] or Ritalin SR 20mg[®]

Y = number of Ritalin 10mg[®] or Ritalin SR 20mg[®] items

Z = average medicine cost per medicine item for Adaphen 10mg[®], Methylphenidate HCl-Douglas[®] or Adaphen XL 20mg[®].

3.6.2 Inferential statistics

3.6.2.1 Effect sizes (d-values)

According to Cohen (1988:9), the effect sizes (d) can be defined as the degree to which the phenomenon is present in the population. The effect sizes can be calculated by using the following equation presented by Steyn (1999:3):

$$d = \frac{x_a - x_b}{S_{\max}}$$

Where:

- d = effect size.
- x_a = the average medicine treatment cost of a (average cost)
- x_b = the average medicine treatment cost of b (average cost).
- S_{\max} = the maximum standard deviation between a and b .

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

- $d = 0.2$: small effect – no practical significance.
- $d = 0.5$: medium effect – effect is observable which may be significant.
- $d = 0.8$: large effect – effect is significant and of practical importance.

For the purpose of this study, the effect sizes were used to compare the average cost per prescription of medicine items of the different years.

3.6.2.2 Cost-prevalence index

Serfontein (1989:180) developed the cost prevalence index to indicate the relation between the number of medicine items per prescription and the total medicine cost associated with these items.

The cost-prevalence index can be calculated by using the following equation/formula by Serfontein.

$$\text{Cost-prevalence index} = \frac{\text{Cost (\%)}}{\text{Prevalence (\%)}}$$

For the purpose of this study:

- Cost index < 1: Indicates that the treatment is relatively inexpensive.
- Cost index = 1: Indicates that there is an equilibrium between the cost and prevalence of treatment.
- Cost index > 1: Indicates that the treatment is relatively expensive.

3.6.2.3 Prescribed daily dose (PDD)

The prescribed daily dose (PDD) is the average daily dose prescribed, as obtained from a representative sample of prescriptions (WHO, 2003:14). The prescribed daily dose (PDD) was calculated by multiplying the strength with the quantity of the product divided by the days supplied. The calculation done is illustrated by the following equation/formula:

$$\text{PDD} = (\text{Strength} * \text{quantity}) / \text{Days supply.}$$

3.7 CHAPTER SUMMARY

This chapter focused on the general and specific objectives as well as the research methodology pertaining to this study.

The results of this investigation are discussed in Chapter 4.

4 CHAPTER 4

Results and discussion

4.1 INTRODUCTION

In this chapter the results of the empirical investigation will be discussed. The results will be presented according to specific study periods namely 2005, 2006 and 2007. The results of this research project were obtained from a medicine claims database of a PBM in a section of the private health care sector of South Africa (refer to section 3.4).

Figure 4.1 illustrates the data analysis process followed in this study.

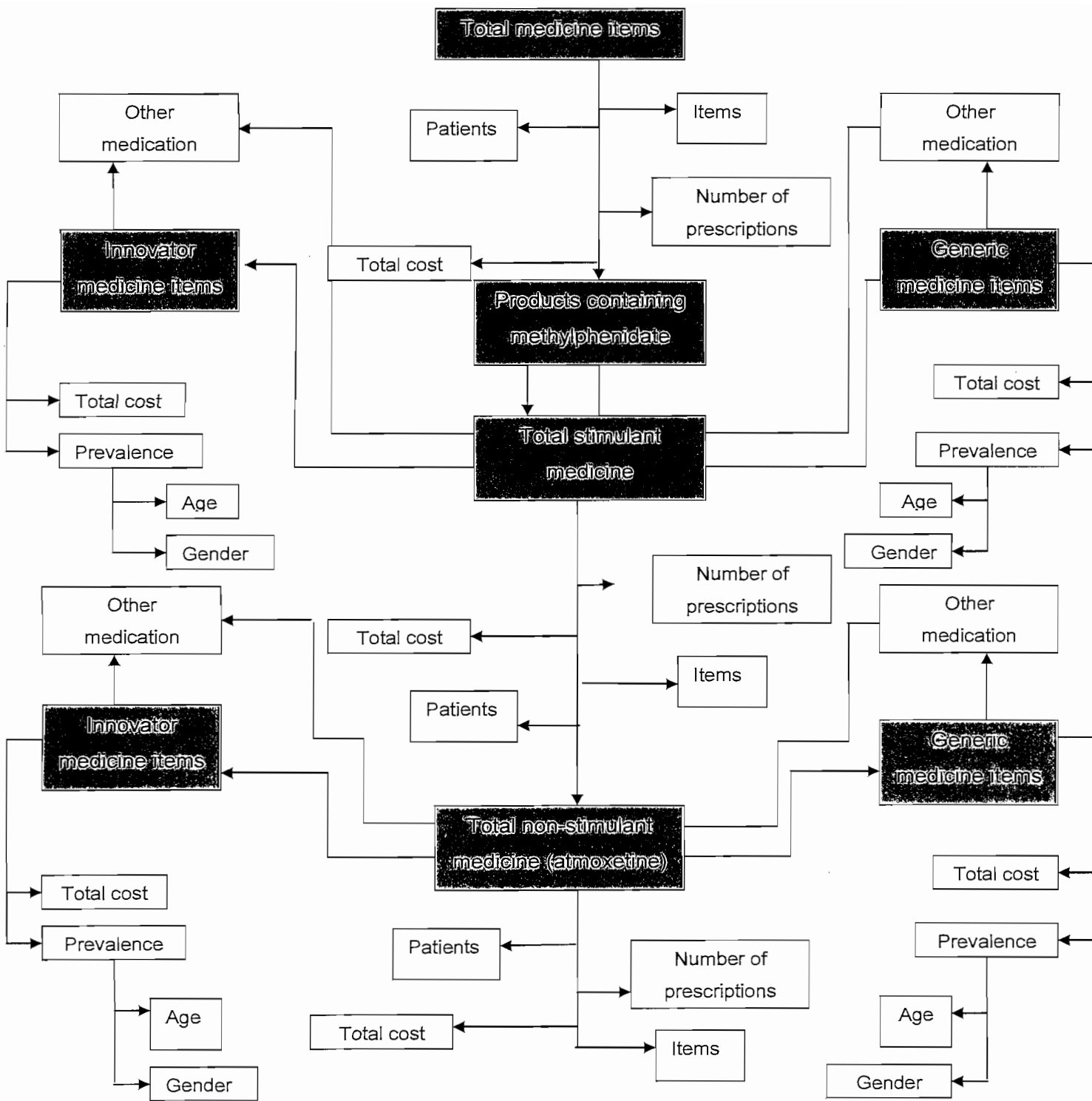


Figure 4.1 Flow diagramme illustrating analysis and presentation of the results

4.2 DEFINITIONS

Patient:	An individual who, on the database received one or more prescriptions during the study period and the prescription was claimed through the PBM.
Total medicine cost:	The total medicine cost is the sum of the patient medicine contribution and the medical scheme contribution to the medicine item.
Patient medicine	The amount payable by the patient or individual contribution responsible for payment as by regulation per medical scheme with reference to the usage of medicine by the patient.
Medical scheme medicine contribution:	The amount payable by the medical scheme as by the regulations per medical scheme with reference to the usage of medicine by the patient.
Prescription:	A written directive for the compounding or dispensing of drugs by a properly authorised person to a particular person. Prescriptions related to restricted drugs must be directed to a qualified pharmacist who can be authorised by a registered medical practitioner to compound or dispense drugs (Anon, 2009). A prescription can consist of more than one item.
Medicine item:	For the purpose of this study the medicine item refers to the pharmacological ingredient for the treatment or prevention of disease.
Active ingredient:	An active ingredient is any component that provides pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of a disease, or that affects the structure or any function of the body of man or animals (FDA, 2009a).
Generic product:	A generic drug contains the same active ingredient as an innovator drug in the same dosage, safety, strength, how it is taken, quality, performance, and intended use. Before approving a generic product, Food and Drug Administration (FDA) requires many rigorous tests and procedures to assure

that the generic drug can be used as substitute, or “therapeutic equivalent”, of innovator drugs on scientific evaluations. By law, a generic drug product must contain the identical amounts of the same active ingredient(s) as the innovator product. Drug products evaluated as “therapeutic equivalent” can be expected to have equal effect and no difference when substituted for the brand name product (FDA, 2009b). According to the Medicines Control Council (MCC), generic substitution is the interchangeable use of different brands of chemically equivalent medications (i.e. those which contain the same active ingredients, the same quantities thereof, in the same pharmaceutical dosage form, or as more commonly named, “generics”)(South Africa, 1965).

Innovator product:

An innovator product is a product that is currently protected by a patent or has previously been protected by a patent. Such medicines may be marketed by the original patent holder or another individual (SA, 2006:8).

Prescribed Daily Dose (PDD):The prescribed daily dose (PDD) is the average daily dose prescribed, as obtained from a representative sample of prescriptions (WHO, 2003:14)

4.3 CLASSIFICATION

The following section contains the classification of the categories of data extracted from the database.

4.3.1 Age

Data obtained were divided into different categories according to age groups as categories indicated in Table 4.1. The division of age groups was obtained from an interview with a paediatrician (Bocking, 2008).

Table 4.1: Age category classification.

Group	Age category (years)	Description
1	≤ 5 years	All patients younger than or equal to 5 years were included in this category – mostly young children.
2	5 < and ≤ 12 years	All patients older than 5 years and younger than or equal to 12 years were included in this category – most of the children were attending school
3	12 < and ≤ 18 years	All patients older than 12 years and younger than or equal to 18 years were included in this category – most of them were adolescents and young adults.
4	> 18 years	All patients older than 18 years were included in this category.

Note: In the tables the frequency of age groups does not add up to the total number of prescriptions due to the fact that in some cases the date of birth (used to calculate the age of the patient on the day of treatment) was not included.

4.3.2 Gender

The gender group is divided into male, female and unknown.

** The frequencies of gender do not add up to the total number of prescriptions due to the unspecified group not included (negligible).

4.3.3 Prescriber

Prescribers of prescriptions were divided into five different groups according to the specialty indicated in the database.

Table 4.2 Prescriber classification

Prescriber
General medical practitioners
Paediatricians
Psychiatrists
Neurologists
Other

Refer to Chapter 3, Section 3.4.4.

4.3.4 Generic indicator of medicine

Various acronyms were used during this study to portray the different types of medicines namely:

Table 4.3: Generic indicators of medicine

Generic indicator	Description
M	Innovator products with patent but the owner of the patent gave permission that the patent may be used by another pharmaceutical company before the expiry date of the patent
N	Innovator products with no generic substitution
O	Innovator products
Y	Generic products

4.4 TOTAL DATABASE

An analysis of the total database will be discussed in this section according to the number of patients, prescriptions and medicine items claimed.

4.4.1 Number of patients

Table 4.4 illustrates the total number of patients for all study years which is sub-divided into gender (refer to Section 3.4.3) and age groups (refer to Section 3.4.2).

Table 4.4: Number of patients in the total database according to gender and age groups for 2005 until 2007

Year	Number of patients	Gender				Age groups (years)							
		Male		Female		≤5 years		>5 and ≤12 years		>12 and ≤18 years		> 18 years	
		n	%	n	%	n	%	n	%	n	%	n	%
2005	1,218,357	540,874	44.39	675,813	55.47	87,898	7.21	117,933	9.68	104,075	8.54	908,445	74.56
2006	1,259,093	559,531	44.44	698,475	55.47	86,085	6.84	116,237	9.23	104,724	8.32	952,032	75.61
2007	911,212	408,734	44.86	502,071	55.10	58,010	6.37	91,508	10.04	86,114	9.45	675,579	74.14

4.4.1.1 Patient general analysis

According to Table 4.4 the number of patients *increased* from 2005 to 2006 with 3.43% followed by a *decrease* in the number of patients with 27.63% from 2006 to 2007. Therefore a *decrease* of 25.21% from 2005 to 2007 could be documented from the data. The results revealed that the number of medical schemes that claimed or the individual members of the medical schemes could have decreased during 2005 to 2007, and this would probably explain the decrease in the number of patients.

4.4.1.2 Patient analysis according to gender

According to Table 4.4, the prevalence percentage of male ($\pm 44\%$) and female ($\pm 55\%$) patients did not change from 2005 to 2007.

4.4.1.3 Patient analysis according to age group

The majority of patients for all study years were in age category 4 (> 18 years) followed by category 2 (> 5 and ≤ 12 years), category 3 (> 12 and ≤ 18 years) and category 1 (≤ 5 years) respectively (refer to Table 4.4).

The results revealed only a small decrease (0.84%) in the percentage prevalence of patients 5 years and younger from 2005 (7.21%) to 2007 (6.37%). This age group was ranked fourth according to the number of patients.

Children aged 5 years to 12 years *increased* only with 0.36% from 2005 (9.68%) to 2007 (10.04%). This age group ranked 2nd for all study years.

The number of adolescents, aged 12 years to 18 years (ranked 3rd) and *increased* with 0.91% from 2005 (8.54%) to 2007 (9.45%).

Most patients were adults (> 18 years) and the percentage prevalence decreased from 2005 (74.56%) to 2007 (74.14%) by 0.42%.

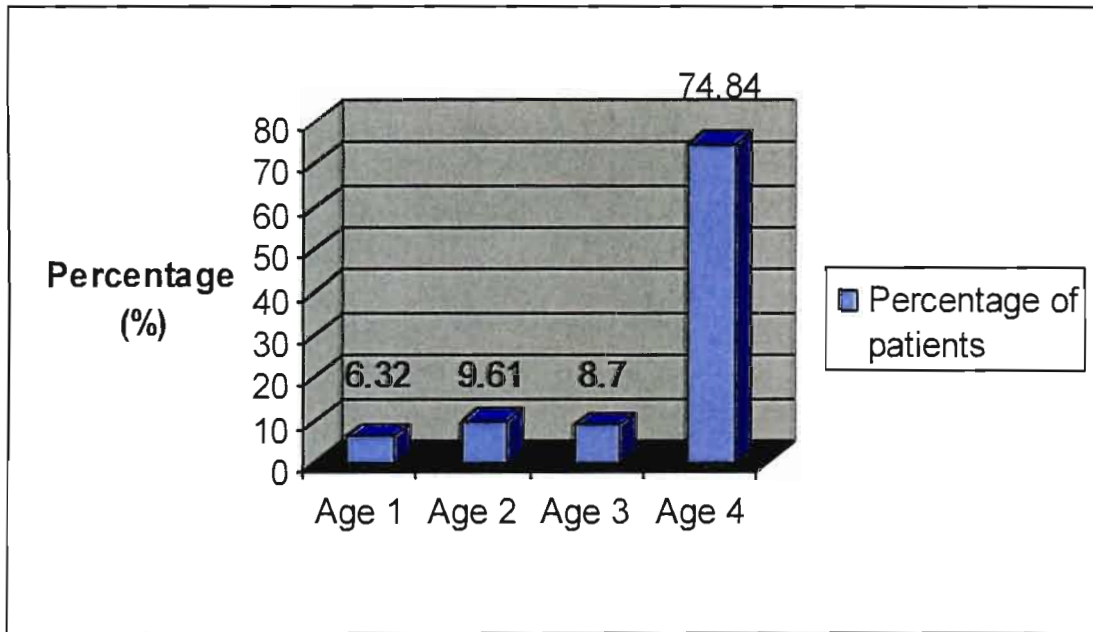


Figure 4.2: Percentage of patients in each age category for all study years

Figure 4.2 is a visual illustration of the prevalence of the number of patients receiving medication for all study years. As can be seen, the majority of patients were 18 years and older.

4.4.2 Number of prescriptions

Table 4.5 is a summarised table, composed from Tables A.1, A.2 and A.3 in Appendix A, and it reflects the general analysis of prescriptions claimed through the PBM during all study years.

Table 4.5: Number of prescriptions in the total database according to gender and age groups for 2005 until 2007.

Year	Number of prescriptions	Gender				Age groups (years)							
		Male		Female		≤ 5 years		5 < and ≤ 12 years		12 < and ≤ 18 years		> 18 years	
		n	%	n	%	n	%	n	%	n	%	n	%
2005	8,522,798	3,403,233	39.93	5,112,373	59.98	391,847	4.60	415,323	4.87	364,879	4.28	7,350,737	86.25
2006	9,048,541	3,621,466	40.02	5,422,200	59.92	405,018	4.48	429,889	4.75	385,402	4.26	7,828,198	86.51
2007	8,015,538	3,196,105	39.87	4,817,599	60.10	324,946	4.05	365,755	4.56	337,548	4.21	6,987,267	87.17

4.4.2.1 Prescriptions general analysis

According to Table 4.5 the number of prescriptions from 2005 to 2006 *increased* by 6.14% with a *decrease* from 2006 to 2007 by 11.42%. Overall the number of prescriptions *decreased* from 2005 to 2007 by 5.95% which may be the result of a decrease in the number of patients as well as medical schemes who claimed through the PBM from 2005 to 2007 (refer to 4.4.1.1) (refer to Table A.1 in Appendix A)

4.4.2.2 Prescription analysis according to gender

Most of the prescriptions claimed through the PBM were for females for all three study years. Prescriptions for females represented 59.98%, 59.92% and 60.10% for 2005, 2006 and 2007 respectively. An *increase* of 0.12% in the number of prescriptions claimed for females was noticed from 2005 to 2007 (refer to Table 4.5). Prescriptions for males represented 39.93% of all prescriptions claimed in 2005, 40.02% in 2006 and 39.87% in 2007. Therefore a *decrease* of 0.06% in the number of prescriptions claimed for males was found from 2005 to 2007 (refer to Table A.2 in Appendix A).

4.4.2.3 Prescription analysis according to age group

The majority of prescriptions for each of the study years were claimed for patients in age category 4 (> 18 years) followed by category 2 (5 < and ≤ 12 years). In 2005 and 2006 it was followed by category 1 (0 < and ≤ 5 years) and in 2007 it was followed by category 3 (12 < and ≤ 18 years) (refer to Table A.3 in Appendix A).

The number of prescriptions claimed for children younger than or equal to 5 years represented 4.60% (n = 391,847) for the year 2005 (N=8,522,798) and 4.48% (n = 405,018) for 2006 (N=9,048,541) and 4.05% (n = 324,946) for 2007 (N=8,015,538). Therefore a *decrease* of 0.55% was found in the number of prescriptions claimed for this age group.

Prescriptions for children aged 5 years to 12 years represented 4.87% in 2005, and in 4.56% (n = 365,755) in 2007. The number of prescriptions decreased by 0.31% from 2005 to 2007.

According to Table 4.5, a total number of 364,879 (4.28%) prescriptions were claimed for adolescents aged 12 years to 18 years in 2005, while in 2007 a total number of 337,548 (4.21%) prescriptions were issued. A decrease of 0.07% was recorded from 2005 to 2007 for this age category.

For adults older than 18 years, a total number of 7,350,737 (86.25%) prescriptions in 2005 and 6,987,267 (87.17%) prescriptions in 2007 were claimed through the PBM with an *increase* of 0.92% from 2005 until 2007.

4.4.3 Number of medicine items

Table 4.6 is a summarised table, composed from Tables A.1, A.2 and A.3 in Appendix A, and it reflects the general analysis of all medicine items claimed during all the study years.

Table 4.6 Number of medicine items in the total database according to gender and age groups for 2005 until 2007.

Year	Number of medicine items	Gender				Age groups							
		Male		Female		≤ 5 years		5 < and ≤ 12 year		> 12 and ≤ 18 years		> 18 years	
		n	%	n	%	n	%	n	%	n	%	n	%
2005	19,606,049	7,777,985	39.67	11,811,901	60.25	974,785	4.97	1,010,808	5.16	834,506	4.26	16,785,929	85.62
2006	21,219,021	8,444,160	39.80	12,764,246	60.15	1,023,923	4.83	1,056,940	4.98	903,193	4.26	18,234,928	85.94
2007	19,146,156	7,590,337	39.64	11,551,895	60.34	827,579	4.32	895,624	4.68	788,341	4.12	16,634,585	86.88

4.4.3.1 Medicine item general analysis

The number of medicine items claimed had *increased* from 2005 (N=19,606,049) to 2006 (N=21,219,021) with 8.23%. From 2006 to 2007 (N=19,146,156) the number of medicine items had *decreased* with 9.77%. Therefore a *decline* in the number of medicine items of 2.35% from 2005 to 2007 has been noticed. A possible explanation for this is that the number of patients who claimed through the database decreased (refer to Section 4.4.1.1) and therefore the number of medicine items could also have decreased from 2005 to 2007.

The results in Appendix A, Table A.1, revealed that the number of medicine items per prescription increased only with 3.91%. Furthermore the number of medicine items per prescription *increased* from 2005 (2.30±1.50) to 2007 (2.39±1.58). However, this increase was not of practical significance ($d < 0.8$).

4.4.3.2 Analysis according to gender

The number of medicine items for females had not really changed from 60.25% (n=11,811,901) in 2005 to 60.34% (n=11,551,895) in 2007. The results further indicated that the number of female patients had not really changed from 2005 to 2007 (refer to Section 4.4.1.2). However, a small change was identified with the average number of medicine items per prescription that *increased* from 2.31±1.53 in 2005 to 2.40±1.61 for female patients by 3.90%. However, this increase was not of practical significance ($d < 0.8$) (refer to table A.2 in Appendix A).

Also for the male group the number of medicine items had not really changed from 39.67% (n=7,777,985) in 2005 to 39.64% (n=7,590,337) in 2007. The number of male patients had also not changed from 2005 to 2007 (refer to Section 4.4.1.2). An *increase* of 3.49% in the average number of medicine items per prescription was noticed from 2005 to 2007.

The following chart (Figure 4.3) illustrates the prevalence percentage of medicine items claimed for the different gender groups for all study years together. (Calculation was done by adding all medicine items for the three-year period per gender group, divided by the added total number of items for study period multiplied by 100).

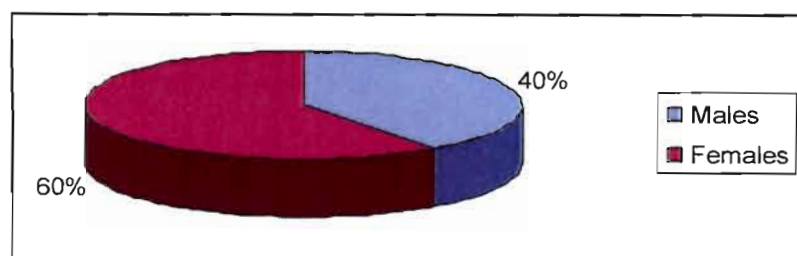


Figure 4.3: Prevalence percentage distribution of the number of medicine items for all study years according to gender groups

4.4.3.3 Analysis according to age groups

The age group 12 years to 18 years (age group 3) had the lowest frequency of prescribed medicine items in all study years. Age group 5 years and younger (age group 1) and 5 years to 12 years (age group 2) had about the same prevalence of prescribed medicine items where age group older than 18 years (age group 4) had the highest frequency in all study years (refer to Table 4.6).

The percentage of children 5 years and younger, according to all medicine items claimed through the South African PBM (refer to Section 2.11.4) for this age group did not really change from 2005 to 2007. The d-value did not reveal any practical significant changes in the number of medicine items per prescription from 2005 (2.49 ± 1.34) to 2007 (2.55 ± 1.38) ($d < 0.8$) for this age group (refer to Table A.3 in Appendix A).

The percentage of medicine items prescribed to children aged 5 to 12 years receiving medicine items during 2005 was 5.16% ($n=1,010,808$) and *decreased* to 4.68% ($n=895,624$) in 2007 with 0.48%. The results revealed that the average number of medicine items per prescription did not change practically significantly from 2005 to 2007 ($d < 0.8$) for this age group (refer to Table A.3 in Appendix A).

The percentage of medicine items prescribed to adolescents aged 12 to 18 years was 4.26% ($n=834,506$) in 2005 and it *decreased* with 0.14% to 4.12% ($n=788,341$) in 2007. From 2005 (2.29 ± 1.30) to 2007 (2.34 ± 1.34), the average number of medicine items per prescription increased by 2.18% (refer to Table A.3 in Appendix A). However, this increase was not of practical significance ($d < 0.8$).

Furthermore, adults older than 18 years received 85.62% ($n=16,785,929$) in 2005 of all medicine items and it *increased* with 1.26% to 86.88% ($n=16,634,585$) in 2007. The number of medicine items per prescription increased from 2.28 ± 1.52 in 2005 to

2.38±1.61 during 2007 by 4.39% (refer to Table A.8 in Appendix B) with no practical significance ($d < 0.8$) (refer to Table A.3 in Appendix A).

4.4.4 Generic indicator of medicine

Tables 4.7 and 4.8 are summarised tables, composed from Tables A.13, A.14 and A.15 in Appendix A. Tables A.13, A.14 and A.15 include the comprehensive data for all study years.

Table 4.7: Number of medicine items in the total database according to generic indicator and gender for 2005 until 2007.

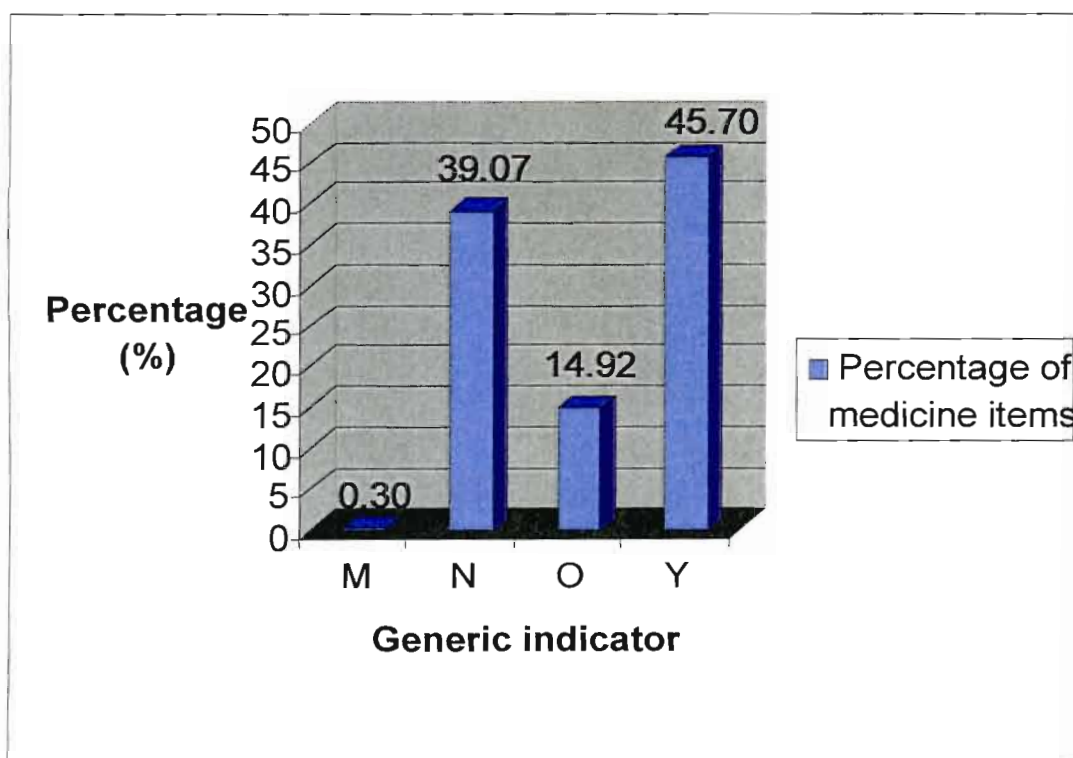
Year	Total number of medicine items	Generic indicator	Number of medicine items		Gender			
					Male		Female	
			N	%	n	%	n	%
2005	19,606,049	M	136,878	0.70	53,691	0.27	83,078	0.42
		N	8,379,008	42.74	3,202,623	16.33	5,170,569	26.37
		O	2,693,298	13.74	1,099,757	5.61	1,591,602	8.12
		Y	8,396,865	42.83	3,421,914	17.45	4,966,652	25.33
	Total		19,606,049	100.01	7,777,985	39.66	6,641,332	60.24
2006	21,219,021	M	32,568	0.15	968	0.00	31,583	0.15
		N	8,026,995	37.83	3,087,130	14.55	4,936,222	23.26
		O	3,242,612	15.28	1,288,989	6.07	1,951,965	9.20
		Y	9,916,846	46.74	4,067,073	19.17	5,844,476	27.54
	Total		21,219,021	100.00	8,444,160	39.79	12,764,246	60.15
2007	19,146,156	M	12,845	0.07	727	0.00	12,118	0.06
		N	7,026,146	36.70	2,626,971	13.72	4,397,480	22.97
		O	3,019,594	15.77	1,262,346	6.59	1,756,460	9.17
		Y	9,087,571	47.46	3,700,293	19.33	5,385,837	28.13
	Total		19,146,156	100.00	7,590,337	39.64	11,551,895	60.33

4.4.4.1 General analysis of medicine items according to the generic indicator

The results in Table 4.7 revealed that the prevalence percentage of generic medicine items ("Y" indicated) *increased* from 42.83% in 2005 to 47.46% in 2007. Thus, an *increase* of 4.63% over the three-year period was documented.

The number of innovator medicine items with patent ("M" indicated) *decreased* from 2005 (0.70%) to 2007 (0.07%) by 0.63%. The number of innovator medicine items with no generic substitutes ("N" indicated) also *decreased* by 6.04% from 2005 (42.74%) to 2007 (36.70%). The number of innovator medicine items ("O" indicated) *increased* from 13.74% in 2005 to 15.77% in 2007. Therefore an *increment* of 2.03% was documented (refer to Table A.13 in Appendix A).

From Table 4.7 it can be seen that the generic medicine items ("Y" indicated) and innovator medicine items with no generic substitutes ("N" indicated) had the highest frequency of all medicine items claimed. Furthermore in 2005 the generic medicine and innovator medicine items with no generic substitutes had about the same frequency where in 2006 and 2007 these varied significantly.



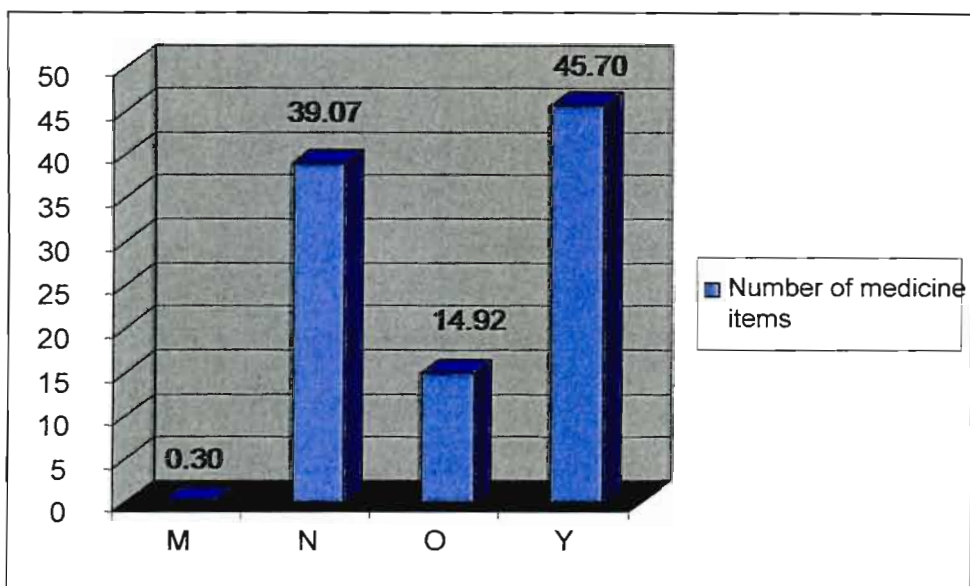


Figure 4.4: Prevalence percentage of the type of medicine items for all three study years

4.4.4.2 Analysis of medicine items according to generic indicator and gender

With regard to females, the prevalence percentage of innovator medicine items with patent (“M” indicated) and innovator medicine items with no generic substitution (“N” indicated) *decreased* from 2005 to 2007 with 0.36% and 3.4% respectively. Whereas the innovator medicine items (“O” indicated) and generic items (“Y” indicated) prevalence percentage *increased* with 1.05% and 2.80% respectively from 2005 to 2007 (refer to Table A.14 in Appendix A).

From afore stated table (Table 4.7), for the males prevalence percentage of the innovator products with patent (“M” indicated) and innovator products with no generic substitution (“N” indicated) *decreased* from 2005 to 2007 by 0.68% and 6.57% respectively. Furthermore, the prevalence percentage of innovator (“O” indicates) and generic medicine items (“Y” indicated) *increased* from 2005 to 2007 by 2.49% and 4.76% respectively (refer to Table A.14 in Appendix A).

The following chart (Figure 4.5) represents in percentage the contribution made by each medicine type to the total number of medicine items claimed during the three study years. For both males and females the original products with no generic substitution (“N” indicated) and generic items indicated had the highest prevalence of all medicine items claimed for both genders. In 2005 there was a small difference between the items indicated “N” and “Y” where in 2006 and 2007 the difference

increased about five times. From Figure 4.5 it can be seen that the number of original products with patent ("M" indicated) is negligible (refer to Table A.14 in Appendix A).

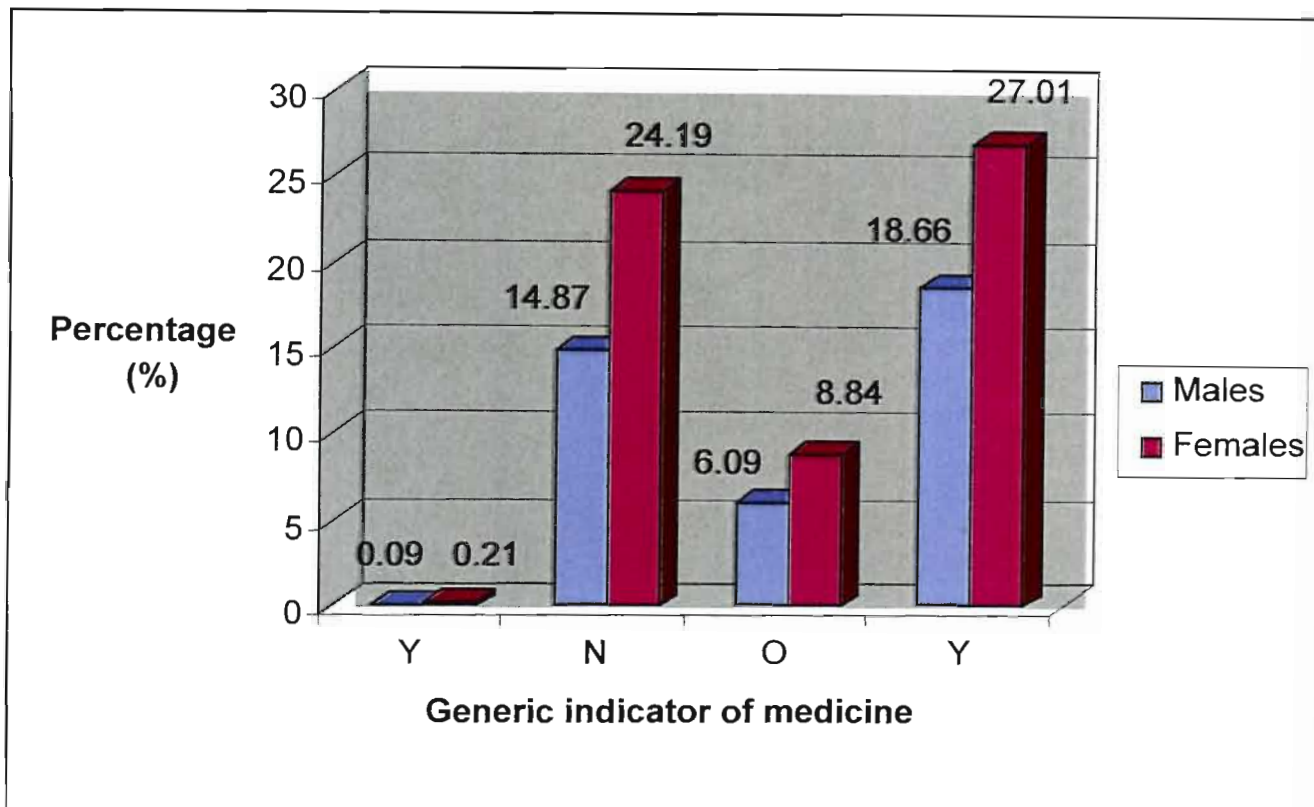


Figure 4.5: Prevalence percentages of the medicine items according to generic indicator and gender for all study years

The following table (Table 4.8) includes the general analysis of all medicine items claimed according to generic indicator for the different age groups (refer to chapter 3, section 3.4.2).

Table 4.8: Number of medicine items in the total database according to generic indicator of medicine and age group for 2005 until 2007.

Year	Total number of medicine items	Generic Indicator	Number of medicine items		Age groups							
					0 < age ≤ 5		6 < age ≤ 12		12 < age ≤ 18		18 < age	
			N	%	n	%	n	%	n	%	n	%
2005	19,606,049	M	136,878	0.70	12,013	0.06	7,484	0.04	8,827	0.05	108,554	0.55
		N	8,379,008	42.74	406,856	2.08	398,394	2.03	319,115	1.63	7,254,628	37.00
		O	2,693,298	13.74	147,341	0.75	140,284	0.72	115,333	0.59	2,290,340	11.68
		Y	8,396,865	42.83	408,575	2.08	464,646	2.37	391,231	2.00	7,132,407	36.38
		Total	19,606,049	100.01	974,785	4.97	1,010,808	5.16	834,506	4.27	16,785,929	85.61
2006	21,219,021	M	32,568	0.15	24	0.00	60	0.00	617	0.00	31,867	0.15
		N	8,026,995	37.83	401,518	1.89	377,809	1.78	316,789	1.49	6,930,845	32.66
		O	3,242,612	15.28	168,320	0.79	166,113	0.78	129,306	0.61	2,778,870	13.10
		Y	9,916,846	46.74	454,061	2.14	512,958	2.42	456,481	2.15	8,493,346	40.03
		Total	21,219,021	100.00	1,023,923	4.82	1,056,940	4.98	903,193	4.25	18,234,928	85.94
2007	19,146,156	M	12,845	0.07	12	0.00	35	0.00	603	0.00	12,195	0.06
		N	7,026,146	36.70	328,831	1.72	321,746	1.68	276,887	1.45	6,098,656	31.85
		O	3,019,594	15.77	138,844	0.73	142,381	0.74	111,643	0.58	2,626,726	13.72
		Y	9,087,571	47.46	359,892	1.88	431,462	2.25	399,208	2.09	7,897,008	41.25
		Total	19,146,156	100.00	827,579	4.33	895,624	4.67	788,341	4.12	16,634,585	86.88

4.4.4.3 Analysis of medicine items according to generic indicator and age groups

As can be seen from Table 4.5 the percentage of innovator medicine with patent ("M" indicated) prescribed to children five years and younger *decreased* with 0.06%, the innovator medicine items with no generic substitution ("N" indicated) *decreased* with 0.36%, the innovator medicine items ("O" indicated) *decreased* by 0.02% and finally generic items ("Y" indicated) also *decreased* by 0.02% from 2005 to 2007 (refer to Table A.15 in Appendix A).

According to Table 4.8 the prevalence percentage of innovator medicine items with patent ("M" indicated) prescribed to children aged 5 years to 12 years *decreased* with 0.04%, the innovator medicine items with no generic substitution ("N" indicated) *decreased* by 0.35%, the innovator medicine items ("O" indicated) *increased* by 0.02% and generic medicine items ("Y" indicated) *decreased* by 0.12% from 2005 to 2007 (refer to Table A.15 in Appendix A).

It was found that the percentage of innovator medicine items with patents ("M" indicated), innovator medicine items with no generic substitution ("N" indicated) and innovator medicine items ("O" indicated) prescribed to adolescents aged 12 years to 18 years *decreased* by 0.05%, 0.18% and 0.01% according to (Table 4.8) Furthermore there was an *increase* of 0.09% in generic medicine items prescribed to this age group ("Y" indicated) from 2005 to 2007 (refer to Table A.15 in Appendix A).

In conjunction with above results, it was indicated in the adult age group 18 years and older that there was a *decrease* in the number of innovator medicine items with patents ("M" indicated) by 0.49% and innovator medicine items with no generic substitution ("N" indicated) by 5.15% from 2005 to 2007. From these results, an *increase* of 2.04% in the innovator medicine items ("O" indicated) and an increase of 4.87% in generic medicine items ("Y" indicated) could be noticed (refer to Table A.15 in Appendix A).

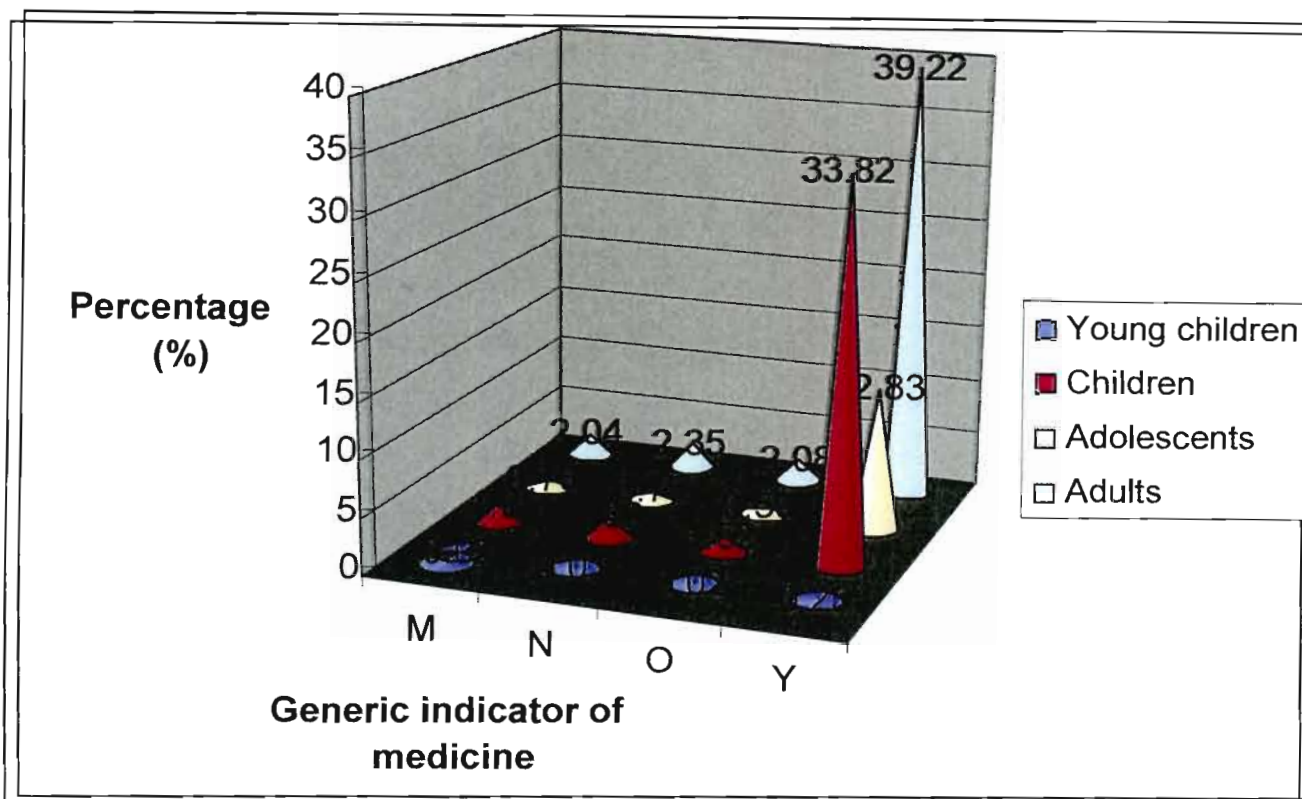


Figure 4.6: Prevalence percentage of the medicine items according to generic indicator and age group for all study years

4.4.5 Medicine cost

For the conversion of RSA Rand value with the three profound currencies in the world the following table was composed. This table may be used to convert the Rand value into an estimated value for profound currencies for international usage. These values were valid at the time of the study.

Table 4.9 Conversion factor from RSA Rand to the international bank rate

Year	Exchange rates	Average (365 days)
2005	RSA Rand/US Dollar	6.38112
	RSA Rand/EURO	7.92944
	RSA Rand/British Pound	11.60356
2006	RSA Rand/US Dollar	6.78812
	RSA Rand/EURO	8.53141
	RSA Rand/British Pound	12.53797
2007	RSA Rand/US Dollar	7.06926
	RSA Rand/EURO	9.67099
	RSA Rand/British Pound	14.14465

4.4.5.1 Total medicine cost

The total medicine cost will be discussed according to a general analysis, an analysis according to gender and age groups and the generic indicators of the medicine (prescriptions).

4.4.5.1.1 General cost analysis

According to Table A.4 in Appendix A the total cost of all the medicine items *increased* from 2005 (R1, 840,663,948.74) to 2007 (R1,933,070,365.79) by 5.02%. In 2006 the total cost of all medicine items reached a maximum of R1,985,049,228.54.

The total medicine item cost was derived from the medical scheme contribution and the patient contribution. In 2005 (N = R1, 840,663,948.74) the medical scheme contribution was R1, 621,622,347.52 while the patient contribution was R219, 041,601.22. In 2006 (N = R1,985,049,228.54) and 2007 (N = R1,933,070,365.79) the medical scheme contribution was R1,721,807,653.68 and R1,627,907,850.83 while the patient contribution was R263,241,574.86 and R305,162,514.96 respectively (refer to Table A.4 in Appendix A).

The results in Figure 4.5 revealed a *decrease* in medical scheme contribution and an *increase* in patient contribution of 3.89% from 2005 to 2007.

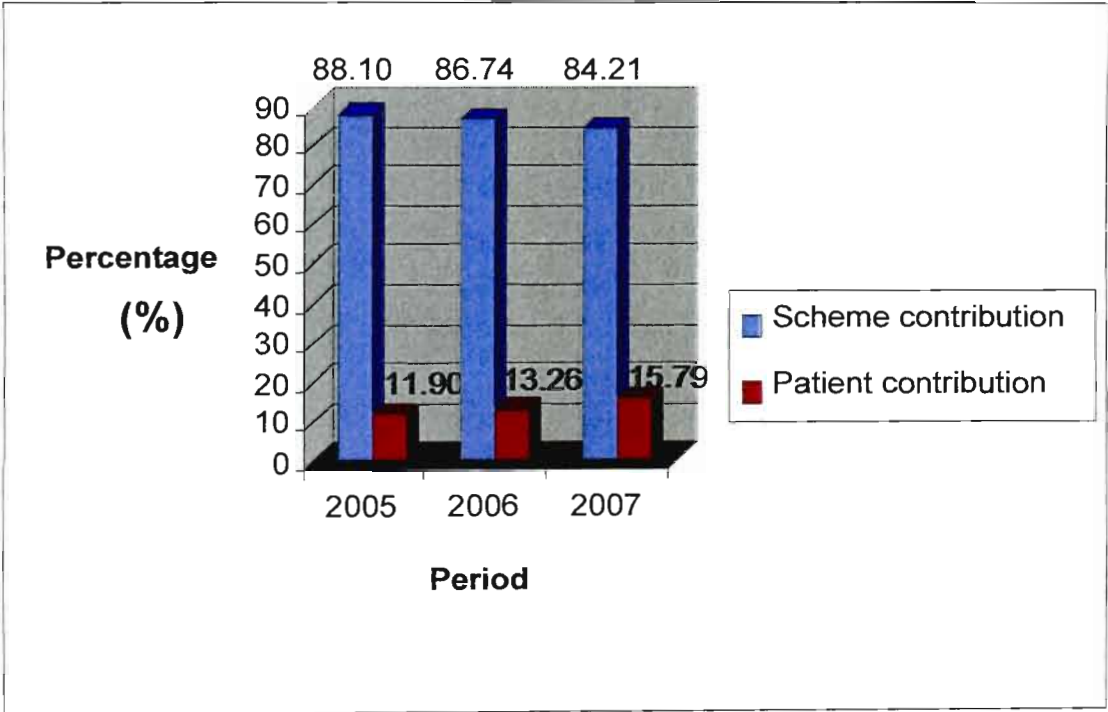


Figure 4.7: Illustrating the percentage cost contribution of medical scheme vs the patient

4.4.5.1.2 Cost analysis according to gender

According to Table A.5 in Appendix A, the total cost of all medicine items for females during 2005 was R1,096,609,592.32 where in 2007 it increased to R1,146,277,609.55 with an *increment* of 4.53%. In 2006 the total cost of medicine items for females reached a maximum of R1,176,562,838.40 although there was not a significant difference for the study period. For males the total cost for 2005 was R742,576,523.73 and in 2007, R786,203,377.57 with once again reaching a maximum in 2006 with R807,352,693.92. An *increment* of 5.88% was noticed from 2005 to 2007 for males. Males and females represented 40.57% and 59.38% of the total cost of all medicine items respectively for the study period.

Derived from Table A.5 from Appendix A the medical scheme contribution for the female gender in 2005 (N = R1, 096,609,592.32) was R958, 684,336.56 while the patient contribution concluded to R137, 925,225.76. For 2006 (N = R1,176,562,838.40) and 2007 (N = R1,146,277,609.55) the medical scheme contributed R1,011,957,533.22 and R955,952,899.90 while the patient contributed R164,605,305.18 and R190,324,709.65 respectively. Medical scheme contribution for females *inclined* by 4.02% from 2005 (12.58%) to 2007 (16.60%).

According to Table A.5 in Appendix A the medical scheme contribution for males in 2005 (N = R742, 576,523.73) was R611, 541,214.39 with a patient contribution of R81, 035,309.34. Furthermore in 2006 (N = R807,352,693.92) and 2007 (N = R786,203,377.57) the medical scheme contribution was R708,828,472.95 and R671,441,524.28 with a patient contribution of R98,524,490.97 and R114,761,853.29. In the male category the contribution by the patients *declined* by 3.05% from 2005 (17.65%) to 2007 (14.60%).

4.4.5.1.3 Cost analysis according to age groups

The total medicine cost for young children at the age of 5 years and younger decreased by 13.42% from 2005 (R52,238,121.63) to 2007 (R45,228,627.09). The total medicine cost of children aged 5 to 12 years indicated a decrease from 2005 (R61,472,357.05) to 2007 (R57,973,545.10). Adolescents at the age of 12 years to 18 years had a total cost of R59,734,845.85 in 2005 and it decreased with 2.47% to

R58,293,879.25 in 2007. The total cost for adults older than 18 years increased from 2005 (R1,667,217,371.91) to 2007 (R1,771,572,605.87) by 6.26% (refer to Table A.6 in Appendix A).

Furthermore young children 5 years and younger represented 2.64%, children aged 5 years to 12 years represented 3.19%, adolescents aged 12 years to 18 years represented 3.15% and adults of the age 18 years and older represented 91.02% of the total medicine cost for all study years (refer to Table A.6 in Appendix A).

The patient contribution for young children aged 5 years and younger for 2005 (N = R52, 238,121.63) was R4, 920,632.96 while the medical scheme contributed the additional R47, 317,488.67. In 2007 (N = R45, 228,627.09) patients contributed R7, 831,910.87 to the total cost for this age category while the medical scheme contributed R37, 396,716.22. Therefore an *increase* of 7.90% was noticed in the patient contribution of patients in this age group from 2005 to 2007 (refer to Table A.6 in Appendix A).

For children aged 5 years to 12 years the patient contribution for 2005 (R61, 472,357.05) was 9.27% (R5, 698,875.55) while the medical scheme contributed 90.73% (R55, 773,481.50). In 2007 (R57, 973,545.10) the total patient contribution was 15.17% (R8, 794,231.95) while the medical scheme contributed 84.83% (R49, 179,313.15). Therefore an *increase* of 5.90% in patients' contribution from 2005 to 2007 was noticed (refer to Table A.6 in Appendix A).

The percentage of patient contribution for patients aged 12 years to 18 years for 2005 (N = R59, 734,845.85) was R6, 359,256.25 while the medical scheme contributed the additional R59, 734,845.85. In 2007 (N = R58, 293,879.25) patients contributed R9, 368,436.03 to the total cost for this age category while the medical scheme contributed R48, 925,443.22. Therefore an *increase* of 5.42% in patient contribution from 2005 to 2007 was documented for this age group (refer to Table A.6 in Appendix A).

In 2005 adults 18 years and older (N = R1, 667,217,371.92) had a patient contribution of R202, 062,836.46 while the medical scheme contributed R1, 465,154,535.46. In 2007 (N = R1, 771,572,605.87) the patients contributed R279, 167,880.10 while the medical scheme contributed the additional R1, 492,404,725.78. Therefore an *increment* of 3.64% was noticed in patient contribution from 2005 to 2007 (refer to Table A.6 in Appendix A).

4.4.5.2 Average medicine cost per prescription containing methylphenidate and/or atomoxetine

The average medicine cost per prescription will be discussed according to general analysis, and an analysis according to gender and age groups (refer to Tables A.4, A.5 and A.6).

4.4.5.2.1 General analysis of the average cost per prescriptions

According to Table A.4 in Appendix A the average cost per prescription for 2005 was R215.97±347.98. For 2006 and 2007 the average cost per prescription was R219.38±401.76 and R241.17±601.64 respectively. No practically significant difference was found in the average cost per prescription between the different years ($d < 0.8$).

In 2005 the average medical scheme contribution per prescription was R190.27±330.01 while the average patient contribution per prescription was R25.70±81.75. In 2006 and 2007 the average medical scheme contribution per prescription was R190.29±384.99 and R203.09±565.94 while the average patient contribution per prescription was R29.09±88.81 and R38.07±171.88 respectively. The average patient contribution per prescription *increased* from 2005 to 2007 by 48.13% and the average medical scheme contribution *increased* by 6.74%. However, these changes were not of practical significance ($d < 0.8$) (refer to Table A.4 in Appendix A).

4.4.5.2.2 Average medicine cost per prescription: analysis according to gender

According to Table A.5 in Appendix A, the average medicine cost per prescription for females during 2005 was R214.50±336.72, which progressively *increased* with 10.93% to R237.94±559.63 in 2007. For males the average medicine cost per prescription during 2005 was R218.20±363.47 while in 2007 it was R245.99±659.85 with an *increase* of 12.74%. The results revealed that there was no practically significant difference in the average medicine cost per prescription in the changes between males and females over the study period.

For female patients in 2005 (R214.50±336.72) the average patient contribution per prescription was R26.98±81.75 while the average medical scheme contribution per prescription was R187.52±317.49. For 2006 (R216.90±385.90) and 2007 (R237.94±559.63) the average patient contribution per prescription was R30.56±90.34 and R39.51±150.13 while the average medical scheme contribution

per prescription was R186.63±367.71 and R198.43±529.85 respectively (refer to Table A.5 in Appendix A). Therefore the patient contribution *increased* by 46.44% and the medical scheme contribution decreased by 5.82% from 2005 to 2007.

In 2005 male patients (R218.20±363.47) contributed R23.81±81.76 to the average medicine cost per prescription while the medical scheme contributed an average of R194.39±347.11 per prescription. In 2006 (R222.94±424.19) and 2007 (R245.99±659.85) the average patient contribution per prescription was R27.21±86.47 and R35.91±200.27 while the average medical scheme contribution per prescription was R195.73±409.24 and R210.08±616.21 respectively (refer to Table A.5 in Appendix A). The average patient contribution per prescription had increased from 2005 to 2007 by 50.82%.

4.4.5.2.3 Average medicine cost per prescription: analysis according to age groups

According to Table A.6 in Appendix A, young children aged 5 years and younger had an average medicine cost per prescription of R133.31±139.25 in 2005 and in 2007 R139.19±252.74, showing an *increase* of 4.50%. The average medicine cost per prescription of children aged 5 years to 12 years *increased* with 7.09% from 2005 (R148.01±153.84) to 2007 (R158.50±188.70). Adolescents aged 12 years to 18 years had an average medicine cost per prescription of R163.71±210.48 in 2005 and R172.70±334.44 in 2007 with an *increase* of 5.49%. Adults older than 18 years had an average medicine cost per prescription of R226.81±367.36 in 2005 and in 2007 it amounted to R253.54±635.44 with an *increase* of 11.79%.

Children 5 years and younger (R133.31±139.25) contributed on average R12.56±44.02 in 2005 while the medical scheme contributed R120.76±131.79. In 2007 (R139.19±252.74) patients contributed R24.10±182.76 and the medical scheme contributed the additional R115.09±164.23. A *increase* of 91.88% in patient contribution was found from 2005 to 2007. No practically significant difference was found for the average cost per prescription for the age groups for the years 2005 to 2007 ($d < 0.8$) (refer to Table A.6 in Appendix A).

Children 5 years to 12 years contributed R148.01±153.84 in 2005, on average, R13.72±44.32 per prescription while the medical scheme contributed R134.29±145.96. In 2007 (R158.50±188.70) the patients contributed R24.04±63.60 where the medical scheme contributed the additional R134.46±172.46. Patient contribution *increased* with 75.22% from 2005 to 2007 (refer to Table A.6 in Appendix

A). The results revealed that there was no practically significant difference in the average medicine cost per prescription in this age group from 2005 to 2007 ($d < 0.8$).

Adolescents 12 years to 18 years ($R163.71 \pm 210.48$) contributed on average $R17.43 \pm 54.85$ in 2005 where the medical scheme contributed $R146.28 \pm 200.17$. In 2007 ($R172.70 \pm 334.44$) patients contributed on average $R27.75 \pm 114.01$ while the medical scheme contributed $R114.94 \pm 308.53$ to the average medicine cost per prescription. Patient contribution *increased* from 2005 to 2007 with 5.42% (refer to Table A.6 in Appendix A). However, these results reveal that there were no practically significant differences between the patient contributions from 2005 to 2007. The same results were found for the medical scheme contribution ($d < 0.8$).

Adults older than 18 years ($R226.81 \pm 367.36$) contributed on average $R27.49 \pm 85.79$ per prescription while the medical scheme contributed $R199.32 \pm 348.62$ in 2005. In 2007 ($R253.54 \pm 635.44$) the medical scheme contributed on average $R213.59 \pm 599.27$ to the largest part of the average medicine cost per prescription where the patients contributed the additional $R39.95 \pm 177.40$. The patient contribution *increased* from 2005 to 2007 by 45.33% (refer to Table A.6 in Appendix A). As the results revealed, there were no practically significant differences in the patient as well as the medical scheme contributions from 2005 to 2007 ($d < 0.8$).

4.4.5.3 Average cost per medicine item

4.4.5.3.1 General analysis of average cost per medicine item

According to Table A.13 in Appendix A, the average medicine cost per medicine item was $R93.88 \pm 173.01$ in 2005 and it progressively *increased* to $R100.96 \pm 329.82$ in 2007 (7.54%). From 2005 to 2007 there were no changes of practical significance ($d < 0.8$) in the average medicine cost per medicine item.

In 2005 the average cost per medicine item was $R93.88 \pm 173.01$ with an average patient contribution of $R11.17 \pm 43.20$ and a medical scheme contribution of $R82.71 \pm 165.92$. In 2006 ($R93.55 \pm 204.23$) and 2007 ($R100.96 \pm 329.82$) the average contribution by patients per medicine item was $R12.41 \pm 45.92$ and $R15.94 \pm 102.35$ while the average medical scheme contribution was $R81.14 \pm 197.88$ and $R85.03 \pm 309.61$ respectively. An *increase* in the average patient contribution and medical scheme contribution from 2005 to 2007 by 42.70% and 2.80% was identified respectively (refer to Table A.13 in Appendix A).

4.4.5.3.2 Analysis of average cost per medicine item according to gender

According to Table A.14 in Appendix A, females had an average cost per medicine item of R92.84±165.28 in 2005 and in 2007 of R99.23±305.38 with an increase of 6.88%. Furthermore for males the average medicine cost per medicine item was R95.47±183.68 in 2005 and R103.58±363.80 in 2007 with an increment of 8.49%. The d-value calculated between the average cost per medicine item for males and females during 2005 to 2007 was 0.02, which is a small effect that indicated that the effect had no practical significance ($d < 0.8$).

For 2005 (R92.84±165.28) the average medical scheme contribution for females was R81.16±158.05 while patients contributed R11.68±42.24. In 2006 (R92.18±195.39) and 2007 (R99.23±305.38) patients contributed on average R12.90±46.11 and R16.48±85.48 while medical schemes contributed on average R79.18±188.75 and R82.75±290.74 respectively (refer to Table A.14 in Appendix A). The patient contribution increased from 2005 (12.58%) to 2007 (16.61%) with 41.10%.

In 2005 (R95.47±183.68) the patients' contribution to the average cost per medicine items for males was R10.42±44.62 while the medical scheme contributed on average R85.05±176.71. In 2006 (R95.61±216.68) and 2007 (R103.58±36.80) the medical scheme contributed on average R83.84±210.69 and R88.46±336.18 while patients only contributed on average R11.67±45.64 and R15.12±123.71 respectively (refer to Table A.14 in Appendix A). Therefore an *increase* in the patient contribution from 2005 (10.91%) to 2007 (14.60%) was noticeable by 45.11%.

4.4.5.3.3 Analysis of average cost per medicine item according to age groups

Analysis according to age groups was done by extracting data from Table A.15 in Appendix A.

Young children patients aged 5 years and younger had an average cost per medicine item of R53.59±68.48 in 2005 and it *increased* to R54.65±124.86 in 2007 by 1.98%. Children aged 5 and to 12 years had an *increase* of 6.43% in the average cost per medicine item from 2005 (R60.82±81.60) to 2007 (R64.73±99.63). Furthermore adolescents aged 12 years to 18 years had an average cost per medicine item of R71.58±116.04 in 2005 and of R73.95±197.82 in 2007 with an *increase* of 3.31%, and adults older than 18 years had an average cost per medicine item of R99.32±182.77 in 2005 and in 2007 of R106.50±349.00 with an *increase* of 7.23% (refer to Table A.15 in Appendix A).

Young children 5 years and younger (R53.59±68.48) contributed on average R5.05±22.72 in 2005 while the medical scheme contributed on average R48.54±64.36 per medicine item. In 2007 (R54.65±124.86) patients contributed on average R9.46±88.53 per medicine item and the medical scheme contributed the additional R115.09±164.23. An *increase* of 87.33% in patient contribution from 2005 to 2007 was noticeable (refer to Table A.15 in Appendix A). The d-value calculated for this age group was 0.01 which indicated a small effect and therefore there were no practically significant differences in the patient and medical scheme contributions from 2005 to 2007 ($d < 0.8$).

Children aged 5 years to 12 years (R60.82±81.60) contributed R5.63±23.62 on average per medicine item, while the medical schemes contributed R55.18±77.08. In 2007 (R64.73±99.63) the patients contributed R9.82±34.15 where the medical scheme contributed the additional R54.91±90.78. The patient contribution per medicine item *increased* with 74.42% from 2005 to 2007 (refer to Table A.15 in Appendix A). The results revealed no practically significant differences in the patients' and medical schemes' contributions from 2005 to 2007 ($d < 0.8$).

Adolescents aged 12 years to 18 years (R71.58±116.04) contributed on average R7.62±30.74 in 2005 where the medical scheme contributed R63.96±109.95. In 2007 (R73.95±197.82) patients contributed on average R11.88±70.12 while the medical scheme contributed R62.06±181.36 to the average medicine cost per prescription. The average patient contribution *increased* from 2005 to 2007 with 55.91% (refer to Table A.15 in Appendix A). For adolescents aged 12 years to 18 years the d-value was calculated as 0.01 which indicated that there was a small effect with no practically significant differences in the patient and medical scheme contributions from 2005 to 2007 ($d < 0.8$).

Adults older than 18 years and older (R99.32±182.77) contributed on average R12.04±45.42 per medicine item in 2005 while the medical scheme contributed R87.28±175.51. In 2007 (R106.50±349.00) the medical scheme contributed on average R89.72±328.33 and the patients contributed the additional R16.78±106.52. The patient contribution *increased* from 2005 to 2007 by 39.37% (refer to Table A.15 in Appendix A). For adults from the age of 18 years and older the d-value was calculated as 0.02 which indicated that there was a small effect with no practically significant differences in the patient and medical scheme contributions from 2005 to 2007 ($d < 0.8$).

4.4.5.4 Average medicine cost per generic indicator of medicine

4.4.5.4.1 General analysis of the average cost per medicine item according to generic indicator

Data were extracted from Tables A.13, A.14 and A.15 from Appendix A.

According to Table A.13 in Appendix A, the average cost per medicine item for innovator products with patents ("M" indicated) was R86.69±86.46 in 2005 and *decreased* by 45.72% to R59.49±69.22 in 2007. Innovator products with no generic substitution ("N" indicated) had an average cost of R137.32±236.94 per medicine item in 2005 and *increased* by 12.44% to R154.40±518.90 in 2007. Furthermore the innovator products ("O" indicated) had an *increase* of 2.65% from 2005 (R99.81±138.25) to 2007 (R102.45±179.48). Generic products ("Y" indicated) *increased* from R48.76±60.72 in 2005 to R59.21±79.67 by 21.43% in 2007.

In 2005 (R86.69±86.46) the average contribution by patients per innovator product with a patent ("M" indicated) was R8.50±26.74 and the medical scheme contributed R78.19±79.82. In 2006 (R95.62±38) and 2007 (R59.49±69.22) the patients contributed on average R13.15±26.15 and R18.79±35.04 respectively. The medical scheme contributed on average R82.47±43.43 and R40.71±67.40 for 2006 and 2007 respectively (refer to Table A.13 in Appendix A). An *increase* in the patient contribution from 9.81% in 2005 to 31.59% in 2007 by 121.06% was found.

In 2005 (R137.32±236.94) patients contributed on average R15.05±59.08 for innovator products with no generic item ("N" indicated) while the medical scheme contributed R122.26±228.73. In 2006 (R141.36±299.36) and 2007 (R154.40±518.90) the average patient's medicine contribution was R17.23±64.69 and R21.85±162.76 respectively. The medical scheme contributed on average R124.13±292.18 and R132.55±487.70 for each study year respectively. The patient contribution *increased* from 2005 (10.96%) to 2007 (14.15%) by 45.18%. No practically significant differences in the patient and medical scheme contribution were found from 2005 to 2007 ($d < 0.8$).

Innovator products ("O" indicated) (R99.81±138.25) showed an average patient contribution of R18.38±40.68 in 2005 where the average medical scheme contribution was R81.43±131.75. In 2006 (R102.52±160.23) and 2007 (R102.45±179.48) the patient contributed on average R20.55±46.01 and R26.18±53.18 respectively. The medical scheme contributed on average R81.97±153.00 and R76.27±168.60 respectively for 2006 and 2007. An *increase* in

the patient contribution from 2005 (18.41%) to 2007 (25.55%) was noticeable by 42.44%. The results revealed that there was no practically significant differences during 2005 to 2007 ($d < 0.8$) for patient contribution or medical scheme contribution (refer to Table A.13 in Appendix A).

Generic products ("Y" indicated)(R48.76±60.72) indicated an average patient contribution of R 5.03±16.16 in 2005 while the medical scheme contributed on average R43.73±57.63. In 2006 (R51.91±68.57) and 2007 (R59.21±79.67) the patients contributed on average R5.83±18.62 and R7.96±22.90. The medical scheme contribution on average R46.08±65.55 and R51.25±75.42 respectively for 2006 and 2007 (refer to table A.13 in appendix A). An *increase* in patient contribution of 58.25% from 2005 (10.32%) to 2007 (13.44%) was documented with no practical significance ($d < 0.8$).

In conclusion the medical scheme contribution in all categories had decreased from 2005 to 2007. The average cost per medicine for innovator products with patent ("M" indicated) was the only medicine type that decreased from 2005 to 2007 whereas the others increased.

4.5 ANALYSIS OF METHYLPHENIDATE AND ATOMOXETINE CONTAINING PRODUCTS

This section will address the number of patients, prescriptions and medicine items claimed through the medicine claims database for individuals with specific reference to products containing methylphenidate and atomoxetine.

4.5.1 Number of patients

Table 4.10 reveals the number of patients who received prescriptions for methylphenidate and atomoxetine containing products.

Table 4.10 Number of patients who received products containing methylphenidate and atomoxetine for the years 2005 until 2007

Year	Number of patients	Gender				Age groups (years)							
		Male		Female		≤ 5 years		>5 and ≤12 years		> 12 and ≤18 years		> 18 years	
		N	%	n	%	n	%	n	%	n	%	n	%
2005	7,990	5,755	72.03	2,217	27.75	73	0.91	4,284	53.62	2,103	26.32	1,530	19.15
2006	8,575	6,184	72.12	2,380	27.76	79	0.92	4,474	52.17	2,283	26.62	1,739	20.28
2007	7,828	5,549	70.89	2,274	29.05	87	1.11	3,854	49.23	2,143	27.38	1,744	22.28

4.5.1.1 General analysis of patients who received products containing methylphenidate and atomoxetine

From the total number of patients on the database in 2005 (N=1,218,357) a total of 7,990 (0.66%) received products containing methylphenidate and atomoxetine. The same trend was experienced in 2006 (N = 1,259,093) with 0.68% (n = 8,575). In 2007 (N = 911,212) the number of patients receiving products containing methylphenidate and atomoxetine represented 0.86% (n = 7,828) (Refer to Tables 4.10 and 4.4). The percentage of patients who received methylphenidate and atomoxetine containing products did not really change from 2005 to 2007.

Table 4.10 reveals an *increase* of 7.32% from 2005 to 2006 and a further *decrease* of 8.71% from 2006 to 2007 in the number of patients who received one or more prescriptions containing methylphenidate and atomoxetine products. From 2005 to 2007 a decrease of 2.03% in the number of patients who received prescriptions with methylphenidate and atomoxetine containing products was observed.

4.5.1.2 Analysis of patients who received products containing methylphenidate and atomoxetine according to gender

In 2005 (N=675,813) female patients who received products containing methylphenidate and atomoxetine represented 0.33% (n = 2,217) of all female patients on the database. They represented 0.45% (n = 2,274) of all female patients in 2007 (N = 502,071) (Refer to Tables 4.4 and 4.10).

Of all patients who received products containing methylphenidate and atomoxetine, females represented 27.75% in 2005 and 29.05% in 2007 (Refer to Tables 4.4 and 4.10).

Male patients who received products containing methylphenidate and atomoxetine represented 1.06% (n = 5,755) of the total number of male patients in 2005 (N = 540,874). In 2007 (N=408,734) they represented 1.36% of all male patients on the database. Of all patients who received products containing methylphenidate and atomoxetine, males represented 72.03% in 2005 and decreased with 1.14% in 2007 to 70.89% (Refer to Tables 4.4 and 4.10).

The ratios between males to females for 2005, 2006 and 2007 were 2.60 to 1, 2.60 to 1 and 2.44 to 1. A ratio of ± 2.55 to 1 for the study period of 2005 to 2007 was calculated whereas Marcetti *et al.* (2001:1905) identified an *international standard* ratio of 3 to 1 for males to females.

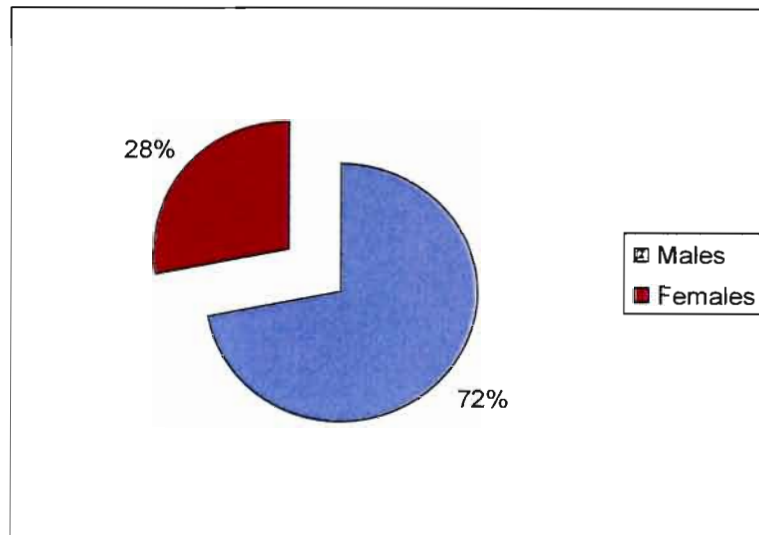


Figure 4.8: Prevalence percentages of products containing methylphenidate and atomoxetine for males and females during all three study years

4.5.1.3 Analysis of patients who received products containing methylphenidate and atomoxetine according to age groups

In 2005 young children 5 years and younger who received products containing methylphenidate and atomoxetine represented only 0.08% (n = 73) of the total number of patients in this age group (N = 87,989). Furthermore, in 2007 (n = 58,010) they represented 0.15% (n = 87) of all patients in the age group 5 years and younger (Refer to Tables 4.4 and 4.10).).

Of all children aged 5 years to 12 years (n = 117,933), 3.63% (n = 4,284) of patients received products containing methylphenidate and atomoxetine in 2005. They *increased* to 4.21% (n=3,854) of all patients (n = 91,508) in this age group during 2007 (Refer to Tables 4.4 and 4.10).

Of the 104,075 adolescents aged 12 years to 18 years, only 2,103 (2.02%) patients received products containing methylphenidate and atomoxetine in 2005. They increased to 2,143 (2.49%) in 2007 (N = 86,114) (Refer to Table A.10 in Appendix A).

Adults older than 18 years who received products containing methylphenidate and atomoxetine represented 0.17% (n = 1,530) of the total number of patients (n = 908,445) during 2005. They increased to 0.26 % (n = 1,744) during 2007 (n = 675,579) (Refer to Tables 4.4 and 4.10).

The results revealed that the majority of patients who received prescriptions for products containing methylphenidate and atomoxetine were children 5 years to 12 years (51.70%, n=12,612), followed by adolescents 12 years to 18 years with 26.77% (n=6,529), adults older than 18 years with 20.55% (n=5,013) and lastly young children aged 5 years and younger (n=239) with 0.98% for all study years (n=24,393) (Refer to Table 4.10) .

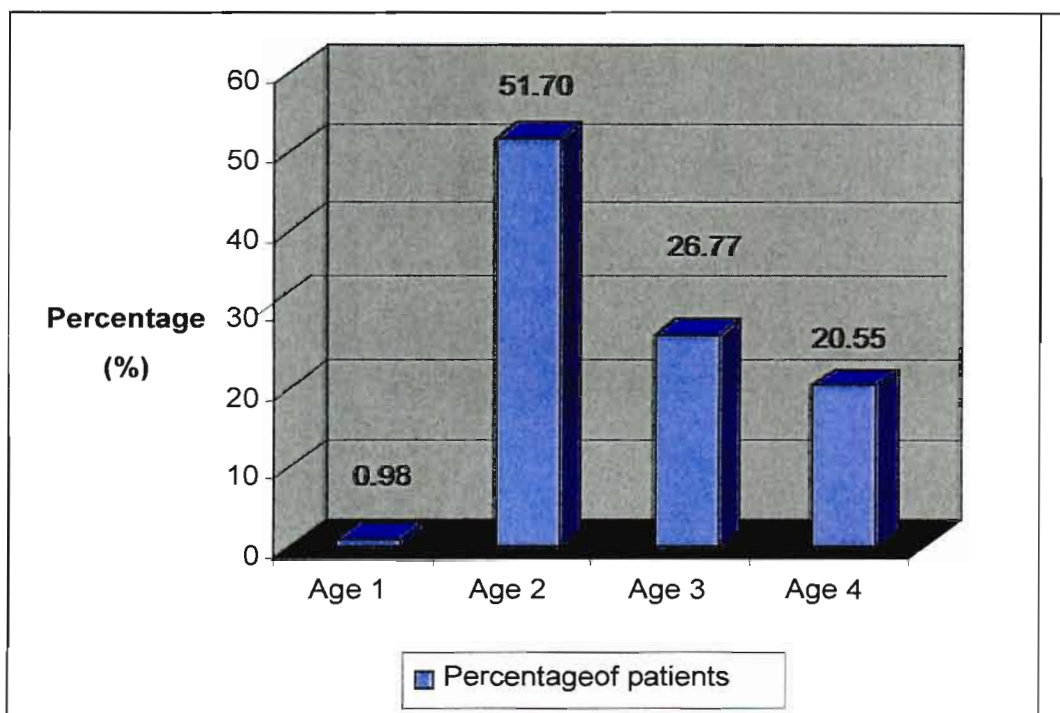


Figure 4.9: Percentage of patients in different age groups who received products containing methylphenidate and atomoxetine for all patients from 2005 to 2007

The results in Table 4.10 revealed that 0.91% of patients who received prescriptions for products containing methylphenidate and atomoxetine were in the age group 5 years and younger in 2005. They represented 1.11% of all patients who received products containing methylphenidate and atomoxetine.

The number of children aged 5 years to 12 years *declined* from 2005 (53.62%) to 2007 (49.23%) by 11.16% (Refer to Table 4.10). In 2005 the number of adolescents aged 12 years to 18 years was 2,103 (26.32%) while in 2007 they increased to 2,143 (27.38%) patients. Therefore an *increase* in the number of patients during 2005 to

2007 with 1.90% was documented (Refer to Tables 4.4 and 4.10). Adults older than 18 years *increased* from 2005 (19.15%) to 2007 (22.28%) with 13.99%.

4.5.2 Number of methylphenidate and atomoxetine containing prescriptions

The following Table consists of the number of prescriptions containing products that contained methylphenidate and atomoxetine containing products which is further sub-divided into gender and age groups.

Table 4.11 Number of methylphenidate and atomoxetine containing prescriptions according to gender and age groups (data extracted from Tables A.7, A.8 and A.9 in Appendix A)

Year	Total number of prescriptions	Gender				Age groups							
		Male		Female		≤ 5 years		> 5 and ≤ 12 years		> 12 and ≤ 18 years		> 18 years	
		n	%	n	%	n	%	n	%	n	%	n	%
2005	27,680	20,511	74.10	7,113	25.70	140	0.51	16,151	58.35	7,569	27.34	3,820	13.80
2006	31,577	23,505	74.44	8,013	25.38	154	0.49	17,995	56.99	8,929	28.28	4,499	14.25
2007	32,647	24,165	74.02	8,466	25.93	203	0.62	17,902	54.84	9,533	29.20	5,009	15.34

4.5.2.1 General analysis of methylphenidate and atomoxetine containing prescriptions

From the total number of prescriptions dispensed in 2005 (N=8,522,798), only 27,680 (0.33%) prescriptions contained methylphenidate or atomoxetine products from where it increased in 2007 (N=8,015,538) to 32,647 (0.41%) prescriptions.

According to Table 4.11 the number of prescriptions containing methylphenidate and atomoxetine products increased from 2005 (N=27,680) to 2006 (N=32,577) with 17.69%. From 2006 (N=32,577) to 2007 (N=32,647) the number of prescriptions increased even further with 0.22% (Refer to Table A.7 in Appendix A). Therefore an increase of 17.94% was noticed from 2005 to 2007 in the number of prescriptions that contained methylphenidate and atomoxetine containing products.

4.5.2.2 Gender analysis of methylphenidate and atomoxetine containing prescriptions

Female patients receiving prescriptions indicating methylphenidate or atomoxetine containing products represented 0.14% (n = 7,113) of the total number of prescriptions prescribed for females (N=5,112,373) in 2005. They represented 0.18% (n = 8,466) of all prescriptions claimed for female patients in 2007 (N=4,817,599) (Refer to Table A.8 in Appendix A). Therefore a conclusion can be made that approximately the same percentage of prescriptions indicating methylphenidate and atomoxetine containing products were claimed for female patients from 2005 to 2007.

According to Table 4.11 the number of prescriptions indicating methylphenidate and/or atomoxetine products for female patients was 25.70% with regard to the total number of prescriptions containing methylphenidate or atomoxetine products during 2005. In 2006 and 2007 the female gender represented 25.38% and 25.93% of the total number of prescriptions containing methylphenidate and/or atomoxetine products claimed in each study year (Refer to Table A.8 in Appendix A). Therefore there was almost no change in the number of prescriptions containing methylphenidate or atomoxetine products for females during 2005 (25.70%) to 2007 (25.93%).

Of the 3,403,233 prescriptions claimed for males in 2005, a total of 20,511 (0.60%) prescriptions included methylphenidate and atomoxetine containing products where in 2007 (N=3,196,105) males received 24,165 (0.76%) such prescriptions.

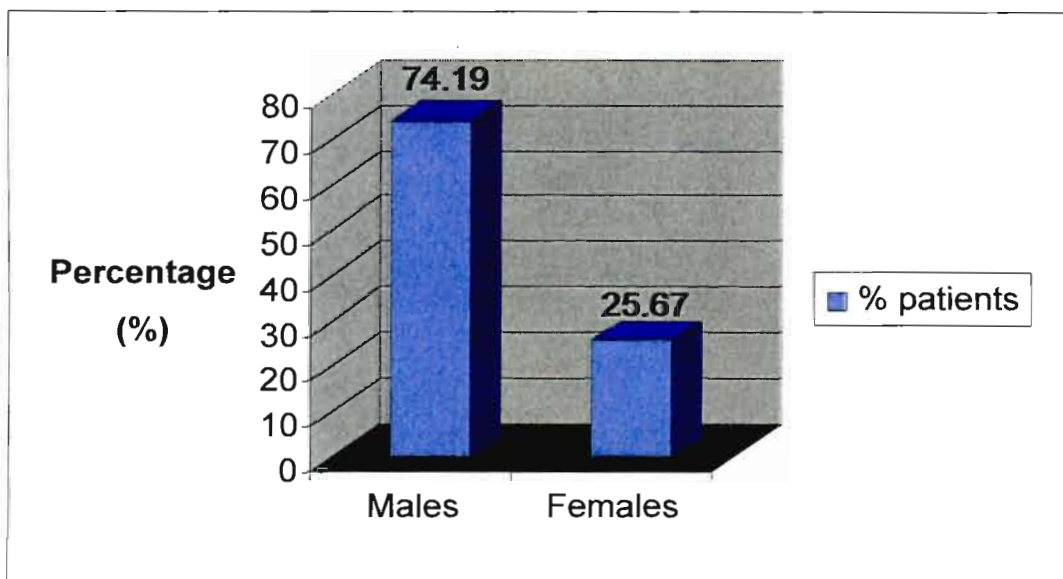


Figure 4.10: The percentage of methylphenidate and atomoxetine containing prescriptions claimed for males and females for the study period.

According to Figure 4.10 it is possible to see the ratio of males to females receiving products containing methylphenidate or atomoxetine. The ratio seen in the figure is 3 to 1 for males to females and is in correlation with some statistics from the United States of America (Marcetti *et al.*, 2001:1905).

4.5.2.3 Analysis according to age groups

The number of young children 5 years and younger receiving prescriptions containing methylphenidate and atomoxetine products during 2005 (N=391,847) was 140 (0.04%) and in 2007 (N=324,946) it was 203 (0.06%). It was observed that the prevalence in young children aged 5 years and younger from 2005 to 2007 proved to be within the same margins. The number of prescriptions containing methylphenidate or atomoxetine products for young children aged 5 years and younger *increased* from 2005 (0.51%) to 2007 (0.62%) by 0.11% (Refer to Table A.9 in Appendix A). This group was ranked 4th.

Prescriptions for children aged 5 years to 12 years that contained methylphenidate and atomoxetine products represented 3.89% (n=16,151) of all prescriptions claimed (N=415,323) during 2005 for this age group. In 2007 (N=365,745) it *increased* to 4.89% (n=17,902) by 1.00%. Children between 5 years to 12 years ranked 1st in the number of prescriptions containing methylphenidate or atomoxetine (Refer to Table A.9 in Appendix A).

Of the 364,879 prescriptions for adolescents, aged 12 years to 18 years, 7,569 (2.07%) prescriptions included products containing methylphenidate and atomoxetine products in 2005. In 2007 (N=337,548) this age group received 9,533 (2.82%) prescriptions containing methylphenidate and atomoxetine products. Ranked second, adolescents between 12 years to 18 years increased during 2005 (27.34%) to 2007 (29.20%) by 1.86% in the number of prescriptions containing methylphenidate and atomoxetine (Refer to Table A.9 in Appendix A).

The number of prescriptions for adults older than 18 years (ranked third) that contained methylphenidate or atomoxetine products did not change noticeably from 2005 (0.05%) to 2007 (0.07%). The number of methylphenidate or atomoxetine containing products prescribed for adults older than 18 years increased from 2005 (13.80%) to 2007 (15.34%) with 1.54% (Refer to Table A.9 in Appendix A).

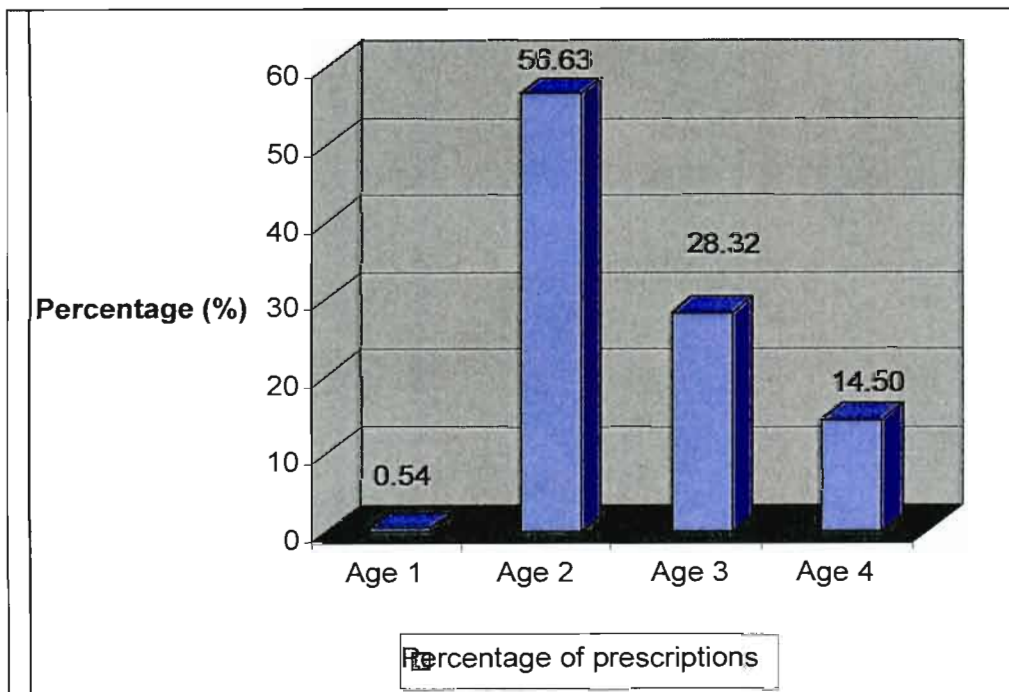


Figure 4.11: Prevalence percentage for prescriptions containing methylphenidate and atomoxetine products for each age group to total number of prescriptions containing methylphenidate or atomoxetine.

Figure 4.11 reveals that the majority of patients receiving products containing methylphenidate or atomoxetine were children aged 5 years to 12 years followed by

adolescents, aged 12 years to 18 years. Young children 5 years and younger received below 1% of the prescriptions during the study period (refer to Figure 4.11).

4.5.3 Number of medicine items containing methylphenidate and atomoxetine

The following Table 4.12 consists of the number of medicine items containing methylphenidate and atomoxetine which is further sub-divided into gender groups and age categories.

Table 4.12: Number of methylphenidate and atomoxetine containing medicine items according to gender and age groups for 2005 to 2007 (Refer to Tables A.7, A.8 and A.9 in Appendix A).

Year	Total number of medicine items	Gender				Age groups (Years)							
		Male		Female		≤ 5 years		> 5 and ≤12 years		> 12 and ≤18 years		> 18 years	
		N	%	n	%	n	%	n	%	n	%	n	%
2005	29,424	21,798	74.08	7,567	25.72	146	0.50	16,936	57.56	8,227	27.96	4,115	13.99
2006	33,576	24,990	74.43	8,525	25.39	160	0.48	18,936	56.40	9,613	28.63	4,867	14.50
2007	34,850	25,833	74.13	9,001	25.83	212	0.61	18,988	54.48	10,216	29.31	5,434	15.59

4.5.3.1 General analysis of methylphenidate and atomoxetine containing medicine items.

Of the 19,606,049 medicine items claimed in 2005, only 29,424 (0.15%) medicine items contained methylphenidate or atomoxetine while in 2007 (N=19,146,156) a total of 34,850 (0.18%) medicine items containing methylphenidate or atomoxetine were claimed. These results revealed no noteworthy difference in the number of medicine items that contained methylphenidate or atomoxetine from 2005 to 2007 (Refer to Table 4.12). The total number of medicine items that contained methylphenidate and atomoxetine *increased* from 2005 (N=29,424) to 2007 (N=34,850) by 18.44%.

4.5.3.2 Analysis according to gender of methylphenidate and atomoxetine containing medicine items

Of the 11,811,901 medicine items claimed in 2005 for females, 7,567 (0.06%) items contained methylphenidate or atomoxetine. In 2007 (N=11,551,895) 9,001 (0.08%) of medicine items contained methylphenidate or atomoxetine (0.08%).

The number of medicine items containing methylphenidate and atomoxetine for the female gender did not change from 2005 (25.72%) to 2007 (25.83%) by 0.11% (Refer to Table A.8 in Appendix A).

In 2005 (N=7,777,985) the number of medicine items containing methylphenidate or atomoxetine prescribed to males was 21,798 (0.28%) while in 2007 (N=7,590,337) it increased to 25,833 (0.34%) (Refer to Table A.8 in Appendix A).

According to Table 4.12 the number of medicine items containing methylphenidate or atomoxetine prescribed for males did not change from 2005 (74.08%) to 2007 (74.13%) by 0.05% (Refer to Table A.8 in Appendix A).

4.5.3.3 Analysis according to age groups of methylphenidate and atomoxetine containing medicine items

Of the 974,785 medicine items claimed to patients 5 years and younger in 2005, only 146 (0.01%) contained methylphenidate or atomoxetine. In 2007 (N=827,579) it concluded to only 212 (0.03%) medicine items (Refer to Table A.9 in Appendix A).

Young children 5 years and younger had the lowest number of medicine items containing methylphenidate or atomoxetine claimed for all the age groups with an average percentage of 0.53% of all medicine items claimed for this age group for all study years. For children aged 5 years to 12 years the number of items containing methylphenidate and atomoxetine for 2005 (n=16,936)

represented 1.68% of the total number of medicine items (N=1,010,808) claimed for this age group. In 2007 (N=895,624) it *increased* to 2.12% (n=18,988) (Refer to Table A.9 in Appendix A).

Methylphenidate and atomoxetine containing items were most frequently prescribed for children aged 5 years to 12 years from 2005 (57.56%) to 2007 (54.48%). A *decline* of 3.08% was found.

In 2005 the number of adolescents 12 years to 18 years (N=834,506) received 8,227 (0.99%) items containing methylphenidate and atomoxetine while during 2007 (N=788,341) adolescents received 10,216 (1.30%). Adolescents aged 12 years to 18 years had the second most claimed methylphenidate or atomoxetine containing items from 2005 (27.96%) to 2007 (29.31%). An *increase* was noticed in the number of medicine items containing methylphenidate or atomoxetine claimed from 2005 (27.96%) to 2007 (29.31%) by 1.35% (Refer to Table A.9 in Appendix A).

Of the 16,785,929 medicine items claimed in 2005 for adults older than 18 years 4,115 (0.03%) medicine items contained methylphenidate or atomoxetine and during 2007 (N=16,634,585) a total of 5,434 (0.03%) medicine items that contained methylphenidate and atomoxetine were claimed (Refer to Table A.9 in Appendix A).

The third highest number of methylphenidate and atomoxetine containing items was prescribed to adults older than 18 years for all study years. An *increase* of 1.60% could be detected in the number of items that contained methylphenidate or atomoxetine as claimed during 2005 (13.99%) to 2007 (15.59%) (Refer to Table A.9 in Appendix A).

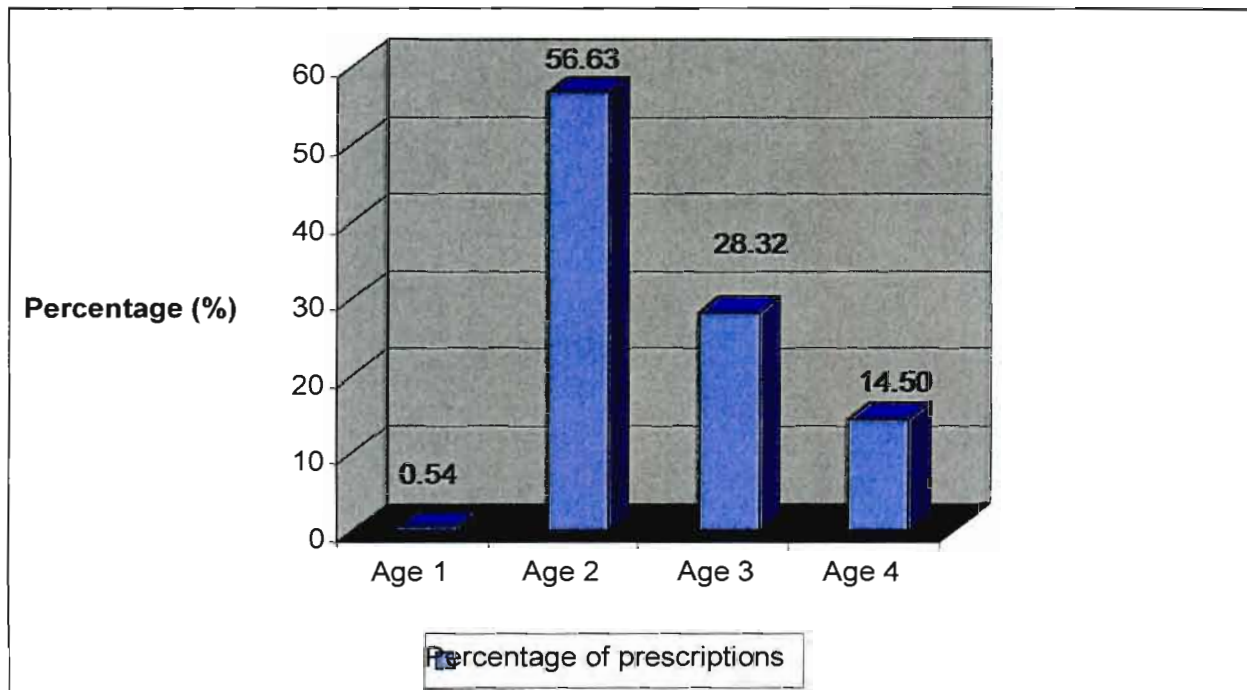


Figure 4.12: Percentage of medicine items that contained methylphenidate or atomoxetine for the different age groups during the three-year study

According to Figure 4.12 children aged 5 to 12 years had the highest prevalence for medicine items containing methylphenidate or atomoxetine (56.07%), and adolescents aged 12 years to 18 years had a prevalence of 28.67%. Young children 5 years and younger had the lowest number of medicine items containing methylphenidate or atomoxetine possible due to the fact that methylphenidate and atomoxetine should not be prescribed to patients under the age of 6 years (Gibbon, 2005).

4.5.3.4 Analysis according to active ingredient of methylphenidate and atomoxetine containing medicine items

4.5.3.4.1 Products containing atomoxetine

The results reveal that products containing atomoxetine represented only 4.69% of all methylphenidate and atomoxetine containing products claimed in 2005 (n=1,379; N=29,424 items) and 12.91% in 2006 (n=4,336; N=33,576 items) and 12.34% in 2007 (n=4,300; N=34,850 items).

These results indicated an *difference* of 7.65% in the number of medicine items containing atomoxetine from 2005 to 2007.

Of all products containing atomoxetine, Strattera 40mg Cap[®] had the *highest* prevalence in 2005 (29.08% with 401 medicine items), in 2006 (40.20% with 1,743 medicine items) and in 2007 (41.95% with 1,804 medicine items). The prevalence of Strattera 40mg Cap[®] increased from 2005 (29.08%) to 2007 (41.95%) with 12.87% difference.

4.5.3.4.2 Products containing methylphenidate

Methylphenidate containing products represented 95.31% (n=28,045; N=29,424 medicine items) in 2005 of the total number of medicine items containing methylphenidate and atomoxetine and 87.09% in 2006 (n=29,240; N=33,576 medicine items) and 87.66% (n=30,550; N=34,850 medicine items) in 2007. A difference of 7.65% was found from 2005 to 2007.

Of all methylphenidate containing products, Ritalin LA 20mg Cap[®] had the highest frequency in 2005 at 31.05% with 8,707 medicine items and in 2006 (25.96%) with 7,592 medicine items and in 2007 with 7,374 (24.14%) medicine items. A *difference* of 6.91% in the number of Ritalin LA 20mg Cap[®] was noticed from 2005 (31.05%) to 2007 (24.14%).

4.5.3.5 Analysis according to prescribers

4.5.3.5.1 General analysis of methylphenidate and atomoxetine containing medicine items

According to Tables A.28 to A.30 from Appendix A atomoxetine and methylphenidate containing medicine items were mostly prescribed by *general medical practitioners (GPs)* with 48.62% in 2005 (n=14,306; N=29,423) and 46.83% in 2006 (n=15,722; N=33,576) and 46.51% in 2007 (n=16,208; N=34,849). A *difference* of 2.11% was observed from 2005 until 2007.

Paediatricians prescribed 33.03% (n=9,717) of all atomoxetine and methylphenidate containing products during 2005 (N=29,423); 33.17% (n=11,137) in 2006; (N=33,576) and 32.72% (n=11,401) in 2007 (N=34,849). These results revealed that the prescribing patterns of paediatricians for products containing methylphenidate or atomoxetine did not really change from 2005 until 2007 (Refer to Tables A.28 to A.30 in Appendix A).

Psychiatrists prescribed 9.58% (n=2,819) of all atomoxetine and methylphenidate containing medicine items during 2005 (N=29,423) and 11.50% in 2006 (n=3,861; N=33,576) and 12.37% in 2007 (n=4,311; N=34,849). An *increment* of 2.79% was observed from 2005 until 2007 (Refer to Tables A.28 to A.30 in Appendix A).

In 2005 (N = 29,423), other medical practitioners (Refer to Chapter 3, Section 3.4.4) prescribed approximately the same percentage of atomoxetine and methylphenidate containing medicine items as *neurologists* with 4.45% (n=1,308) and 4.33% (n=1,273) respectively.

During 2006 (N=33,576), neurologists prescribed more atomoxetine and methylphenidate containing medicine items than other medical practitioners with 4.62% (n=1,552) to 3.88% (n=1,304) and during 2007 (N=34,849) 4.84% (n=1,687; and 3.56% (n=1,242).respectively (Refer to Tables A.21 to A.23 in Appendix A).

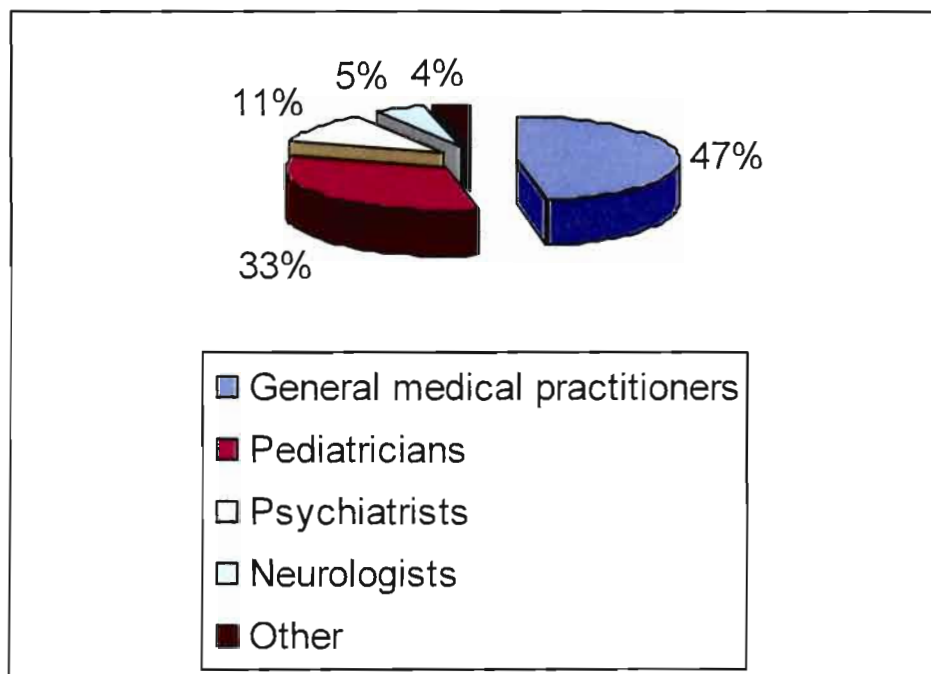


Figure 4.13: Prescribers of atomoxetine and methylphenidate containing products from 2005 until 2007.

In conclusion, according to Figure 4.13, it is possible to see that the general medical practitioners prescribed the majority of products containing methylphenidate or atomoxetine followed by paediatricians. It is interesting that psychiatrists and neurologists who are specialists in behavioural and neurological disturbances, prescribed the lowest number of products that contained methylphenidate and atomoxetine.

4.5.3.5.2 The general analysis of the prescriber group: General medical practitioner (GP)

Atomoxetine containing medicine items represented 7.38% (n=3,411; N=46,236) of all products containing atomoxetine and methylphenidate prescribed by general practitioners for the study period of 2005 until 2007 (Refer to Tables A.21 to A.23 in Appendix A).

During 2005 atomoxetine containing products prescribed by general medical practitioners represented 3.05% (n=437) of all products containing methylphenidate and atomoxetine (N=14,306 items). Strattera 40mg Cap[®] represented 29.52% (n=129; N=437) of the products containing atomoxetine prescribed by general medical practitioners during 2005 (Refer to Table A. 28 in Appendix A). From 2006 (N=15,722) until 2007 (N=16,208) atomoxetine containing products prescribed by general medical practitioners had a prevalence of 10.2% (n=1,575) and 8.63% (n=1,399) of all methylphenidate or atomoxetine containing products prescribed by general medical practitioners. Strattera 40mg Cap[®] represented 35.49% (n=559; N=1,575) and 40.03% (n=560, N=1,399) of all atomoxetine containing products prescribed by general medical practitioners during 2006 and 2007 respectively (Refer to Tables A.28 and A.30 in Appendix A).

Medicine items containing methylphenidate represented 96.95% (n=13,869) of all products containing methylphenidate and atomoxetine prescribed by a general medical practitioner in 2005 (N=14,306). In 2006 (N=15,722) and 2007 (N=16,208) products containing methylphenidate had a frequency of 89.98% (n=14,147) and 91.37% (n=14,809) respectively (Refer to Tables A.28 to A.30 in Appendix A).

Ritalin LA 20mg[®] had the highest frequency of all products containing methylphenidate prescribed by general medical practitioners during 2005 (N=13,869) with 32.20% (n=4,466) followed by 27.79% (n=3,931) in 2006, and in 2007 Ritalin LA 20mg[®] (N=14,809) had a frequency of 27.08% (n=4,010)(Refer to Tables A.28 to A.30 in Appendix A).

Methylphenidate containing products represented 92.62% (n=42,825, N=46,236) of all products prescribed by general medical practitioners and containing methylphenidate and atomoxetine during the study period from 2005 to 2007.

4.5.3.5.3 The general analysis of the prescriber group: Paediatricians

Atomoxetine containing products represented 4.65% (n=452) of all products containing methylphenidate and atomoxetine during 2005 (N=9,717) that were prescribed by paediatricians. Furthermore products containing atomoxetine had a prescribing prevalence of 11.19% (n=1,246) and 11.77% (n=1,342) during 2006 (N=11,137) and 2007 (N=11,401) respectively. Thus an

increment of 7.12% during 2005 to 2007 was observed (Refer to Tables A.28 to A.30 in Appendix A). Atomoxetine represented 9.42% (n=3,040; N=32,255) of all products prescribed by paediatricians and that contained methylphenidate and atomoxetine (Refer to Tables A.28 to A.30 in Appendix A)

Strattera 40mg[®] represented 29.87% (n=135) of all atomoxetine containing products during 2005 (N=452), compared to (N=1,246) in 2006 and (N=1,342) in 2007. Strattera 40mg[®] represented 38.12% (n=475) and 45.23% (n=604) of the atomoxetine containing products prescribed by paediatricians (Refer to Tables A.28 to A.30 in Appendix A).

Methylphenidate containing products represented 95.35% of all the products containing methylphenidate and atomoxetine prescribed by paediatricians in 2005 (n=9,265; N=9717) and 88.81% (n=9,891; N=11,137) in 2006 and 88.23% (n=10,059; N=11,401) in 2007. Therefore a *decline* of 7.12% was observed from 2005 to 2007. Methylphenidate containing products represented 90.58% (n=29,215; N=32,255) of all products prescribed by paediatricians that contained methylphenidate and atomoxetine for the study period (Refer to Tables A.28 to A.30 in Appendix A).

Ritalin LA 20mg Cap[®] represented 31.39% (n=2,908) of all products containing methylphenidate prescribed by paediatricians during 2005 (N=9,265) and in 2007 (N=10,059) 23.50% (n=2,364) (Refer to Tables A.21 and A.23 in Appendix A).

The results revealed that Ritalin 10mg[®] showed the highest prevalence in 2006 with 25.45% (n=2,517)(N=9,891) of all products containing methylphenidate prescribed by paediatricians (Refer to Table A.29 in Appendix A).

4.5.3.5.4 The general analysis of the prescriber group: Psychiatrists

Atomoxetine represented 20.21% (n=2,221; N=10,991) of all products containing methylphenidate or atomoxetine prescribed by psychiatrists during the study period (Refer to Tables A.28 to A.30 in Appendix A).

Atomoxetine represented 10.71% (n=302) of all products containing methylphenidate and atomoxetine prescribed by psychiatrists in 2005 (N=2,819) and 24.19% (n=934) during 2006 (N=3,861) and 22.85% (n=985) in 2007 (N=4,311). Therefore an *increment* of 12.14% from 2005 to 2007 was observed (Refer to Tables A.21 to A.23 in Appendix A). The prescribing patterns of

Strattera 40mg Cap[®] increased by 15.40% from 2005 (29.47%) to 2007 (44.87%) (Refer to Tables A.28 to A.30 in Appendix A).

Methylphenidate represented 79.79% (n=8,770; N=10,991) of products that contained methylphenidate or atomoxetine that were prescribed by psychiatrists. Products containing methylphenidate represented 89.29% (n=2,517) in 2005 (N=2,819) which decreased to 77.15% (n=3,326) in 2007 (N=4,311) with 12.14%. In 2005 (N=2,517) and 2006 (N=2,927) Ritalin LA 20mg Cap[®] had the highest frequency of 26.54% (n=668) and 22.31% (n=653) respectively. (Refer to Tables A.28 to A.30 in Appendix A).

The results revealed that in 2007 (N=3,326) Concerta 36mg Oros[®] represented the highest frequency of 25.35% (n=843) of all products containing methylphenidate that were prescribed by psychiatrists (Refer to Table A.30 in Appendix A).

4.5.3.5.5 The general analysis of the prescriber group: Neurologists

Atomoxetine represented 18.99% (n=857) products that were prescribed by neurologists and that contained methylphenidate or atomoxetine (N=4,512) for all study years.

During 2006 (N=1,552) and 2007 (N=1,687) atomoxetine represented 24.03% (n=373) and 21.87% (n=369) of all products containing methylphenidate and atomoxetine prescribed by neurologists with a decline of 2.16%. In 2005 (N=1,273) atomoxetine represented 9.03% (n=115) of all products containing methylphenidate and atomoxetine prescribed by neurologists (Refer to Tables A.28 to A.30 in Appendix A).

During 2005 (N=115) Strattera 25mg[®] had a prevalence of 32.17% (n=37). The results revealed that in 2006 (N=373) and 2007 (N=369) Strattera 40mg[®] had a prevalence of 44.50% (n=166) and 34.15% (n=126) respectively (Refer to Tables A.28 to A.30 in Appendix A).

Methylphenidate represented 18.01% (n=3,655; N=4,512) of products containing methylphenidate and atomoxetine that were prescribed by neurologists. Products containing methylphenidate represented 75.97% (n=1,179) in 2005 and 78.13% (n=1,318) in 2006 (N=1,552) and 2007 (N=1,687) with an increment of 2.16%. In 2005 (N=1,273) products containing methylphenidate represented 90.97% (n=1,158) (Refer to Tables A.28 to A.30 in Appendix A).

In 2006 (N=1,179) and in 2007 (N=1,318), Concerta 36mg[®] had the highest prevalence of methylphenidate containing products with 22.82% (n=269) and 24.66% (n=325) prescribed respectively prescribed by neurologists. In 2005 (N=1,158) Ritalin LA 20mg[®] had the highest

prevalence of methylphenidate containing products with 24.70% (n=286) (Refer to Tables A.28 to A.30 in Appendix A).

4.5.3.5.6 The general analysis of the prescriber group: Other prescribers

Atomoxetine represented 12.65% (n=486; N=3,843) of prescriptions by other physicians of products containing methylphenidate and atomoxetine by other physicians. Atomoxetine represented 5.60% (n=73) in 2005 (N=1,308), where in 2006 (N=1,301) and 2007 (N=1,234) the percentages were 15.99% (n=208) and 16.61% (n=205) with an increment of 11.01% from 2005 to 2007 (Refer to Tables A.28 to A.30 in Appendix A). Strattera 40mg Cap® represented with the highest frequency during 2005 (N=73) with 36.99% (n=27) and in 2006 (N=208) with 38.94% (n=81) and in 2007 (N=205) with 33.66% (n=69) (Refer to Tables A.28 to A.30 in Appendix A).

Methylphenidate represented 87.35% (n=3,357; N=3,843) of prescriptions by other physicians of products containing methylphenidate and atomoxetine. In 2005 (N=1,308) methylphenidate containing products represented 94.40% (n=1,235) of products containing methylphenidate and atomoxetine prescribed by other physicians. In 2006 (N=1,301) the same represented 84.01% (n=1,093) and in 2007 methylphenidate containing products represented 83.39% (n=1,029) (Refer to Tables A.28, A.29 and A.30 in Appendix A). Ritalin 10mg Tab® had the highest frequency prescribing in 2005 (n=401; N=1,235); 2006 (n=270; N=1,093) and 2007 (n=241; N=1,029) with 32.52%, 24.70% and 23.42% respectively for each study year. A decline of 9.1% was observed (Refer to Tables A.28, A.29 and A.30 in Appendix A).

4.5.3.6 The top five trade name products

Tables A.20 to A.22 in Appendix A, illustrate a complete list of methylphenidate and atomoxetine containing products according to prevalence. A summarised Table to be followed of the top five trade name products according to prevalence for 2005, 2006 and 2007 is concluded in Table 4.13.

Table 4.13: The top five products containing methylphenidate or atomoxetine ranked according to prevalence.

Year	Trade name products	Rank	Number of medicine items	%
2005 N=29,424 items	Ritalin LA 20mg [®]	1	8,707	29.59
	Ritalin 10mg [®]	2	8,173	27.78
	Ritalin LA 30mg [®]	3	2,667	9.06
	Concerta 36mg [®]	4	1,969	6.69
	Methylphenidate HCl-Douglas [®]	5	1,406	4.79
Total			22,922	77.91
2006 N=33,576 items	Ritalin LA 20mg [®]	1	7,592	22.61
	Ritalin 10mg [®]	2	6,828	20.34
	Concerta 36mg [®]	3	4,104	12.22
	Ritalin LA 30mg [®]	4	2,523	7.51
	Concerta 18mg [®]	5	2,399	7.14
Total			23,446	69.82
2007 N=34,850 items	Ritalin LA 20mg [®]	1	7,374	21.78
	Ritalin 10mg [®]	2	6,261	18.50
	Concerta 36mg [®]	3	5,682	16.79
	Concerta 18mg [®]	4	3,193	9.43
	Ritalin LA 30mg [®]	5	2,663	7.87
Total			25,173	74.37

Note: To calculate the percentage per medicine item, the number of items per trade name product was divided by the total number of items ("N" indicated) and then multiplied by 100.

According to Table 4.13 it is indicated that the top five products represented 70% or higher for each study year. It is interesting to note that all products mentioned in Table 4.13 contains methylphenidate. Ritalin LA 20mg[®] and Ritalin 10mg[®] were the two highest ranking products according to prevalence of all products containing methylphenidate and atomoxetine in the consecutive years (Refer to Tables A.24 to A.22 in Appendix A).

Table 4.14: Top five products containing methylphenidate or atomoxetine ranked according to total cost (Rand) (Refer to Tables A.24 to A.22).

Year	Trade name products	Rank	Total cost (R) items	%
2005 N=R8,810,130.56	Ritalin LA 20mg [®]	1	R 2,624,389.50	29.79
	Ritalin 10mg [®]	2	R 1,718,024.48	19.5
	Ritalin LA 30mg [®]	3	R 114,811.63	1.30
	Concerta 36mg [®]	4	R 787,783.76	8.94
	Methylphenidate HCl-Douglas [®]	5	R 180,899.70	2.05
Total			R 5,425,909.07	61.59
2006 N=R11,101,929.25	Ritalin LA 20mg [®]	1	R 2,212,592.13	19.93
	Ritalin 10mg [®]	2	R 1,347,103.52	12.13
	Concerta 36mg [®]	3	R 1,633,882.70	14.72
	Ritalin LA 30mg [®]	4	R 1,058,449.61	9.53
	Concerta 18mg [®]	5	R 864,077.83	7.78
Total			R 7,116,105.79	64.10
2007 N=R11,717,340.70	Ritalin LA 20mg [®]	1	R 2,087,175.47	17.81
	Ritalin 10mg [®]	2	R 1,122,970.43	9.58
	Concerta 36mg [®]	3	R 2,284,550.61	19.50
	Concerta 18mg [®]	4	R 1,116,455.73	9.53
	Ritalin LA 30mg [®]	5	R 1,075,488.27	9.18
Total			R 7,686,640.51	65.60

Note: To calculate the % of medicine item cost to total cost, the total cost of items was divided by the total cost of products containing methylphenidate and atomoxetine and then multiplied by 100.

According to Table 4.14, the top five products represented more than 60% of the total cost of all products containing methylphenidate and atomoxetine for the three-year study period. The cost prevalence index (CPI) can be calculated from Tables 4.13 and 4.14 and follows in Table 4.15.

Table 4.15 Calculated Cost Prevalence Index (CPI) of annual top 5 products

Period	Trade name products	Cost Prevalence Index (CPI)
2005	Ritalin LA 30mg Cap	0.14
	Methylphenidate HCl-Douglas	0.43
	Ritalin 10mg Tab	0.7
	Ritalin LA 20mg Cap	1.01
	Concerta 36mg Oros	1.34
2006	Ritalin 10mg Tab	0.6
	Ritalin LA 20mg Cap	0.88
	Concerta 18mg Oros	1.09
	Concerta 36mg Oros	1.2
	Ritalin LA 30mg Cap	1.27
2007	Ritalin 10mg Tab	0.52
	Ritalin LA 20mg Cap	0.82
	Concerta 18mg Oros	1.01
	Concerta 36mg Oros	1.16
	Ritalin LA 30mg Cap	1.17

According to Table 4.15, in 2005 Ritalin LA 20mg[®] and in 2007 Concerta 18mg[®] and Concerta 36mg[®] had a CPI of 1 which indicated that there was an equilibrium between the cost and prevalence of treatment. Concerta 36mg[®] and Ritalin LA 30mg[®] were the only products throughout the study period to be considered relatively expensive.

4.5.3.6.1 The top trade name products according to gender

In the following section the top products for both atomoxetine and methylphenidate containing products will be discussed according to prevalence. Data were extracted from Tables A.24, A.25 and A.26 in Appendix A.

Table 4.16: Top trade name atomoxetine containing products for males according to prevalence.

Year	Active ingredient	Trade name	Number of medicine items	Percentage (%)
2005	Atomoxetine	Strattera 25mg [®]	299	28.29
		Strattera 40mg [®]	296	28.00
	Total		595	56.29
2006	Atomoxetine	Strattera 40mg [®]	1,276	40.09
		Strattera 25mg [®]	782	24.57
	Total		2,058	64.66
2007	Atomoxetine	Strattera 40mg [®]	1,326	42.71
		Strattera 60mg [®]	669	21.55
		Strattera 25mg [®]	607	19.55
	Total		2,602	83.81

During 2005 products containing atomoxetine for the remaining 43.71% for males consisted of Strattera 18mg[®] (18.35%), Strattera 60mg[®] (13.25%) and Strattera 10mg[®] (12.11%). The results revealed that during 2006 Strattera 60mg[®] (17.22%), Strattera 18mg[®] (11.66%) and Strattera 10mg[®] (6.47%) made up the remaining 35.44% for products containing atomoxetine. Furthermore, Strattera 18mg[®] (10.40%) and Strattera 10mg[®] (5.80%) made up the additional 16.20% of products containing atomoxetine during 2007 (Refer to Tables A.24, A.25 and A.26 in Appendix A).

Table 4.17: Top trade name atomoxetine containing products for females according to prevalence.

Year	Active ingredient	Trade name	Number of medicine items	Percentage (%)
2005	Atomoxetine	Strattera 40mg [®]	103	32.39
		Strattera 25mg [®]	65	20.44
	Total		168	52.83
2006	Atomoxetine	Strattera 40mg [®]	453	40.23
		Strattera 25mg [®]	232	20.6
	Total		685	60.83
2007	Atomoxetine	Strattera 40mg [®]	471	39.71
		Strattera 25mg [®]	271	22.85
		Strattera 60mg [®]	258	21.75
	Total		1,000	84.31

Strattera 18mg[®], Strattera 60mg[®] and Strattera 10mg[®] formed the additional 47.17% for females receiving products containing atomoxetine during 2005 while in 2007 the results revealed that these products contributed 37.44% to products containing atomoxetine for females (refer to Tables A.24, A.25 and A.26 in Appendix A).

According to Table 4.16 and 4.17 Strattera 40mg[®] was prescribed mainly to female patients in 2005 (32.39%), 2006 (40.23%) and 2007 (39.71%) with an increment of 7.32%. Strattera 40mg[®] for males had no significant difference in 2006 to females where in 2007 males (42.71%) used more Strattera 40mg[®] than females (39.71%) (refer to Tables A.24, A.25 and A.26 in Appendix A). For the male gender, prescription of Strattera 40mg[®] increased from 2005 (28.29%) to 2007 (32.39%) by 14.71%.

Table 4.18: Top trade name methylphenidate containing products for males according to prevalence.

Year	Active ingredient	Trade name	Number of medicine items	Percentage (%)
2005	Methylphenidate	Ritalin LA 20 [®]	6,515	31.41
		Ritalin 10mg [®]	5,874	28.32
		Ritalin LA 30mg [®]	2,169	10.46
	Total		14,558	70.19
2006	Methylphenidate	Ritalin LA 20 [®]	5,753	26.38
		Ritalin 10mg [®]	4,885	22.40
		Concerta 36mg [®]	3,052	14.00
	Total		13,690	63.00
2007	Methylphenidate	Ritalin LA 20 [®]	5,547	24.41
		Ritalin 10mg [®]	4,471	19.67
		Concerta 36mg [®]	4,217	18.55
	Total		14,235	63.00

According to Table 4.18, Ritalin LA 20mg and Ritalin 10mg[®] accounted for the most prevalent methylphenidate containing products prescribed to males throughout the study period. It showed a significant decrease during 2005 to 2007 with 15.67%. The additional percentages of methylphenidate containing products are found in Tables A.24, A.25 and A.26 in Appendix A for the years 2005, 2006 and 2007.

Table 4.19: Top trade name methylphenidate containing products for females according to prevalence.

Year	Active ingredient	Trade name	Number of medicine items	Percentage (%)
2005	Methylphenidate	Ritalin 10mg [®]	2,289	31.58
		Ritalin LA 20 [®]	2,173	29.98
	Total		4,462	61.56
2006	Methylphenidate	Ritalin 10mg [®]	1,939	26.21
		Ritalin LA 20 [®]	1,833	24.77
	Total		3,772	50.98
2007	Methylphenidate	Ritalin LA 20 [®]	1,827	23.38
		Ritalin 10mg [®]	1,788	22.88
		Concerta 36mg [®]	1,465	18.75
	Total		5,080	65.01

Methylphenidate containing products Ritalin LA 20mg[®] and Ritalin 10mg[®] presented with the highest prevalence prevalent for females during all study years. These products formed 61.56% during 2005 and 46.26% in 2007 of all methylphenidate containing products and a decline of 15.30% was documented.

For males, Ritalin LA 20mg[®] was most frequently prescribed during 2005 (31.41%) and then showed a prescribed prevalence of 24.41% during 2007 (Refer to Table 4.18). Ritalin 10mg[®] had the highest prescribing frequency for females during 2005 (31.58%) to 2006 (26.21%) while Ritalin LA 20mg[®] was observed as (23.38%) in 2007 (Refer to Table 4.19).

The number of Ritalin LA 20mg[®] items prescribed for males had decreased from 2005 until 2007 by 7.00% where Ritalin 10mg[®] followed with 8.65% (Refer to Table 4.18). The results revealed that the number of Ritalin 10mg[®] items claimed for females decreased from 2005 to 2007 by 8.70%. (Refer to Table 4.19).

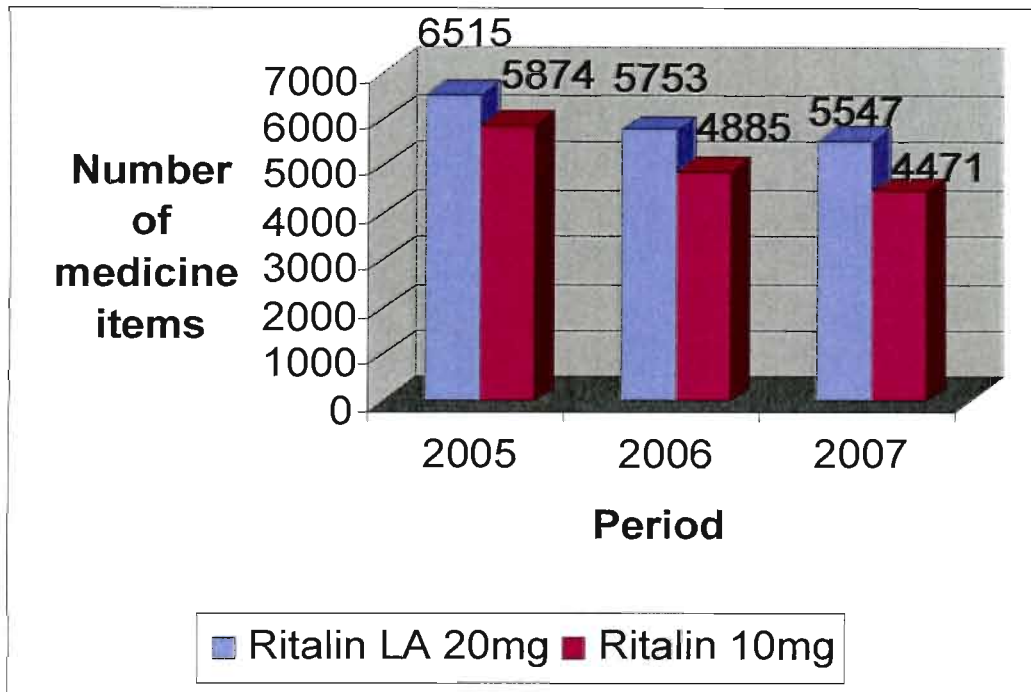


Figure 4.14: Illustration of prevalence of the two top ranked methylphenidate containing products for the study period.

4.5.4 Generic indicator of medicine items containing methylphenidate or atomoxetine.

For all study years the generic indicator of medicine items has been sub-divided into four categories (Refer to section 4.3.4). Analysis is done by extracting data from Table A.19 in Appendix A.

According to Table A.19 in Appendix A the number of innovator products containing methylphenidate or atomoxetine with no generic ("N" indicated) had *increased* from 2005 (61.96%) to 2007 (74.24%) by a staggering 12.28%.

The number of innovator products containing methylphenidate ("O" indicated) dramatically *decreased* from 2005 (29.37%) to 2007 (19.05%) by 10.32% (Refer to Table A.20 in Appendix A).

The number of generic products containing methylphenidate ("Y" indicated) had *decreased* from 2005 (8.67%) to 2007 (6.72%) by 1.95% according to Tables A.20 to A.22 in Appendix A. The average number of generic products containing methylphenidate ("Y" indicated) claimed was 7.93% over the study period (Refer to Tables A.20 to A.22 in Appendix A).

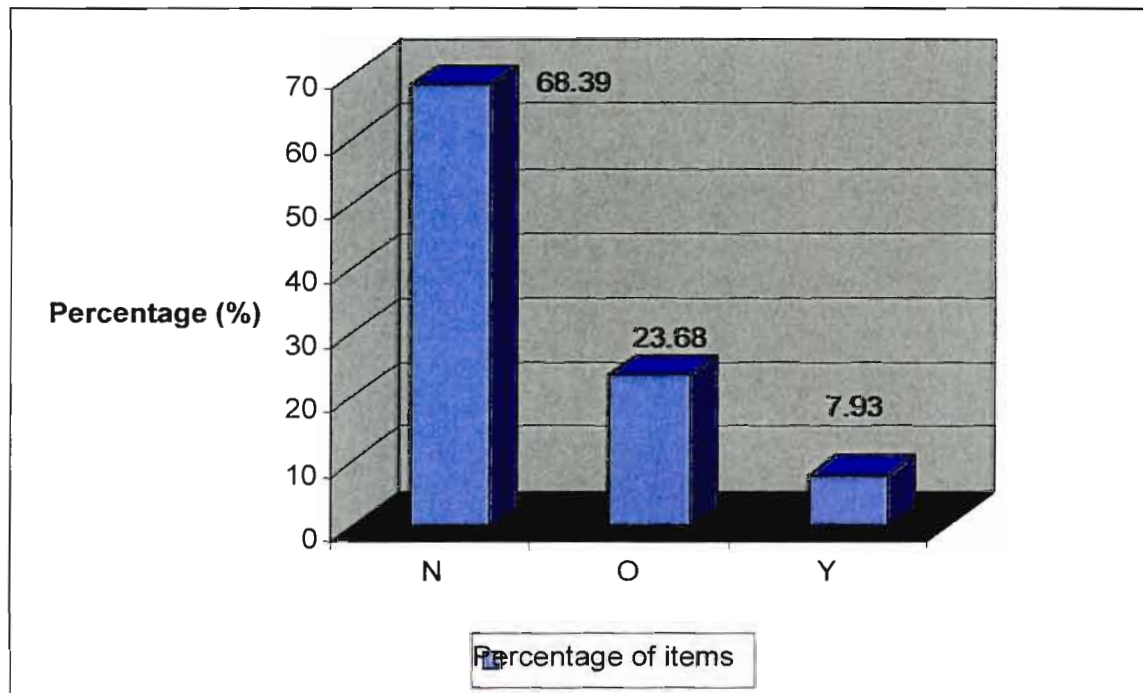


Figure 4.15 The prevalence of products containing methylphenidate or atomoxetine according to generic indicator for all study years together

4.5.4.1 Cost prevalence index (CPI)

Data were extracted from Tables A.19 to A.22 in Appendix A to calculate CPI. The following equations were used to calculate this:

Calculation: Cost (%) / Prevalence (%)

Cost %: Is the sum of the total cost of each medicine type divided by the total cost for the study year,

Prevalence %: Is the total number of items of each medicine type divided by the total number of items for the study year.

In 2005 the cost prevalence index for innovator products containing methylphenidate or atomoxetine with no generic ("N" indicated) calculated to 1.21, which signified that the treatment was relatively expensive. The results revealed that the treatment cost did not really change during 2006 (1.20) or in 2007 (1.17).

Innovator products containing methylphenidate ("O" indicated) calculated a cost prevalence of 0.72 during 2005, signifying that the treatment was relatively inexpensive and remained so from 2006 (0.64) until 2007 (0.55).

During 2005 the cost prevalence index for generic products containing methylphenidate ("Y" indicated) were 0.42 and did really change significantly in 2006 (0.40) or 2007 (0.40). The cost prevalence index for generic products containing methylphenidate ("Y" indicated) signified that the treatment was relatively inexpensive.

4.5.5 Cost of medicine items containing methylphenidate or atomoxetine

4.5.5.1 Total medicine cost

4.5.5.1.1 General cost analysis of methylphenidate or atomoxetine containing products

According to Table A.16 in Appendix A, the total medicine cost for products containing methylphenidate and atomoxetine in 2005 was R8, 810,130.56. It *increased* with 33.00% to R11, 717,340.70 in 2007. The possible reason for the increase in total cost could be that the number of products containing methylphenidate and atomoxetine had increased from 2005 to 2007 (refer to Table 4.9).

In 2005 patients contributed R1, 062,094.81 (12.06%) while medical schemes contributed R7, 748,035.75 (87.94%) of the total medicine item cost (N = R8, 810,130.56) of all products containing methylphenidate and atomoxetine. In 2006 (N = R11,101,929.25) and 2007 (N = R11,717,340.70) patients' medicine contribution was R1,789,523.81 (16.12%) and R2,373,867.59 (20.26%) with the medical scheme contribution of R9,312,405.44 (83.88%) and R9,343,473.11 (79.74%) respectively (refer to Table A.16 in Appendix A). Therefore an increase in the patient medicine contribution of 4.4% was observed during 2005 to 2007.

4.5.5.1.2 Cost analysis of methylphenidate or atomoxetine containing products according to gender.

According to the results in Table A.17 in Appendix A, the contribution females made to the total medicine cost for 2005 was R2,186,354.95 (24.82%) while in 2007 (R11,717,340.70) they contributed R2,958,795.47 (25.25%) of the total medicine cost (N = R8, 810,130.56) of all products containing methylphenidate and atomoxetine. In 2005 male patients contributed R6, 605,662.72 (74.98%) of the total medicine cost (N = R8, 810,130.56) of all products containing methylphenidate and atomoxetine. Furthermore during 2007 they contributed R8, 750,509.01 (74.68%) of the total medicine item cost (N = R11, 717,340.70) of all products containing methylphenidate and

atomoxetine. These results indicated that the contribution of males and females to the total cost of products containing methylphenidate and atomoxetine did not really change from 2005 to 2007.

Of the total cost of products containing methylphenidate and atomoxetine claimed for females in 2005 (N = R2, 186,354.95) the patient medicine contribution for females was R285, 633.90 (13.06%) and the medical scheme contribution was R1, 900,721.05 (86.94%). In 2006 (N = R2,761,186.49) and 2007 (N = R2,958,795.47) the patient contribution was R468,223.09 (16.96%) and R629,883.02 (21.29%) where the medical scheme contributed R2,292,963.40 (83.04%) and R2,328,912.45 (78.71%) respectively. An *increase* in the patient medicine contribution for females was documented from 2005 to 2007 by 8.23% (Table A.17 in Appendix A).

Of the total cost of products containing methylphenidate and atomoxetine claimed for males during 2005 (R6, 605,662.72) the patient contribution was R774, 640.85 (11.73%) and the medical scheme contribution was R5, 831,021.87 (88.27%). In 2006 (R8,315,888.20) and 2007 (R8,750,509.01) the patient contributions were R1,314,440.27 (15.81%) and R1,742,841.70 (19.92%) with a medical scheme contribution of R7,001,447.93 (84.19%) and R7,007,667.31 (80.08%) respectively. An *increase* in the patient contribution for males was found from 2005 to 2007 by 8.19% (Table A.31 un Appendix A).

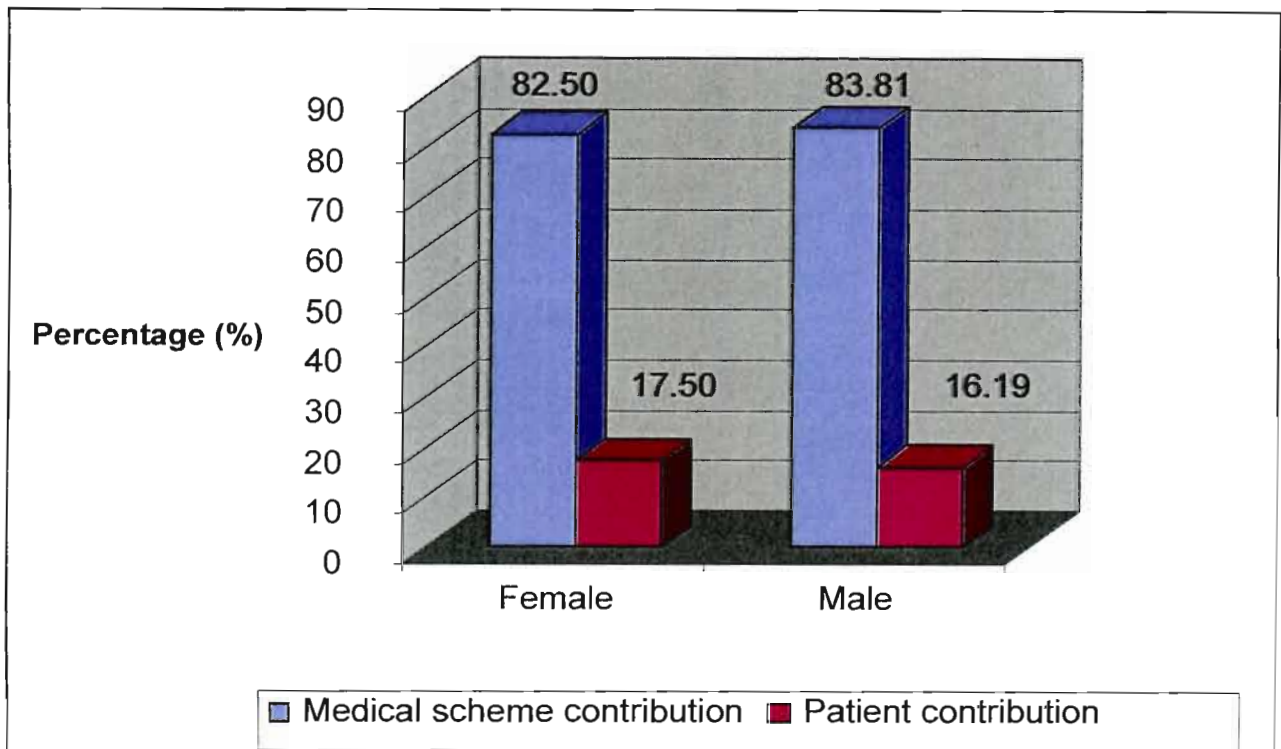


Figure 4.16 Percentage of medical scheme contribution to patient contribution for males and females receiving products containing methylphenidate or atomoxetine for all study years.

4.5.5.1.3 Cost analysis according to age groups of methylphenidate or atomoxetine containing products

According to Table A.18 in Appendix A, the total cost of all products containing methylphenidate or atomoxetine prescribed to children 5 years and younger was R30, 721.29 (0.35%) in 2005 (N = R8, 810,130.56) and R63,656.22 (0.50%) in 2007 (N = R11, 717,340.70).

Children aged 5 years to 12 years had the highest contribution to the total cost of products containing methylphenidate or atomoxetine (N = R8, 810,130.56) with R4, 750,026.83 (53.92%) in 2005 while in 2007 (N = R11, 717,340.70) it was R5,997,324.08 (51.18%). Adolescents aged 12 years to 18 years had the second highest contribution to the total cost of products containing methylphenidate or atomoxetine during 2005 with R2, 705,082.80 (30.70%) and R3,757,107.43 (32.06%) in 2007. Adults, older than 18 years, contributed R1, 324,299.64 (15.03%) to the total cost of products containing methylphenidate or atomoxetine (N = R8, 810,130.56) in 2005 and in 2007 (N = R11, 717,340.70) with R1,899,252.97 (16.21%) (refer to Table A.18 in Appendix A).

These results revealed that there was no noteworthy change in the contribution made by each age group who received products containing methylphenidate or atomoxetine to the total medicine cost from 2005 to 2007 ($d < 0.8$).

In 2005 (N = R30, 721.29) the patient contribution of children 5 years and younger was R3, 618.80 (11.78%) and the medical scheme medicine contribution was R27, 102.49 (88.22%) to the total cost of products containing methylphenidate or atomoxetine. In 2006 (N = R35, 835.02) and 2007 (N = R63, 656.22) patients contributed R8, 241.47 (23.00%) and R16, 882.19(26.52%) respectively to the contribution of children 5 years and younger towards the total cost of products containing methylphenidate or atomoxetine, where the medical scheme contributed R27, 593.55 (78.00%) and R46, 774.03 (73.48%). Therefore a *increase* of 14.74% in children 5 years and younger patient's contribution towards the total cost of products containing methylphenidate and/or atomoxetine was documented during 2005 to 2007 (refer to Table A.18 in Appendix A).

According to Table A.18 in Appendix A, children aged 5 to 12 years contributed R522, 678.66 (11.00%) during 2005 (N = R4, 750,026.83) while the medical scheme medicine contribution was R4, 227,348.17 (89.00%). In 2006 (N = R5,898,701.75) and 2007 (N = R5,997,324.08) the patients contributed R887,231.32 (15.04%) and R1,160,324.31 (19.35%) while the medical schemes contributed R5,011,470.43 (84.96%) and R4,836,999.77 (80.65%) respectively. An *increase* can be documented in the patient contribution from 2005 (11.00%) to 2007 (19.35%) by 8.35%.

Adolescents aged 12 to 18 years contributed R318, 835.13 (11.79%) in 2005 (N = R2, 705,082.80) and the medical schemes' contribution was R2, 386,247.67 (88.21%). In 2006 (N = R3,510,932.53) and 2007 (N = R3,757,107.43) the patients contributed R521,582.33 (14.86%) and R663,894.56 (17.67%) where the medical scheme contributed R2,989,350.20 (85.14%) and R3,093,212.87 (82.33%) (Refer to Table A.18 in Appendix A). Patient contribution for adolescents aged 12 years to 18 years *increased* from 2005 (11.79%) to 2007 (17.67%) by 5.88%.

The results in Table A.32 in Appendix A revealed that adults older than 18 years in 2005 (N = R1, 324,299.64) contributed R216, 962.22 (16.38%) towards the total cost of products containing methylphenidate or atomoxetine that were prescribed to this age group, where the medical scheme contributed R1, 107,337.42 (83.62%). In 2006 (N = R1,656,459.95) and 2007 (N = R1,899,252.97) the patients contributed R372,468.69 (22.49%) and R532,766.53 (28.05%) to the total cost and the medical scheme contributed R1,283,991.26 (77.51%) and R1,366,486.44 (71.95%) respectively. From these results an *increase* of 11.67% in the patient contribution of adults 18 years and older

towards the total cost of products containing methylphenidate or atomoxetine that were prescribed to adults was observed from 2005 (16.38%) to 2007 (28.05%) (refer to Table A.32 in Appendix A).

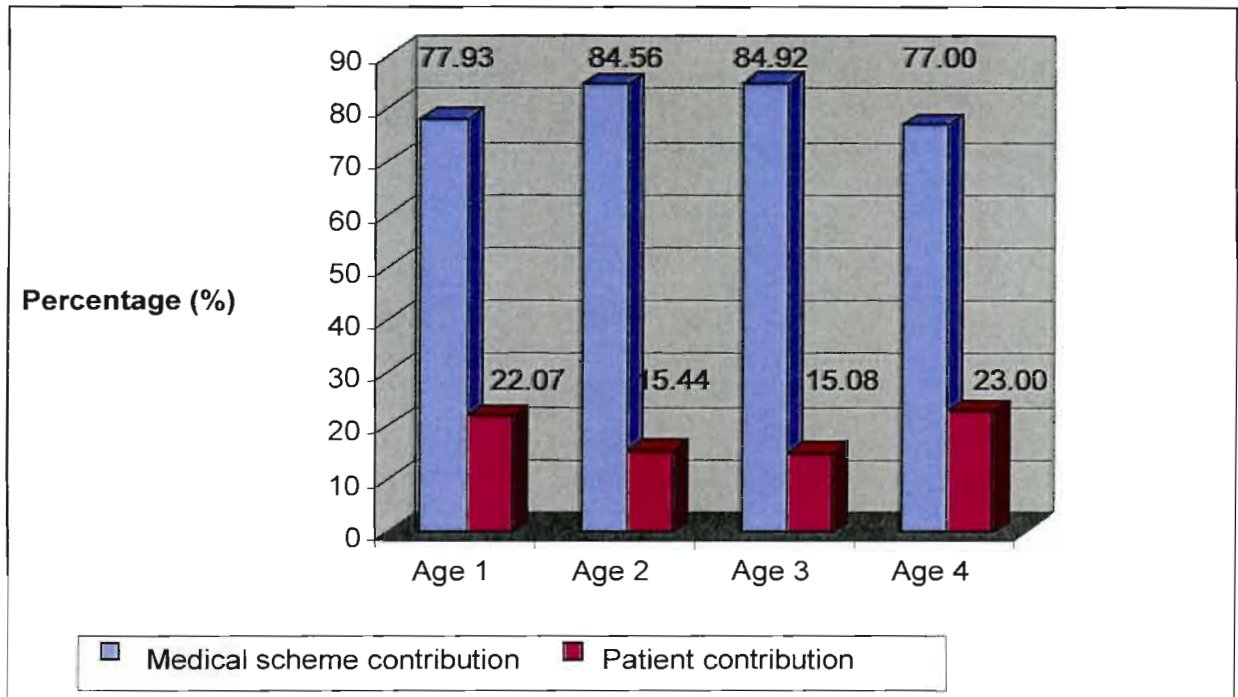


Figure 4.17: Percentage of medical scheme contribution to patient contribution for products containing methylphenidate or atomoxetine in the different age groups for all study years.

4.5.5.2 Average cost per prescription of products containing methylphenidate or atomoxetine

The average medicine cost per prescription of products containing methylphenidate or atomoxetine will be discussed according to general analysis, gender and age groups.

4.5.5.2.1 General analysis average cost per prescription

In 2005 the average medicine cost per prescription for products containing methylphenidate or atomoxetine was R318.29±162.09 and in 2007 it was R358.91±208.10. The results in Appendix A, Table A.10 revealed that the average medicine cost per prescription increased with 12.76% from 2005 to 2007. However, this was not of practical significance ($d < 0.8$)

The results in Table A.10 from Appendix A revealed that in 2005 the average patient medicine cost contribution was R38.37±91.88 where the medical scheme contributed on average

R279.91±163.12 to the total cost of products containing methylphenidate or atomoxetine. In 2006 and 2007 the patients contributed R56.67±120.24 and R72.71±134.27 and the medical schemes contributed on average R294.91±193.51 and R286.20±205.25 respectively. For both the patient and medical scheme average the medicine cost contribution had no change of practical significance ($d < 0.8$) (refer to Table A.10 in Appendix A).

4.5.5.2.2 Average medicine cost analysis per prescription according to gender

The results in Appendix A, Table A.11 revealed that the average medicine cost per prescription for products containing methylphenidate or atomoxetine for females was R307.37±158.54 in 2005 and it increased to R349.49±208.08 in 2007. For the male group the average medicine cost per prescription for these products was R322.05±163.13 in 2005 and R362.12±208.01 in 2007. However, the differences between 2005 and 2007 were not practically significant for both groups ($d < 0.8$) (refer to Table A.11 in Appendix A).

In 2005 the average medicine contribution per prescription for products containing methylphenidate or atomoxetine prescribed for female patients was R40.16±93.98 where medical schemes contributed on average R267.22±158.90. In 2006 and 2007 female patients contributed on average R58.43±122.21 and R74.40±137.65 respectively per prescription for these products while the medical scheme contributed R286.16±192.55 and R275.09±202.35 respectively. Although there was an *increase* in female patients' contribution per prescription and a decrease in medical schemes contribution per prescription from 2005 to 2007 the difference was not practically significant ($d < 0.8$) (refer to Table A.11 in Appendix A).

In 2005 males' medicine cost contribution per prescription for products containing methylphenidate or atomoxetine was R37.77±91.13 and the medical schemes contributed on average R284.29±164.32. The medical schemes' contributions to the average cost per prescription for these products for 2006 and 2007 were R297.87±193.68 and R289.99±206.12 respectively. Patients contributed on average R55.92±119.15 and R72.12±133.11 respectively per prescription for 2006 and 2007 for prescriptions containing methylphenidate or atomoxetine. Although the average patient contribution per prescription *increased* from 2005 to 2007, it was not practically significant ($d < 0.8$) (refer to Table A.11 in Appendix A). The average medical scheme's medicine contribution on prescriptions containing methylphenidate or atomoxetine did not decrease practically significantly from 2005 to 2007.

4.5.5.2.3 Average medicine cost analysis per prescription according to age groups

According to Table A.12 in Appendix A, children 5 years and younger had an average medicine cost per prescription containing methylphenidate or atomoxetine products of R219.44±157.23 in 2005 and it increased to R313.58±251.07 in 2007. Children aged 5 years to 12 years resulted in an average medicine cost per prescription containing methylphenidate or atomoxetine products of R294.10±145.96 in 2005 while it increased to R335.01±193.43 in 2007.

Adolescents aged 12 years to 18 years had the highest average medicine cost per prescription during 2005 (R357.39±159.05) to 2007(R394.12±203.62) for these products. The results in Table A.35 in Appendix A documented that adults older than 18 years showed an average medicine cost per prescription of R346.68±206.48 for products containing methylphenidate or atomoxetine in 2005 and R379.17±249.40 in 2007. These results revealed that the average cost per prescription of products containing methylphenidate or atomoxetine did not change practically significantly ($d < 0.8$) from 2005 to 2007 for all age groups (refer to Table A.12 in Appendix A).

In 2005 the average medicine cost per prescription for products containing methylphenidate or atomoxetine in children 5 years and younger was R219.44±157.23, the average patient medicine contribution was R25.85±64.25 and the medical scheme contributed on average R193.59±160.73. In 2006 and 2007 most of the medicine cost was covered by the medical schemes with average contributions of R179.18±162.01 and R230.41±229.93 followed by the patient's contribution of R53.52±104.76 and R83.16±173.40 respectively (refer to Table A.12 in Appendix A). The results revealed that there were no practically significant changes in the contributions by patients or medical schemes for products containing methylphenidate or atomoxetine for children age 5 years and younger from 2005 to 2007 ($d < 0.8$).

For children aged 5 years to 12 years during 2005 the medical schemes contributed mostly to the cost of prescriptions containing methylphenidate or atomoxetine products (R261.74±149.58) while patients contributed on average only R32.36±79.44. For 2006 and 2007 medical schemes contributed mostly to the average cost per prescription for these products (R278.49±181.79 vs R270.19±192.08) followed by patients' contributions of R49.30±106.00 and R64.82±119.08 respectively (refer to Table A.12 in Appendix A).

However, these results revealed that both the patient medicine contribution and medical scheme's contribution for products containing methylphenidate or atomoxetine did not show a practically significant change from 2005 to 2007 ($d < 0.8$).

Adolescents, aged 12 years to 18 years, had the third highest frequency of prescriptions. In 2005 the patients' medicine contribution was only R42.12±100.25 where the medical schemes contributed the additional R315.27±164.76. In 2006 and 2007 the medical schemes contributed the greater part of medicine cost per prescription with an average of R334.79±199.78 and R324.47±208.98. Furthermore patients contributed R58.41±125.22 and R69.64±131.23 for 2006 and 2007 respectively (refer to Table A.12 in Appendix A).

An *increase* in the patient contribution of 65.34% for products containing methylphenidate and/or atomoxetine was identified from 2005 to 2007. However, this increase was not practically significant ($d < 0.8$)

For adults, older than 18 years, the greater part of the medicine cost of products containing methylphenidate or atomoxetine was covered by the medical scheme with R289.88±198.11 in 2005 while patients contributed on average R56.80±117.95. For 2006 and 2007 the patient contribution was R82.79±155.37 and R106.36±177.41 and the medical scheme contributed R285.39±213.95 and R272.81±231.26 respectively (refer to Table A.12 in Appendix A). Again the changes in both patients' medicine contribution and medical schemes' contribution were of no practical significance ($d < 0.8$) from 2005 to 2007.

4.5.5.3 Average cost per medicine item containing methylphenidate or atomoxetine

4.5.5.3.1 General analysis of average cost per medicine item containing methylphenidate or atomoxetine

According to Table A.16 in Appendix A, the average cost per medicine item of products containing methylphenidate or atomoxetine during 2005 was R299.42±144.97 where it increased to R336.22±192.02 in 2007. These results disclosed that the changes from 2005 to 2007 were not practically significant ($d < 0.8$).

During 2005 the average cost per medicine item of products containing methylphenidate or atomoxetine was covered by the medical scheme with R263.32±149.21 while patients contributed R36.10±84.71. In 2006 and 2007 the average patient contribution to the cost per medicine item of these products was R53.30±112.25 and R68.12±125.18 and the medical scheme contributed R277.35±180.57 and R268.11±192.46 respectively (refer to Table A.16 in Appendix A).

An *increase* in the patient contribution was observed from 2005 to 2007. Therefore a decrease of the same value was observed for medical scheme contribution. However, the results revealed that these differences were not practically significant ($d < 0.8$).

4.5.5.3.2 Analysis of average cost per medicine item containing methylphenidate or atomoxetine according to gender

During 2005 the average cost per medicine item of products containing methylphenidate or atomoxetine for females was R288.93±142.50 and it increased during 2007 to R328.72±193.90. On the other hand for the male group, the average cost per medicine item for products containing methylphenidate or atomoxetine during 2005 was R303.04±145.65 which increased to R338.73±191.28 with 11.77% in 2007. As the results revealed, there were no practically significant differences between males or females in the average cost per medicine item for products containing methylphenidate or atomoxetine from 2005 until 2007 ($d < 0.8$) (refer to Table A.17 in Appendix A).

According to Table A.17 in Appendix A, the average medical scheme contribution of females for products containing methylphenidate or atomoxetine during 2005 ($N = R288.93\pm142.50$) was R251.19±145.98 while an average patient contribution concluded to R37.75±87.02. For 2007 ($N = R328.72\pm193.90$) the average medical scheme contribution for females for products containing methylphenidate or atomoxetine was R258.74±191.51 while the average patient medicine contribution was R69.98±128.59. On average female patient medicine contribution *increased* with 85.38% where the average medical scheme contribution for products containing methylphenidate or atomoxetine did not really change. The results revealed that there were no practical significant differences in either the patient medicine contribution or the medical scheme contribution for products containing methylphenidate or atomoxetine ($d < 0.8$) from 2005 to 2007 (refer to Table A.17 in Appendix A).

In 2005 male patients ($R303.04\pm145.65$) contributed R35.54±83.90 to the average medicine cost per medicine item for products containing methylphenidate or atomoxetine while the medical scheme contributed an average of R267.50±150.09. In 2007 ($R338.73\pm191.28$) the average patient medicine contribution per medicine item for products containing methylphenidate and/or atomoxetine was R271.27±192.67 where the patients contributed on average R67.47±124.01. The average male patient contribution per medicine item for products containing methylphenidate or atomoxetine had increased from 2005 to 2007 with 89.84% where the average medical scheme contribution did not really change (refer to Table A.17 in Appendix A) . The results revealed that there were no practically significant differences in either the patient medicine contribution or the medical scheme contribution for products containing methylphenidate or atomoxetine in males ($d < 0.8$).

4.5.5.3.3 Analysis of average cost per medicine item containing methylphenidate or atomoxetine according to age groups

According to Table A.18 in Appendix A, children 5 years and younger had an average cost per medicine item for products containing methylphenidate or atomoxetine during 2005 of R210.42±141.61 which increased to R300.27±222.09 in 2007. Children aged 5 years to 12 years on the other hand had an average cost per medicine item for products containing methylphenidate or atomoxetine of R280.47±132.31 in 2005 and R315.85±181.63 in 2007 respectively. Furthermore adolescents, aged 12 years to 18 years, had the highest average cost per medicine item for products containing methylphenidate or atomoxetine of all the age groups during 2005 (R328.81±38.75) to 2007 (R367.77±189.22) which was followed by adult patients, older than 18 years, with R321.82±184.35 in 2005 and R349.51±220.06 in 2007 (refer to Table A.18 in Appendix A). The results revealed that there were no practically significant differences ($d < 0.8$) between the average medicine cost for products containing methylphenidate or atomoxetine from 2005 to 2007 for all age groups.

For children aged 5 years and younger during 2005 (R210.42±141.61) the majority of the average cost per medicine item for products containing methylphenidate or atomoxetine was covered by the medical scheme with R185.63±144.68 followed by the patient contribution of R24.79±62.99. In 2006 (R223.97±160.01) and 2007 (R300.27±222.09) the patients contributed R51.51±101.98 and R79.63±160.28 while the medical scheme contributed R172.46±157.57 and R220.63±207.77 for products containing methylphenidate or atomoxetine respectively. The average patient contribution had increased as the medical scheme contribution decreased from 2005 to 2007 by 14.74% for products containing methylphenidate or atomoxetine (refer to Table A.18 in Appendix A). The results disclosed that there were no practically significant differences ($d < 0.8$) in the patient's medicine contribution or medical schemes' contribution for products containing methylphenidate or atomoxetine in children 5 years and younger from 2005 to 2007.

In 2005 (R280.47±132.31) the contribution for children aged 5 years to 12 years concluded to R30.86±74.71 and the medical scheme contributed the greater part to the average cost per medicine item of R249.61±138.04 for products containing methylphenidate or atomoxetine. In 2006 (R311.51±163.72) and 2007 (R315.85±181.63) the greater part of the cost was covered by the medical scheme with R264.65±171.62 and R254.74±182.16 respectively. The rest of the expenses were covered by patients with R46.85±100.78 and R61.11±112.63 respectively.

The average patient contribution for products containing methylphenidate or atomoxetine increased from 2005 to 2007 by 8.35% (refer to Table A.18 in Appendix A). The results from the patient

medicine contribution and medical scheme contribution revealed that there were no practically significant changes from 2005 to 2007 ($d < 0.8$), in the contributions made for this age group.

The greater part of the expenses for adolescents aged 12 years to 18 years to the average cost per medicine item for products containing methylphenidate or atomoxetine was covered during 2005 (R328.81±38.75) by the medical scheme with R290.05±149.51. The rest was covered by the patients with R38.75±90.62. In 2006 (R365.23±172.02) and 2007 (R367.77±189.22) patients contributed R54.26±115.93 and R64.99±122.72 and the medical scheme contributed R310.97±183.94 and R302.78±196.36 respectively to the average medicine cost per medicine item for products containing methylphenidate or atomoxetine. Patient contribution increased from 2005 (11.78%) to 2007 (17.67%) by 5.89% (refer to Table A.18 in Appendix A).

For adolescents, aged 12 years to 18 years, there was no practically significant differences in the patient medicine contribution or the medical scheme contribution towards the cost of products containing methylphenidate or atomoxetine from 2005 to 2007 ($d < 0.8$).

In 2005 (R321.82±184.35) the total patient contribution for adults older than 18 years to the average cost per medicine item for products containing methylphenidate or atomoxetine was R52.72±106.67 as the medical scheme contributed R269.10±181.41. For 2006 (R340.35±201.64) and 2007 (R349.51±220.06) the greater part of the expenses for products containing methylphenidate or atomoxetine was carried by the medical scheme with R263.82±198.28 and R251.47±210.25 and the patients contributed R76.53±140.80 and R98.04±160.53 respectively.

Patient contribution for products containing methylphenidate or atomoxetine increased from 2005 (16.38%) to 2007 (28.05%) by 11.67%.

These results revealed that there were no changes or differences of practical significance in either in the patient medicine contribution or the medical scheme contribution for products containing methylphenidate or atomoxetine during 2005 to 2007 ($d < 0.8$) for adults older than 18 years (refer to table A.18 in Appendix A).

4.5.6 Average medicine cost per generic indicator of medicine items containing methylphenidate or atomoxetine

4.5.6.1 General analysis of average medicine cost per medicine item according to generic indicator

In 2005 the average medicine cost for innovator products with no generic ("N" indicated) containing methylphenidate or atomoxetine was R363.27±119.53 and in 2007 it was R393.77±177.76. For the

innovator products ("O" indicated) containing methylphenidate expenses showed an average medicine cost of R215.85±125.05 in 2005 and in 2007 it was R184.20±128.74. As for generic products ("Y" indicated) containing methylphenidate the average medicine cost during 2005 was R126.26±67.48 while in 2007 it concluded to R131.32±92.65 (refer to Tables A.19 and A.20 in Appendix A). The results established that there was no practical significance in the average cost per medicine item for various generic indicators of medicine from 2005 to 2007 ($d < 0.8$).

The average medicine cost for innovator products containing methylphenidate and/or atomoxetine with no generic ("N" indicated) amounted to (R363.27±119.53) in 2005 and was covered mostly by the medical scheme with R324.12±135.04 and patients contributed R39.15±95.98. In 2006 (R397.28±153.43) and 2007 (R393.77±177.76) patients contributed R56.72±127.04 and R71.81±137.78 and the medical scheme contributed most of the average cost with R340.56±171.75 and R321.95±187.51 respectively. Patient contribution *increased* from 2005 (10.78%) to 2007 (18.24%) by 83.42% as did the medical schemes contribution *decrease* by 0.67% for innovator products containing methylphenidate or atomoxetine with no generic ("N" indicated) (refer to Tables A.19 and A.20 in Appendix A). As the results showed, there was no practically significant difference in the patients or the medical scheme's contribution to innovator products containing methylphenidate or atomoxetine with no generic ("N" indicated) from 2005 to 2007 ($d < 0.8$).

In 2005 (R215.85±125.05) innovator products containing methylphenidate ("O" indicated) had a patient contribution of R37.35±66.94 and the medical schemes contributed R178.50±121.04. In 2006 (R221.36±128.37) and 2007 (R184.20±128.74) the medical schemes contributed most of the average cost with R153.00±122.47 and R113.65±104.97 and the patients contributed R58.35±75.73 and R70.55±80.07 respectively. Patient contribution *increased* from 2005 (17.30%) to 2007 (38.30%) by a staggering 88.89% for innovator products containing methylphenidate ("O" indicated) as there was a *decrease* in the medical scheme contribution of identical value (refer to Tables A.19 and A.20 in Appendix A). The results revealed that there was no practical significance in the patient's medicine contribution during 2005 to 2007 for innovator products containing methylphenidate ("O" indicated) and the same applied to contributions by medical schemes ($d < 0.8$).

The average medicine cost for generic products containing methylphenidate ("Y" indicated) in 2005 was R126.26±67.48 with a patient contribution of R9.99±31.76 and a medical scheme contribution of R116.28±66.64. In 2006 (R128.83±77.04) and 2007 (R131.32±92.65) the medical schemes contributed R116.67±75.16 and R110.96±85.21 respectively. Patients contributed R12.16±38.34

and R20.36±53.50 for 2006 and 2007 respectively. An *increase* in the patient contribution and a decrease in medical scheme contribution in generic products containing methylphenidate (“Y” indicated) during 2005 (7.91%) to 2007 (15.50%) by **95.96%** was documented (refer to Tables A.19 and A.20 in Appendix A). The results revealed that both the patient medicine contribution and medical scheme contribution for generic products containing methylphenidate (“Y” indicated) showed no practical significance ($d < 0.8$).

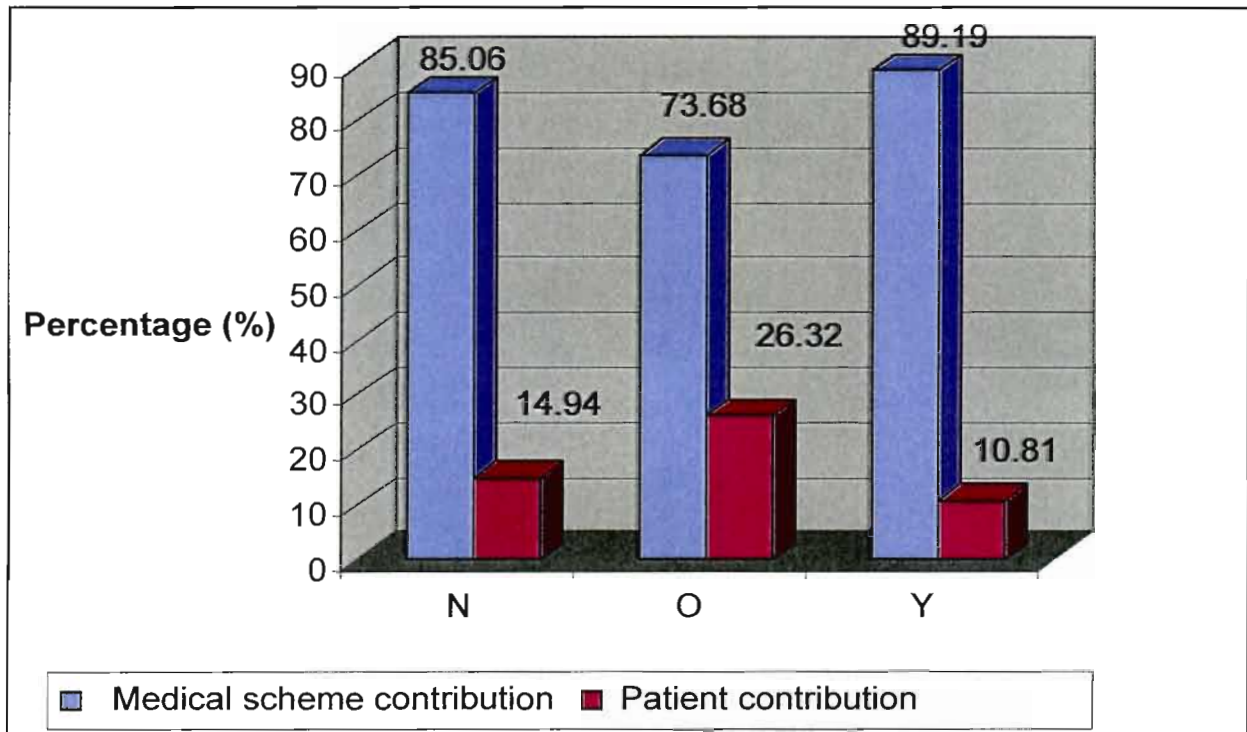


Figure 4.18: Percentage contributions of medical schemes and patients to the total cost of products containing methylphenidate or atomoxetine according to generic indicator for 2005 to 2007.

**Calculation for figure 4.14 was done by adding the total medical scheme contributions and patient contributions of the different generic indicators respectively for all study years and dividing the total by the sum of the total cost of each medicine type.

4.5.6.2 Cost saving with the substitution of innovator products for generic products.

**Calculations for this section were done by multiplying the number of innovator products containing methylphenidate (“O” indicated) with the average cost per medicine item of generic products

containing methylphenidate ("Y" indicated) where the dosage of the active ingredient corresponded with each other (refer to chapter 3, section 3.6.1.3). Data were extracted from Tables A.20 to A.22 in Appendix A.

In 2005 Ritalin 10mg[®] Tab could be substituted for Adaphen 10mg[®] and Methylphenidate HCl-Douglas[®]. When Ritalin 10mg[®] Tab is substituted for Adaphen 10mg[®], the total cost saving would be R718, 342.36 annually. For Ritalin 10mg[®] to be substituted for Methylphenidate HCl-Douglas[®] cost saving would be R666, 464.56. Ritalin SR 20mg[®] could be substituted for Adaphen XL 20mg[®] in which the cost saving would be R45, 153.25 (refer to Table A.20 in Appendix A).

The following equation was used to calculate this:

Calculation: $X - (Y*Z)$

X = total cost of Ritalin 10mg[®] (R1, 718,024.48) or Ritalin SR 20mg[®] (R147, 606.98)

Y = number of Ritalin 10mg[®] items (n=8,173) or Ritalin SR 20mg[®] (n=470)

Z = average medicine cost per medicine item for Adaphen 10mg[®] (R122.32),

Methylphenidate HCl-Douglas[®] (R128.67) or Adaphen XL 20mg[®] (R218.00)

In 2006 Ritalin 10mg[®] could be substituted for Adaphen 10mg[®] and Methylphenidate HCl-Douglas[®]. Where Ritalin 10mg[®] was substituted for Adaphen 10mg[®], the total cost saving could be R503, 945.85 annually. For Ritalin 10mg[®] to be substituted for Methylphenidate HCl-Douglas[®] cost saving would be R498, 327.40.

If Ritalin SR 20mg[®] could be substituted for Adaphen XL 20mg[®] the cost saving could be R70, 749.07 (refer to Table A.21 in Appendix A).

Calculation: $X - (Y*Z)$

X = total cost of Ritalin 10mg[®] (R1, 347,103.52) or Ritalin SR 20mg[®] (R321, 125.97)

Y = number of Ritalin 10mg[®] items (n=6,828) or Ritalin SR 20mg[®] (n=1,065)

Z = average medicine cost per medicine item for Adaphen 10mg[®] (R123.49), Methylphenidate HCl-Douglas[®] (R124.31) or Adaphen XL 20mg[®] (R235.10).

In 2007 Ritalin 10mg[®] could be substituted for Adaphen 10mg[®] and Methylphenidate HCl-Douglas[®]. If Ritalin 10mg[®] were to be substituted for Adaphen 10mg[®], the total cost saving could be R274, 730.46 annually. For Ritalin 10mg[®] to be substituted for Methylphenidate HCl-Douglas[®] cost saving could be R351, 232.63.

Bu substituting Ritalin SR 20mg[®] for Adaphen XL 20mg[®] a cost saving of R18, 476.99 would be possible (refer to Table A.22 in Appendix A).

Calculation: $X - (Y * Z)$

X = total cost of Ritalin 10mg[®] (R1, 112,970.43) or Ritalin SR 20mg[®] (R99, 765.04)

Y = number of Ritalin 10mg[®] items (n=6,261) or Ritalin SR 20mg[®] (n=377)

Z = average medicine cost per medicine item for Adaphen 10mg[®] (R135.48), Methylphenidate HCl-Douglas[®] (R123.26) or Adaphen XL 20mg[®] (R215.62)

A limitation of this method is that the calculation was done assuming that generic substitution had occurred in 100% of the cases. In practice doctors do not always prescribe generic products and pharmacists do not always substitute innovator products for generic products. In conclusion a total of R1,497,018.67 could be saved over the three years if Ritalin 10mg[®] were substituted for Adaphen 10mg[®] and R1,516,024.59 could be saved if Ritalin 10mg[®] were substituted for methylphenidate HCl-Douglas. If Ritalin SR 20mg was substituted for Adaphen XL 20mg, R134,379.31 could be saved over the three-year period.

4.5.6.3 Potential drug interactions

For this section the potential drug-drug interactions between methylphenidate or atomoxetine containing products and other central nervous system (CNS) drugs will be discussed. Data were extracted from Tables B.1, B.2 and B.3 in Appendix B.

The results revealed that the percentage of prescriptions containing CNS products in combination with products containing methylphenidate or atomoxetine in relation to the total number of prescriptions containing methylphenidate or atomoxetine stayed the same during 2005 (N = 27,724) with 652 (2.00%) and 749 (2.00%) in 2007 (N = 32,712).

In 2005 (N=652) imipramine was prescribed in combination with methylphenidate or atomoxetine containing products in 363 prescriptions. In 2006 (N=751) and 2007 (N=749) imipramine was prescribed in combination with methylphenidate or atomoxetine containing products annually in 357

and 354 prescriptions (refer to chapter 2, section 2.11.1.8) (refer to Tables B.1 to B.3 in Appendix B).

In 2005 (N=652) amitriptyline ranked second and was prescribed with methylphenidate containing products in 193 prescriptions. In 2006 (N=751) and 2007 (N=749) amitriptyline was prescribed in combination with methylphenidate or atomoxetine containing products in 239 and 274 prescriptions (refer to chapter 2, section 2.11.1.6) (refer to Tables B.1 to B.3 in Appendix B).

In 2005 (N=652) carbamazepine was prescribed with methylphenidate containing products in 76 prescriptions. In 2006 (N=751) and 2007 (N=749) carbamazepine was prescribed in combination with methylphenidate or atomoxetine containing products annually in 132 and 94 prescriptions (refer to chapter 2, section 2.11.1.3) (refer to Tables B.1 to B.3 in Appendix B).

In 2005 (N=652) clomipramine was prescribed with methylphenidate containing products in 24 prescriptions. In both 2006 (N=751) and 2007 (N=749) clomipramine was prescribed in combination with methylphenidate or atomoxetine containing products annually in 28 and 24 prescriptions (refer to chapter 2, section 2.11.1.7) (refer to Tables B.1 to B.3 in Appendix B).

In 2005 (N=652) trimipramine was prescribed with methylphenidate containing products in one prescription. In 2006 (N=751) and 2007 (N=749) trimipramine was prescribed in combination with methylphenidate or atomoxetine containing products annually in five and five prescriptions (refer to chapter 2, section 2.11.1.9) (refer to Tables B.1 to B.3 in Appendix B).

In 2005 (N=652) phenytoin was prescribed with methylphenidate containing products in three prescriptions. In both 2006 (N=751) and 2007 (N=749) phenytoin was prescribed in combination with methylphenidate or atomoxetine containing products annually in 0 and 0 prescription (refer to chapter 2, section 2.11.1.9) (refer to Tables B.1 to B.3 in Appendix B).

4.5.6.4 Number of prescriptions consisting of products containing methylphenidate and/or atomoxetine and other CNS products: Top ten

Data were extracted from Tables B.1; B.2 and B3 from Appendix B.

**Table 4.20, Table 4.21 and Table 4.22 indicate the top 50 (according to prevalence) prescriptions containing methylphenidate or atomoxetine products in combination with other CNS products as a percentage of the total number of prescriptions containing CNS medicine items as well as methylphenidate and atomoxetine containing products.

Table 4.20 Number of prescriptions of products containing methylphenidate and atomoxetine in combination with other central nervous system (CNS) products for 2005 (N=652)

Year	Product	Item	Frequency (n)	Percentage (%) to total number of prescriptions
2005	Methylphenidate or atomoxetine	Citalopram	3	0.46
		Escitalopram	4	0.61
		Buspirone	19	2.91
		Clomipramine	24	3.68
		Risperidone	26	3.99
		Lamotrigine	40	6.13
		Fluoxetine	58	8.90
		Carbamazepine	76	11.66
		Amitriptyline	193	29.60
		Imipramine	363	55.67

Table 4.21 Number of prescriptions of products containing methylphenidate and atomoxetine in combination with other central nervous system (CNS) products for 2006 (N=751).

Year	Product	Item	Frequency (n)	Percentage (%) to total number of combinations
2006	Methylphenidate or atomoxetine	Escitalopram	4	0.53
		Trimipramine	5	0.67
		Lamotrigine	8	1.07
		Citalopram	11	1.46
		Clomipramine	28	3.73
		Valproate (sodium)	29	3.86
		Risperidone	60	7.99
		Carbamazepine	132	17.58
		Amitriptyline	239	31.82
		Imipramine	357	47.27

Table 4.22 Number of prescriptions of products containing methylphenidate and atomoxetine in combination with other central nervous system (CNS) products for 2007 (N=749)

Year	Product	Item	Frequency (n)	Percentage (%) to total number of combinations
2007	Methylphenidate or atomoxetine	Trimipramine	5	0.67
		Citalopram	8	1.07
		Lamotrigine	14	1.87
		Citalopram	15	2.00
		Clomipramine	24	3.20
		Risperidone	33	4.41
		Valproate (sodium)	49	6.54
		Carbamazepine	94	12.55
		Amitriptyline	274	36.58
		Imipramine	353	47.13

Risperidone is a product indicated for acute and chronic schizophrenic psychoses with positive and/or negative symptoms, or when affective symptoms are prominent. It is also used for the management of behavioural symptoms (aggression, wandering, and agitation) and psychosis associated with dementia (Gibbon. 2005:428). The number of Risperidone prescriptions increased from 2005 (3.99%) to 2007 (4.41%) with 0.42% (refer to Table 4.20 and 4.22).

Imipramine has the same indications as amitriptyline and is also used in the management of panic disorders. Imipramine is better studied than amitriptyline and is therefore preferred (Gibbon, 2005:439). The number of imipramine items prescribed in combination with products containing methylphenidate decreased during 2005 (55.67%) to 2007 (47.13%) by 8.54% (refer to Tables 4.20 and 4.22).

Amitriptyline is indicated for the management of depressive illness and is also used in the management of anxiety disorders and as an adjuvant to pain relief in chronic pain syndromes (unregistered indications) as well as for nocturnal enuresis (adjunctive therapy) in children over six years of age, after exclusion of organic pathology (Gibbon., 2005:438). During 2005 (29.60%) to 2007 (36.58%) the number of products containing amitriptyline in combination increased with 6.98% (refer to Table 4.20 and 4.22).

4.5.6.5 Possible reasons for the other combinations

Escitalopram and citalopram are selective serotonin re-uptake inhibitors (SSRIs) which are as effective as the tricyclic antidepressants in the management of depressive disorders, and have the advantage of fewer anticholinergic and cardiovascular effects. These drugs have a lower potential for drug interactions than the other SSRI's (Gibbon., 2005:439).

Valproate sodium is indicated for all forms of epilepsy and is the drug of first choice in the treatment of tonic-clonic seizures as part of the syndrome of primary generalised epilepsy. It is also used for prophylaxis of migraine and for control of the acute manic phase of bipolar disorder (unregistered indications) (Gibbon, 2005:407).

Lamotrigine is indicated as monotherapy or add-on therapy of partial epilepsy with or without secondary generalised tonic-clonic seizures and in primary generalised tonic-clonic seizures. It is registered as adjunctive therapy for children with Lennox-Gastaut syndrome (Gibbon. 2005:489).

Fluoxetine is indicated for depressive disorders, bulimia nervosa and obsessive compulsive disorder. It is also used off-label for anxiety disorders; especially panic states and generalised anxiety disorder (Gibbon. 2005:439).

Carbamazepine is used as a first-line agent for the management of generalised tonic-clonic epilepsy (primary, or secondary to a focal discharge). It is also a drug of choice in controlling partial seizures (simple or complex), but is not effective in the treatment of absence seizures (petit mal) or atonic seizures. While not primarily an analgesic, it may be of benefit in the management of pain such as trigeminal neuralgia, the neuralgic states associated with multiple sclerosis and nerve trauma as well as diabetic and post herpetic neuralgias. It has been used to control neurohypophyseal diabetes insipidus, chronic dystonic disorders and intractable hiccups, and also as a successful alternative to lithium in the prophylactic treatment of bipolar affective disorders (Gibbon. 2005:405).

Buspirone is a non-sedating anti-anxiety agent with insignificant abuse and misuse potential (Gibbon. 2005:434).

Clonidine is used in the prevention of recurrent migraine, vascular headache, and menopausal flushing (Gibbon. 2005:399).

4.5.7 Prescribed daily dose (PDD)

In this section the prescribed daily dose (PDD) was determined between the innovator and generic products of products containing methylphenidate and atomoxetine (refer to chapter 3, section 3.6.2.3). This section will include a discussion on Ritalin LA 20mg[®], Ritalin 10mg[®], Ritalin LA 30mg[®], Concerta 36mg[®], Concerta 18mg[®] and Methylphenidate HCl-Douglas[®].

4.5.7.1 Ritalin LA 20mg[®]

According to Gibbon (2007:3) Ritalin LA 20mg[®] tablets are to be given once daily to replace 10mg methylphenidate twice daily or Ritalin SR 20mg[®] once daily. The effect was illustrated in figure 2.11.2 in chapter 2.

During 2005 Ritalin LA 20mg[®] (N = 8,707) was primarily prescribed (93.15%) according to the recommended PDD of 20mg per day (n=8,111) followed by a PDD dose of 40mg per day (n=239). A further 23 items were prescribed with a PDD of 600mg. Also in 2006 Ritalin LA 20mg[®] (N = 7,592) was mainly prescribed in a PDD of 20mg (n = 7,100) followed by 60mg daily (n=195) and with an unexpected case of 450mg (n =1) per day. In 2007 Ritalin LA 20mg Cap[®] (N=7,374) was prescribed in a PDD of 20mg and ranked 1st with 6,680 cases followed by 229 cases with PDD of 40mg. The results further identified 210 cases with PDD of 60mg (refer to Tables A.36 to and A.38 in Appendix A).

The average PDD for Ritalin LA 20mg[®] during 2005 was 28.17mg±49.79 where 94.27% received below the average PDD dose. Furthermore the average PDD during 2007 was 21.81mg±7.57 mg where the results reported that 93.38% of the individuals received below the average PDD. The influence of the age group on the PDD will be discussed in 4.5.3.1.

4.5.7.2 Ritalin 10mg[®]

According to Gibbon (2007:3) the average PDD for Ritalin 10mg Tab[®] is 20-30mg daily with two to three divided dosages where some patients require 40-60mg daily.

In 2005 (N=8,173) Ritalin 10mg[®] was prescribed in 4,307 (52.70%) cases according to a PDD of 10mg followed by 20mg daily with 1,497 (18.32%) cases. A further 484 items were prescribed at a PDD of 30mg and one patient received a startling PDD of 1200mg (n = 1). During 2006 (N=6,828) the majority of Ritalin 10mg[®] prescriptions had a PPD of 10mg (n =3,680) followed by 20mg daily (n = 1,317). Also during 2006 Ritalin 10mg[®] was prescribed in a PDD of 30mg (n= 327) while in two cases there was a PPD of 1200mg. In 2007 Ritalin

10mg[®] (N=6,261) was prescribed at a PDD of 10mg with 3,416 cases followed by 20mg in 1,240 cases. Meanwhile it was surprising to find that in 2007 the highest dosage was 110mg (n = 1) (refer to Tables A.36 to and A.38 in Appendix A). The results revealed that the average PDD during 2005 was 21.45mg±44.36 mg where 84.67% of patients receiving Ritalin 10mg[®] received less than that. Meanwhile during 2007 the average PDD was 16.11mg±11.39 mg and 67.23% of the patients receiving Ritalin 10mg[®] received less than 16.11mg±11.39 mg.

4.5.7.3 Concerta 36mg[®]

The results revealed that Concerta 36mg[®] ranked third in both 2006 (N = 4,104) and 2007 (N = 5,682) whereas in 2005 it ranked 4th. During 2005 (N = 1,969) the PDD was 36mg in 1,911 (97.05%) cases, followed by 540mg (n = 37) and with an outlier of 1080mg (n = 1) (refer to Table A.36). During 2006 and 2007 Concerta 36mg[®] had a PDD of 36mg in 4,044 (98.55%) and 5,475 (96.36%) cases with an outlier of 540mg in 14 cases and 108mg (n = 1) for each study year respectively (refer to Table A.37 to A.43). According to Gibbon (2007:2) Concerta 36mg[®] should be administered once daily in the morning and a maximum of 54mg per day. During 2006 a total of 98.76% patients receiving Concerta 36mg[®] received less than the average PDD of 38.02mg±29.67. Furthermore during 2007 the average PDD was 37.14mg±6.36 where the results reported that 93.38% of patients received less than 37.14mg±6.36.

Ritalin LA 30mg[®] shifted from third ranked methylphenidate containing products in 2005 to 4th in 2006 and 5th in 2007. During 2005 (N = 2,667) Ritalin LA 30mg[®] showed a PDD of 30mg (n = 2,489) with an outlier of 900mg (n = 2) (refer to Table A.36). The results revealed that approximately 94.64% of patients receiving Ritalin LA 30mg[®] received less than the average PDD of 40.22mg±63.51 mg.

In 2006 (N = 2,523), the PDD was 30mg (n = 2,338) with a frequency of 92.67% and an outlier of 450mg (n = 13). Also in 2007 (N = 2,663) Ritalin LA 30mg[®] was mostly prescribed in a PDD of 30mg (n = 2,481) followed by 60mg (n = 210) and an outlier of 300mg (n = 2) (refer to Table A.38). According to Gibbon (2007:3) Ritalin LA 30mg Cap[®] once daily can replace 15mg methylphenidate twice daily. During 2006 only about 93.54% of patients received less than the average PDD (35.10mg±35.24 mg) while in 2007 (31.68mg±10.99mg) only 94.44% of patients received less than the average PDD Ritalin LA 30mg[®].

4.5.7.4 Prescribed daily dose according to age groups

4.5.7.4.1 Ritalin LA 20mg[®]

During 2005 (N=8,707) Ritalin LA 20mg[®] was mainly prescribed for children aged 5 years to 12 years in 60.31% (n=5,251) of cases. Ritalin LA 20mg[®] was prescribed in a PDD of 20mg in 4,999 cases followed by 13 outlier cases of 600mg daily. The results revealed that adolescents aged 12 years to 18 year had a PDD of 20mg in 2,364 cases where only six outlier prescriptions of 600mg daily were documented (refer to Table A.42 in Appendix A). During 2005 about 96.31% of children aged 5 years to 12 years had an average PDD of 27.43mg±48.74mg or less while adolescents, aged 12 years to 18 years (93.82%), received an average PDD of 28.69mg±50.43mg or less (Refer to table A.42 in Appendix A).

During 2006, Ritalin LA 20mg[®] (N = 7,592) showed a frequency for children aged 5 years to 12 years of 58.29% (n = 4,425) which was followed by adolescents aged 12 years to 18 years with 29.74% (n = 2,258). The PDD for both age groups was 20mg at a frequency of 4,237 and 2,082 cases respectively. The outlier PDD for Ritalin LA 20mg[®] during 2006 was 300mg (n = 29) for children aged 5 years to 12 years and during 2007 the 600mg (n = 1) was documented for adolescents, aged 12 years to 18 years, (refer to Tables A.43 and A.44). The results revealed that for children aged 5 years to 12 years about 95.22% of these patients received an average PDD of 21.34mg±6.69mg or less where in the case of adolescents, aged 12 years to 18 years, more of them (94.06%) received the average PDD of 21.62mg±7.43mg or less.

4.5.7.4.2 Ritalin 10mg[®]

Children aged 5 years to 12 years represented 65.13% (n=5,323) of all age groups that received Ritalin 10mg Tab[®] during 2005 (N=8,173). Children aged 5 years to 12 years showed a PDD of 10mg (n=2,932) followed by an outlier prescription (450mg) during 2005 (N = 5,323). Adolescents, aged 12 years to 18 years, showed a PDD of 10mg in 779 cases with a single outlier prescription of 1200mg (refer to Table A.42). During 2006, Ritalin 10mg Tab[®] (N = 6,828) was ranked second for children aged 5 years to 12 years at a frequency of 63.93% (n=4,364). Adolescents, aged 12 years to 18 years, showed a PDD of 10mg at a frequency of 2,457 cases where adults older than 18 years presented with 650 cases. Furthermore the outlier prescription frequency for adolescents, aged 12 years to 18 years, was for 320mg (n = 1) where in the case of adults, older than 18 years, one prescription had a PPD of 1200mg (refer to Table A.43 in Appendix A).

During 2007 Ritalin 10mg Tab[®] (N=6,261) ranked 2nd where children aged 5 years to 12 years represented 64.67% (n=4,049) followed by adolescents aged 12 years to 18 years with

18.14% (n=1,136) (refer to Table A.44 in Appendix A). Children aged 5 to 12 years who received the average dose or less showed a reported 71.46% (17.67mg±25.81) during 2005 and 63.40% (14.60mg±9.38mg) in 2007.

4.5.7.4.3 Ritalin LA 30mg[®]

During 2005 approximately 81.07% of adolescents aged 12 years to 18 years had an average PDD of 23.50mg±53.81mg or less while in 2007 about 63.87% had an average PDD of 17.07mg±12.40mg or less. Ritalin LA 30mg Cap[®] (N=2,667) indicated the highest prevalence during 2005 for adolescents, aged 12 years to 18 years (n=1,239), with 46.46% followed by children aged 5 years to 12 years with 41.32% (n=1,102). During 2005 adolescents, aged 12 years to 18 years (n = 1,031), and adults, older than 18 years (n = 1,163) showed a prescribed daily dose of 30mg. For children aged 5 years and younger or equal to 12 years, 21 prescriptions showed a PDD dose of 450mg where adolescents aged 12 years to 18 years showed a PDD of 900mg (n = 1) (refer to Table A.42 in Appendix A) .

During 2006 (N=2,523) adolescents, aged 12 years to 18 years, indicated a prevalence of 45.50% (n=1,148) followed by children aged 5 years and younger or equal 12 years with 38.68% (n=976) for Ritalin LA 30mg[®]. It was not prescribed to children age 5 years and younger. A PDD of 30mg for children aged 5 years to 12 years was prescribed in 1,082 cases followed by adolescents aged 12 years to 18 years in 915 cases. Outlier dosages of 450mg for children aged 5 years to 12 years and had been documented in seven cases where for adolescents, aged 12 years to 18 years, it was documented in five cases during 2006 (refer to Table A.43 in Appendix A). Ritalin LA 30mg[®] at (N = 2,663) in 2007 was prescribed to adolescents, aged 12 years to 18 years, in 1,215 cases (45.63%) where children aged 5 years to 12 years followed closely with 38.98% (n=1,038). PDD for children aged 5 years to 12 years at 30mg had been documented in 978 cases where as for adolescents, aged 12 years to 18 years, the PDD was documented in 1,138 cases (refer to Table A.44 in Appendix A). With regard to the average PDD, children aged 5 years to 12 years showed that approximately 95.10% (39.12mg±58.19mg) had received the average PDD or less during 2005 while in 2007 about 96.92% (30.46mg±5.66mg) did. Furthermore about 95.24% and 93.91% of adolescents, aged 12 years to 18 years, received less than the average PDD of 40.80mg±66.00mg and 31.59mg±6.72mg respectively for 2005 and 2007.

4.5.7.4.4 Concerta 36mg[®]

During 2005 (N=1,969) the results revealed that children aged 5 years to 12 years had a prevalence of 50.76% (n=999) in relation to all age groups receiving Concerta 36mg[®] followed by adolescents, aged 12 years to 18 years, with 34.99% (n=689). The PDD of 36mg

for children aged 5 years to 12 years was documented in 982 cases and for adolescents, aged 12 years to 18 years, only 665 cases had been reported. The results revealed an outlier dosage of 1080mg (n = 1) for children aged 5 years to 12 years and was followed by 540mg (n = 18) for adolescents, aged 12 years to 18 years (refer to Table A.42 in Appendix A).

Concerta 36mg[®] ranked first during 2006 (N = 4,104) for children aged 5 years to 12 years with 51.34% (n=2,107) followed by adolescents aged 12 years to 18 years with 37.13% (n=1,524). The PDD of 36mg had been reported in 2,096 cases for children aged 5 years to 12 years. The results revealed that adolescents aged 12 years to 18 years showed a reported 1,484 cases at a PDD of 36mg during 2006.

The outlier PDD for both children aged 5 years and younger or equal 12 years (n = 4) and adolescents aged 12 years to 18 years (n = 8) was at 540mg (refer to Table A.43 in Appendix A).

Concerta 36mg[®] during 2007 (N=5,682) was most frequently prescribed to children aged 5 years to 12 years at a frequency of 50.30% (n=2,858) and adolescents, aged 12 years to 18 years, followed with 35.69% (n=2,028). During 2007 children aged 5 years to 12 years documented 2,822 cases at a PDD of 36mg which was followed by adolescents, aged 12 years to 18 years, with 1,915 cases. The results revealed that these two age groups received 2 tablets daily (PPD of 72mg) in 23 cases and 98 cases respectively during 2007 (refer to Table A.44 in Appendix A). Referring to the average PDD, children aged 5 years to 12 years (98.60%) had received an average PDD of 42.08mg±58.95mg during 2005 and in 2007 about 98.88% had received an average PDD of 36.30mg±3.33mg or less. Adolescents, aged 12 years to 18 years, who received the average PDD or less showed a reported 96.66% (50.02mg±81.92mg) during 2005 and 94.87% (37.75mg±7.79mg) in 2007.

4.5.7.4.5 Methylphenidate HCl-Douglas[®]

Methylphenidate HCl-Douglas[®] ranked 5th during 2005 (N=1,406) showed a prevalence of 63.44% (n=892) for children aged 5 years to 12 years followed by adolescents, aged 12 years to 18 years, at 19.63% (n=276). For children aged 5 years to 12 years, a PDD of 10mg was documented in 373 cases where for adolescents, aged 12 years to 18 years, the results revealed a PDD in 118 cases. Outlier PDD for children aged 5 years and younger or equal 12 years (n = 6) and adolescents aged 12 years to 18 years (n = 1) was documented at 300mg (refer to Table A.42 in Appendix A). The average PDD during 2005 for children aged 5 years to 12 years was 22.19mg±35.28mg or less at a reported 81.17% while adolescents aged 12 years to 18 years reported at 80.80% (19.00mg±20.76mg) or less.

4.5.7.4.6 Concerta 18mg[®]

Concerta 18mg[®] (N= 2,399) was ranked fifth in 2006 where children aged 5 years to 12 years showed a prevalence of 75.03% (n=1,800). The results revealed that for children aged 5 years to 12 years there was a reported 1,732 cases at a PPD of 18mg. The PPD for adolescents aged 12 years to 18 years at 18mg had been documented in 351 cases. Outlier PDD of 270mg had been reported for children aged 5 years to 12 years (n = 7). The outlier PDD was 270mg with a frequency of 7 items while for adolescents aged 12 years to 18 years outlier dosage at 54mg had been documented in 4 cases during 2006 (refer to Table A.43 in Appendix A).

Concerta 18mg[®] (N=3,193) ranked fourth according to prevalence for products containing methylphenidate or atomoxetine during 2007 where children aged 5 years to 12 years received 71.81% (n=2,293) followed by adolescents, aged 12 years to 18 years, with 17.26% (n=551) (refer to Table A.44 in Appendix A). A PDD of 18mg had been reported in 2,196 cases for children aged 5 years and younger or equal to 12 years and at the same time for adolescents aged 12 years to 18 years in 517 cases. The outlier PDD for Concerta 18mg[®] during 2007 was 54mg (n = 33) for children aged 5 years and younger or equal 12 years and for adolescents aged 12 years to 18 years (n = 12). Children aged 5 to 12 years who received an average PDD of 19.76mg±16.38 or less, were reported at 96.72% during 2006 and 96.17% (18.86mg±4.68) in 2007. The results revealed that during 2005 approximately 95.94% of adolescents, aged 12 years to 18 years, had an average PDD of 18.87mg±4.89mg or less while in 2007 about 94.37% had an average PDD of 19.43mg±6.26mg or less.

4.5.7.5 Prescribed daily dose according to gender

The male gender represented 74.82% (n=6,515) of the total number of Ritalin LA 20mg[®] (N=8,707) claimed where females represented 24.96% (n=2,173) and therefore a ratio of 3 to 1 existed in coordination with international ratio (Marcetti *et al.*, 2001:1905).

4.5.7.5.1 Ritalin LA 20mg[®]

For both males and females most of the prescriptions of Ritalin LA 20mg[®] were prescribed at a PDD of 20mg at a frequency of 6,074 and 2019 prescriptions with outlier prescriptions with PDD at 600mg daily at a frequency of 15 and 8 prescriptions respectively during 2005 (refer to Table A.45 on Appendix A). For Ritalin LA 20mg[®] (N=7,592) usage males indicated the highest prevalence with 75.78% (n=5,753) followed by females with 24.14% (n=1,833) with a ratio of 3.14 to 1 during 2006 (refer to Table A.46 in Appendix A). The results revealed that during 2007 (N=7,374) at a PPD of 20mg males reported 5,178 cases while females had

documented 1,827 cases. Outlier PDD during 2007 for males was reported at 120mg (n = 1). Females (N = 1,827) showed a PDD of 20mg in 1,682 cases with outlier dosages at 60mg (n = 61) (refer to Table A.47).

During 2005 the number of female patients receiving an average PDD (29.11mg±54.00mg) and for male patients (27.87mg±48.37mg) was below 94.43% and 94.24% respectively. Furthermore during 2007 about 92.61% in females and 93.64% of males received lower dosages than the average dose of 22.02mg±8.02mg and 21.74mg±7.42mg respectively.

4.5.7.5.2 Ritalin 10mg[®]

The results revealed that Ritalin 10mg Tab[®] (N=8,173) usage for females represented 27.99% (n=2,288) cases, whereas in males it represented 71.87% (n=5,874). A ratio of 2.57 to 1 between males and females are present for Ritalin 10mg Tab[®] usage. For both gender groups the PDD was 10mg at a frequency of 3,063 and 1,237 for males and females respectively. For males and females there was one prescription with an outlier PDD of 1050mg and 1200mg respectively (refer to Table A.45 in Appendix A). As for Ritalin 10mg Tab[®] (N=6,828) the prevalence for males was higher than for females with 71.54% (n=4,885) and 28.40% (n=1,939) respectively. A ratio of 2.52 to 1 was detected for males to females during 2006 (refer to Table A.46 in Appendix A). During 2007 (N=6,259) it showed a prevalence of 71.43% (n=4,471) for males. A PPD for males at 10mg was reported in 2,431 cases and 124 cases at a outlier dosage of 60mg. Females (n= 1,788) at a 10mg PPD was documented in 983 cases with an outlier PDD of 110mg (n = 1) (refer to Table A.47 in Appendix A). During 2005 results revealed that female patients (85.93%) received less than the average PDD of 23.28mg±54.80mg while male patients (84.07%) received less than 20.74mg±39.57. During 2007 approximately 66.89% of females (16.49mg±12.33mg) and 67.41% of males (16.00mg±10.99mg) received less than the average PDD.

4.5.7.5.3 Ritalin LA 30mg[®]

Males received 81.33% (n=2,169) whereas females received 18.22% (n=486) of Ritalin LA 30mg[®] prescriptions during 2005 (N = 2,667) with a ratio of 4.46 to 1. The PPD during 2005 for males was 30mg in 2,027 cases whereas for females it was documented at 450 cases. The outlier PDD for males and females during 2005 was 900mg (n = 2) and 450mg (n = 12) respectively (refer to Table A.45 in Appendix A). The results revealed that for all Ritalin LA 30mg[®] claimed during 2006 (N = 2,523), males showed a prevalence of 78.80% (n=1,988) while females reported 21.13% (n=533) at a ratio of 3.73 to 1 (refer to Table A.46 in Appendix A). During 2007 (N=2,663) the results revealed that males had a prevalence of 80.40% (n=2,141) for all Ritalin LA 30mg[®] claimed. During 2007 for a PDD at 30mg males

were documented in 1,986 cases where in eight cases there were reports of 120mg doses. Females showed a prevalence of 19.60% (n=522) for all Ritalin LA 30mg[®] (N = 2,663) claimed during 2007. A PDD of 30mg was documented for females in 495 cases and there were two reported cases with a PDD of 300mg (refer to Table A.47 in Appendix A).

During 2005 approximately 66.89% of females (16.49mg±12.33mg) and 67.41% of males (16.00mg±10.99) claimed less than the average PDD of Ritalin LA 30mg[®]. Furthermore, during 2007 about 93.21% of females and 94.11% males received less than the average PDD of 32.05mg±17.67 and 31.59mg±8.61mg respectively.

4.5.7.5.4 Concerta 36mg[®]

The results revealed that Concerta 36mg[®] (N=1,969) had a prevalence of 1,429 (72.57%) for males and females in 536 (27.22%) cases respectively at a ratio of 2.67 to 1 during 2005. For males 1,398 cases during 2005 were documented at a PDD where as for females only 509 cases were reported. According to the results a PDD of 540mg was reported for females (n = 21) during 2005 and for one male a staggering PDD of 1080mg was documented (refer to Table A.45 in Appendix A). Concerta 36mg[®] claimed during 2007 (N=5,682) for males generated a prevalence of 74.22% (n=4,217). A documented PDD of 36mg was reported in 4,048 cases while in only one case the PDD was 108mg. Females showed a prevalence of 25.78% (n=1,465) of all claimed Concerta 36mg[®] during 2007 (N = 5,682). A PDD of 36mg was reported in 1,427 cases and the outlier doses showed in 28 cases with a PDD of 72mg (refer to Table A.47 in Appendix A).

Female patients (95.71%) received less than the average PDD of 56.52mg±98.87mg while male patients (98.11%) had less than 43.08mg±61.15mg during 2005. During 2007 approximately 97.68% of females (36.68mg±5.02mg) and 96.11% of males (37.30mg±6.76mg) received less than the average PDD.

4.5.7.5.5 Methylphenidate HCl-Douglas[®]

As for Methylphenidate HCl-Douglas[®] at (N=1,406) in 2005, males represented 71.91% (n=1,011) whereas females reported at 27.81% (n=391) at a ratio of 2.59 to 1 respectively. A PDD of 10mg for males (n = 398) and females (n = 148) was documented during 2005. During 2005 one male reported to have an outlier PDD of 600mg and for females at 300mg (n = 1). (Refer to Table A.45 in Appendix A). During 2005 patients received Methylphenidate HCl-Douglas[®] at an average PDD of (25.81mg±37.45mg) for females and at (21.92mg±34.30mg) for males and below 78.26% and 76.66% respectively

4.5.7.5.6 Concerta 18mg®

During 2006 (N=2,399) males represented 72.78% (n=1,746) and females 27.22% (n=653) of all Concerta 18mg® claimed at a ratio of 2.67 to 1 (refer to Table A.46 in Appendix A). Males receiving Concerta 18mg® during 2007 (N=3,192) revealed a frequency of 75.00% (n=2,394). For a PDD at 18mg the results revealed that males reported in 2,290 cases with outlier dosages (54mg) in 34 cases (54mg).

During the same period females showed a prevalence of 25.00% (n=798) for all Concerta 18mg® claimed and at a PDD at 18mg (n = 738). The outlier PDD during 2007 for females was at 54mg (n = 21) (refer to Table A.47 in Appendix A).

During 2006 95.87% of female patients receiving Concerta 18mg® had received less than the average daily dose of 20.46mg±20.26mg. The results revealed that during 2007 the average PDD for males was 19.58mg±14.42mg and it was reported that 96.51% received less than that.

4.6 CHAPTER SUMMARY

In this chapter the results were presented and discussed. The conclusions with regard to the different objectives of this study as well as the proposed recommendations will be presented in Chapter 5.

5 CHAPTER 5

Conclusions and recommendations

5.1 INTRODUCTION

The conclusions and recommendations in this chapter are based on the results of the literature review and the empirical research. Limitations of this study will be mentioned and possible suggestions for future studies will also be stated in this chapter.

5.2 CONCLUSIONS

5.2.1 Conclusions based on the literature study

The following conclusions are based on the specific objectives of the literature study (refer to chapter 1, section 1.4.2.1).

The **first specific research objective** of this study was to conceptualise ADHD as a disease from available literature. ADHD is one of the most common psychiatric disorders in children (Leibson & Long, 2003:1239). It is characterised by impulsivity, over-emotional involvement or reactions, academic underachievement, inattention, hyperactivity, restlessness, impulsivity, distractibility and can carry on into adolescence and adulthood (Leibson & Long, 2003:1239; Mercugliano, 1999:84). According to Karande (2005:59) and Spencer (2009b:S4) ADHD can be categorised into three different subgroups. These groups include the inattentive type (ADHD/I), hyperactive-impulsive type (ADHD/HI) and the combined type (ADHD/C) (refer to Chapter 2, Section 2.1). According to ADHDSA the exact cause of ADHD is unknown. Various authors identified neurological, environmental, biological and genetic causes as described in Chapter 2, Section 2.2.

The **second specific research objective** of this research project was to determine from the literature the prevalence of ADHD on an international level as well as in South Africa. According to Leibson and Long (2003:1240) the reported prevalence of ADHD during 2001 in the United States was 9.2% for males and 2.9% for females. It can, therefore, be concluded that for every 3 boys only one girl had ADHD. This statement could be supported by a study done by Truter (2005:61) in South Africa that showed that the majority of the patients were males.

The **third specific research objective** of this study was to determine from the literature the co-morbid diseases with ADHD. The following psychiatric disorders have correlating symptoms that could be associated with ADHD and these include, inter alia: oppositional

defiant disorder (ODD), bipolar disorder, obsessive compulsive disorder (OCD), depression, anxiety, developmental co-ordination disorder and learning disabilities (refer to Chapter 2, Section 2.6).

The **fourth specific research objective** was to establish the medicine treatment for ADHD. The psycho stimulant, methylphenidate, is the most commonly prescribed drug for the treatment of attention deficit hyperactivity disorder (ADHD) as well as the registered non-stimulant atomoxetine prescribed to patients with ADHD (Chamberlain *et al.*, 2007:977). Possible side-effects include, inter alia, insomnia, nausea, loss of appetite and an elevated heart rate which is rare (refer to Chapter 2, Section 2.7.2).

The **fifth specific research objective** of this study was to determine from the literature possible drug-drug interactions between atomoxetine and methylphenidate containing products on the one hand and other drugs on the other hand. It was found that methylphenidate or atomoxetine may present with drug-drug interactions with, for example, monoamine oxidase inhibitors, tricyclic anti-depressants, selective serotonin re-uptake inhibitors (SSRIs), carbamazepine and phenytoin. These drug-drug interactions were briefly discussed in Section 2.7.1.

The **sixth specific research objective** of this study was to investigate from the literature the cost associated with ADHD treatment. The cost associated with ADHD treatment includes the direct cost to the medical schemes and/or parent of children with ADHD. Furthermore indirect cost includes, inter alia, absenteeism from work and efficacy at workplace. Problems that adults with ADHD will suffer from may include poor job performance and lower occupational status which has an effect on the cost to ADHD treatment. Other cost associated with ADHD includes cost to families, cost of co-morbid disorders and work loss (refer to Chapter 2, Section 2.8.9).

The **seventh specific research objective** of this study was to establish the importance of disease management, DUR, pharmacoeconomics, evidence-based medicine, drug classification systems, prescribed minimum benefits (PMB). This was done with an overview of the literature regarding disease management, DUR, pharmacoeconomics, evidence-based medicine, drug classification systems and PMB.

Drug utilisation review (DUR) was defined and retrospective, prospective or concurrent DUR processes were briefly described (refer to chapter 2, section 2.8.2). The ATC classification system and prescribed minimum benefits were also reviewed (refer to chapter 2, sections 2.8.4 and 2.8.5). Through the literature the concepts of pharmacoeconomics and evidence-based medicine have been reviewed. Pharmacoeconomics can be seen as the evaluation of

the economic, humanistic and clinical outcomes connected to pharmaceutical services and products. Pharmacoeconomics was also discussed according to cost-minimisation analysis (CMA), cost-effective analysis (CEA), cost-utility analysis (CUA) and cost-benefit analysis (CBA) (refer to Chapter 2, Section 2.8.3). It can be concluded that pharmacoeconomics is an extensive subject that has valuable application in health care, e.g. analysing the cost associated with the treatment of ADHD through drug utilisation review. The concept and steps that need to be followed during evidence-based medicine have been discussed in the literature and briefly applied to the treatment of ADHD.

5.2.2 Conclusions based on the empirical study

The following conclusions are based on the specific objectives of the **empirical** study (Refer to Chapter 3, Section 3.2.2.2).

The ***eighth specific research objective*** of this study was to determine the usage patterns and cost of drugs in general according to all medicine items and prescriptions in the total database for the study period 2005 to 2007.

A decrease of 5.95% in the number of prescriptions claimed through the PBM was observed from 2005 to 2007 (refer to Chapter 4, Section 4.4.2.1) whereas the number of medicine items also decreased with 2.35% (refer to Chapter 4, Section 4.4.3.1). This may be the result of a decrease in the number of patients who claimed through the PBM during the study period (refer to Chapter 4, Section 4.4.1.1). The total medicine cost of all medicine items claimed through the PBM increased by 5.02% (refer to Chapter 4, Section 4.4.5.1). A decrease in medical scheme contribution and an increase in patient contribution of 3.89% towards the total cost of all medicine items claimed were observed from 2005 to 2007. (refer to Chapter 4, Section 4.4.5.1.1).

The ***ninth specific research objective*** was to analyse the prescribing patterns and cost of methylphenidate or atomoxetine containing products and prescriptions in a section of the private health care sector of South Africa.

An increase (17.94%) in the number of prescriptions containing methylphenidate or atomoxetine was found from 2005 to 2007 (Refer to Chapter 4, Section 4.5.2.1). An increase of 18.44% was also observed for medicine items containing methylphenidate or atomoxetine claimed through the PBM from 2005 to 2007 (Refer to Chapter 4, Section 4.5.3.1). The total medicine cost for products containing methylphenidate or atomoxetine had increased with 33.00% from 2005 to 2007 (refer to Chapter 4, Section 4.5.5.1.1). This may be the result of

an increase in the number of prescriptions and medicine items claimed through the PBM from 2005 to 2007

The results revealed that atomoxetine containing products represented only 4.69% of all methylphenidate or atomoxetine containing products claimed in 2005 and 12.91% in 2006 and 12.34% in 2007. These results indicate an *increase* of 7.65% in the number of medicine items containing atomoxetine from 2005 to 2007. Of all products containing atomoxetine, Strattera 40mg Cap® had the *highest* frequency in all three study years (refer to Chapter 4, Section 4.5.3.4.1).

Methylphenidate containing products represented 95.31% of the total number of medicine items containing methylphenidate or atomoxetine in 2005 and 87.09% in 2006 and 87.66% in 2007. A decrease of 7.65% was found from 2005 to 2007.(refer to Chapter 4, Section 4.5.3.4.2). Of all products containing methylphenidate or atomoxetine, Ritalin LA 20mg® was most frequently prescribed during all three study years (refer to Chapter 4, Section 4.5.3.4.2)

It was observed that atomoxetine or methylphenidate containing products were mostly prescribed by general medical practitioners and paediatricians (refer to Chapter 4, Section 4.5.3.5).

The ***tenth specific research objective*** reviewed the influence of age and gender on the prescribing patterns of all medicine items and prescriptions with special reference to methylphenidate or atomoxetine containing products in a section of the private health care sector.

It was observed that the percentage of prescriptions for methylphenidate and atomoxetine containing products claimed for males (74.11%) or females (25.78%) did not change from 2005 to 2007 (refer to Chapter 4, Section 4.5.2.2). The same trend was experienced with the number of medicine items containing methylphenidate and atomoxetine (refer to Chapter 4, Section 4.5.3.2).

The percentage of prescriptions for methylphenidate or atomoxetine containing products claimed for adolescents, aged 12 to 18 years, from 2005 to 2007 increased by 1.86%. Those prescribed to adults, aged 18 years and older, also increased with 1.54% from 2005 to 2007. The percentage of prescriptions for methylphenidate or atomoxetine containing products claimed for children younger than 5 years and children aged 5 to 12 years did not really change from 2005 to 2007 (refer to Chapter 4, Section 4.5.2.3).

The **eleventh specific research objective** reviewed the total cost, medical scheme and patient cost contribution of all medication and methylphenidate or atomoxetine containing products specifically in a section of the private health care sector of South Africa.

The total cost of all medicine items claimed through the PBM increased with 5.02% from 2005 to 2007. With regard to the medical scheme contribution, it decreased with 3.89% while the patient contribution increased with the same value from 2005 to 2007 (refer to Chapter 4, Section 4.4.5.1.1). For products containing methylphenidate or atomoxetine the total cost increased with 33.00% from 2005 to 2007. The results revealed an increase in the patient medicine contribution and a decrease in medical scheme contribution by 4.14% (refer to Chapter 4, Section 4.5.5.1.1).

The **twelfth specific research objective** reviewed the prescribed daily doses (PDD) of methylphenidate or atomoxetine containing products in patients of different age groups, gender, and prescribed by different types of prescribers (e.g. general practitioners, specialists, etc.).

The PDD was discussed with regard to Ritalin LA 20mg[®], Ritalin 10mg[®], Ritalin LA 30mg[®], Concerta 36mg[®], Concerta 18mg[®] and Methylphenidate-Douglas[®] respectively (refer to Chapter 4, Section 4.5.5).

Ritalin LA 20mg[®] was mainly prescribed to children aged 5 to 12 years at a PDD of 27.43mg±48.74mg during 2005 and 21.34mg±6.69mg during 2007 (refer to Chapter 4, Section 4.5.5.5.2). Children aged 5 to 12 years received Ritalin 10mg[®] at a PDD of 17.67mg±25.81mg during 2007 (refer to Chapter 4, Section 4.5.5.5.2). Children aged 5 to 12 years received a PDD of 39.12mg±58.19mg during 2005 and 30.46mg±5.66mg during 2007 for Ritalin LA 30mg[®] (refer to Chapter 4, Section 4.5.5.5.2).

Adolescents aged 12 to 18 years received Concerta 36mg[®] at an average PDD of 50.02mg±81.92mg during 2005 and 37.75mg±7.79mg in 2007 (refer to Chapter 4, Section 4.5.5.5.2). The results revealed that Methylphenidate HCl-Douglas[®] was prescribed during 2005 at an average PDD of 19.00mg±20.76mg for this age group (refer to Chapter 4, Section 4.5.5.5.2). Concerta 18mg[®] showed a PDD of 18.87mg±4.89mg for adolescents aged 12 to 18 years during 2005 and 19.43mg±6.26mg during 2007 (refer to Chapter 4, Section 4.5.5.5.2).

The results showed that females received Ritalin LA 20mg[®] at a PDD of 29.11mg±54.00mg during 2005 and males 27.87mg±48.37mg. During 2007 females had an average PDD of 22.02mg±8.02mg and 21.47mg±7.42mg for males (refer to Chapter 4, Section 4.5.5.6.1).

Ritalin 10mg[®] showed a PDD of 23.28mg±54.80mg during 2005 and 16.49mg±12.33mg during 2007 where males revealed a PDD of 20.74mg±39.57mg and 16.00mg±10.99mg respectively for 2005 and 2007 (refer to Chapter 4, Section 4.5.5.6.2). As for Ritalin LA 30mg[®] females showed a PDD of 16.49mg±12.33mg during 2005 and 32.05mg±17.67mg while males received 16.00mg±10.99mg and 31.59mg±8.61mg (refer to Chapter 4, Section 4.5.5.6.4).

Females received a PDD of 56.52mg±98.87mg of Concerta 36mg[®] during 2005 and 36.68mg±5.02mg during 2007 where males documented a PDD of 43.08mg±61.15mg and 37.30mg±6.76mg respectively (refer to Chapter 4, Section 4.5.5.6.4). Where females received Methylphenidate HCl-Douglas[®] the results revealed a PDD of 25.81mg±37.45mg and males 21.92mg±34.30mg during 2005 (refer to Chapter 4, Section 4.5.5.6.5). As for Concerta 18mg[®], females reported a PDD of 20.46mg±20.26mg and during 2007 males presented a PDD of 19.58mg±14.42mg (refer to Chapter 4, Section 4.5.5.6.6).

The **thirteenth specific research objective** was to identify the potential cost savings that could be generated by practising generic prescribing/substitution for methylphenidate containing products.

As the results revealed a total of R1, 497,018.67 could have been saved over the three years if Ritalin 10mg[®] had been substituted for Adaphen 10mg[®] and R1, 516,024.59 could have been saved if Ritalin 10mg had been substituted for Methylphenidate HCl-Douglas[®]. If Ritalin SR 20mg[®] had been substituted for Adaphen XL 20mg[®] over the three years R134,379.31 could have been saved (refer to Chapter 4, Section 4.5.4.2).

The **fourteenth specific research objective** was to investigate the prevalence of possible drug-drug interactions between methylphenidate or atomoxetine containing products and other central nervous system medication on prescriptions.

As the results revealed, imipramine, amitriptyline and carbamazepine were the highest ranking central nervous system products prescribed together on prescriptions with products containing methylphenidate or atomoxetine, which can cause possible drug-drug interactions (refer to Chapter 4, Section 4.5.4.3). Other products prescribed on the same prescriptions as products containing methylphenidate or atomoxetine which can cause possible drug-drug interactions include clomipramine, trimipramine and phenytoin (refer to Chapter 4, Section 4.5.4.3).

Risperidone, imipramine and amitriptyline were the highest ranking CNS products prescribed together with products containing methylphenidate or atomoxetine on prescriptions (Refer to

Chapter 4, Section 4.5.4.5). From these results it was reported that the prevalence of risperidone decreased with 6.23% from 2005 to 2007. Imipramine in combination with methylphenidate or atomoxetine containing products decreased with 7.74% from 2005 to 2006 and did not really change during 2007. Furthermore the percentage of prescriptions with amitriptyline containing products and products containing methylphenidate or atomoxetine decreased with 2.70% from 2005 to 2006 and did not really change during 2007.

These results revealed that there was a large number of CNS products being prescribed in combination with products containing methylphenidate and atomoxetine. Some of these products are indicated for psychiatric disorders. Due to this, there should be a more in-depth evaluation done by physicians who specialise in psychiatric disorders (e.g. psychiatrist). A more specific diagnosis could be done to evaluate whether an individual has ADHD or any other psychiatric disorder. The research showed that it may not always be appropriate to prescribe products containing methylphenidate or atomoxetine with certain CNS drugs due to possible drug-drug interactions (Refer to Chapter 4, Section 4.5.2.5).

5.3 RECOMMENDATIONS

The following recommendations have been formulated:

- Appropriate data systems and strategies to monitor the usage and prescribing patterns of products containing methylphenidate or atomoxetine should be developed and implemented in the South African private health care sector.
- Corrective intervention strategies for prescribers and providers should be formulated and put into practice to ensure appropriate prescribing and dispensing of products containing methylphenidate or atomoxetine, especially when other CNS drugs are prescribed simultaneously.
- Since several potential DDIs have been identified between products containing methylphenidate and atomoxetine and other CNS drugs further studies should be performed in the public health care sector of SA to make comparisons with the results obtained in the private sector.
- It is recommended that generic use of products containing methylphenidate should be further promoted to reduce the costs of these relatively expensive drugs

5.4 LIMITATIONS AND SHORTCOMINGS OF THIS STUDY

The following limitations and shortcomings should be taken into account when evaluating the results and conclusions of this study:

- All the data obtained from the pharmacy benefit management company database were considered to be accurate and correct.
- External validity is limited, implying that the results can only be generalised to the specific database and study population in the private health care sector of South Africa.
- Demographic data were limited to patient age and gender. Certain patients were not classified into age groups or gender as their date of birth or gender had not been recorded in the data.

5.5 CHAPTER SUMMARY

This chapter focused on the discussion of the results as presented in Chapter 3. The general findings of the study were discussed according to the empirical objectives as outlined in Chapters 1 and 3. For each research objective, results were briefly discussed; conclusions and limitations of the study were discussed together with recommendations. Finally general recommendations have been made. Thereby the objectives of this study have been met.

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APPENDIX A

Table A.1: General prescription analysis for the study period 2005 to 2007

Study period	Number of prescriptions	Average number of medicine items per prescription	Standard deviation (\pm)	Number of medicine items
2005	8,522,798	2.30	1.50	19,606,049
2006	9,048,541	2.35	1.53	21,219,021
2007	8,015,538	2.39	1.58	19,146,156

Table A.2: General prescription analysis according to gender for the study period 2005 to 2007

Study period	Gender	Number of prescriptions	Number of medicine items	Average number of medicine items per prescription	Standard deviation (\pm)
2005	Female (F)	5,112,373	11,811,901	2.31	1.53
	Male (M)	3,403,233	7,777,985	2.29	1.45
	Unspecified (U)	7,192	16,163	2.25	1.36
	Total	8,522,798	19,606,049	2.30	1.50
2006	Female (F)	5,422,200	12,764,246	2.35	1.56
	Male (M)	3,621,466	8,444,160	2.33	1.49
	Unspecified (U)	4,875	10,615	2.18	1.39
	Total	9,048,541	21,219,021	2.35	1.53
2007	Female (F)	4,817,599	11,551,895	2.40	1.61
	Male (M)	3,196,105	7,590,337	2.37	1.53
	Unspecified (U)	1,834	3,924	2.14	1.46
	Total	8,015,538	19,146,156	2.39	1.58

Table A.3: General prescription analysis according to age group for the study period 2005 to 2007

Study period	Age group	Number of prescriptions	Number of medicine items	Average number of medicine items per prescription	Standard deviation (\pm)
2005	≤ 5 years	391,847	974,785	2.49	1.34
	5< and ≤ 12 years	415,323	1,010,808	2.43	1.32
	12< and ≤ 18 years	364,879	834,506	2.29	1.30
	> 18 years	7,350,591	16,785,929	2.28	1.52
	Total for 2005	8,522,640	19,606,028	2.30	1.50
2006	≤ 5 years	405,014	1,023,923	2.53	1.36
	5< and ≤ 12 years	429,889	1,056,940	2.46	1.34
	12< and ≤ 18 years	385,401	903,193	2.34	1.34
	> 18 years	7,826,733	18,234,928	2.33	1.56
	Total for 2006	9,047,037	21,218,984	2.35	1.53
2007	≤ 5 years	324,935	827,579	2.55	1.38
	5< and ≤ 12 years	365,745	895,624	2.45	1.35
	12< and ≤ 18 years	337,542	788,341	2.34	1.34
	> 18 years	6,981,151	16,634,585	2.38	1.61
	Total for 2007	8,009,373	19,146,129	2.39	1.58

Table A.4 : Cost analysis of all prescriptions for the study period 2005 to 2007

Study period	Number of prescriptions	Contribution (R)	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2005	8,522,798	Total cost	215.97	347.98	1,840,663,948.74
		Total patient contribution	25.70	81.75	219,041,601.22
		Total scheme contribution	190.27	330.01	1,621,622,347.52
2006	9,048,541	Total cost	219.38	401.76	1,985,049,228.54
		Total patient contribution	29.09	88.81	263,241,574.86
		Total scheme contribution	190.29	384.99	1,721,807,653.68
2007	8,015,538	Total cost	241.17	601.64	1,933,070,365.79
		Total patient contribution	38.07	171.88	305,162,514.96
		Total scheme contribution	203.09	565.94	1,627,907,850.83

Appendix A

Table A.5 : Cost analysis of all prescriptions according to gender for the study period 2005 to 2007

Study period	Gender	Number of prescriptions	Contribution (R)	Average cost (R)	Standard deviation (R)	Total cost (R)
2005	Female (F)	5,112,373	Total cost	214.50	336.72	1,096,609,592.32
			Total patient contribution	26.98	81.75	137,925,255.76
			Total scheme contribution	187.52	317.49	958,684,336.56
	Male (M)	3,403,233	Total cost	218.20	363.47	742,576,523.73
			Total patient contribution	23.81	81.76	81,035,309.34
			Total scheme contribution	194.39	347.11	661,541,214.39
	Unspecified (U)	7,192	Total cost	205.48	620.43	1,477,832.69
			Total patient contribution	11.27	40.89	81,036.12
			Total scheme contribution	194.22	613.72	1,396,796.57
	Total for 2005	8,522,798	Total cost	215.97	347.98	1,840,663,948.74
			Total patient contribution	25.70	81.75	219,041,601.22
			Total scheme contribution	190.27	330.01	1,621,622,347.52
2006	Female (F)	5,422,200	Total cost	216.99	385.90	1,176,562,838.40
			Total patient contribution	30.36	90.34	164,605,305.18
			Total scheme contribution	186.63	367.71	1,011,957,533.22
	Male (M)	3,621,466	Total cost	222.94	424.19	807,352,963.92
			Total patient contribution	27.21	86.47	98,524,490.97
			Total scheme contribution	195.73	409.24	708,828,472.95
	Unspecified (U)	4,875	Total cost	232.50	532.08	1,133,426.22
			Total patient contribution	22.93	58.69	111,778.71
			Total scheme contribution	209.57	526.96	1,021,647.51
	Total for 2006	9,048,541	Total cost	219.38	401.76	1,985,049,228.54
			Total patient contribution	29.09	88.81	263,241,574.86
			Total scheme contribution	190.29	384.99	1,721,807,653.68

Table A.5 : Cost analysis of all prescriptions according to gender for the study period 2005 to 2007 (continued)

Study period	Gender	Number of prescriptions	Contribution (R)	Average cost (R)	Standard deviation (±)	Total cost (R)
2007	Female (F)	4,817,599	Total cost	237.94	559.63	1,146,277,609.55
			Total patient contribution	39.51	150.13	190,324,709.65
			Total scheme contribution	198.43	529.85	955,952,899.90
	Male (M)	3,196,105	Total cost	245.99	659.85	786,203,377.57
			Total patient contribution	35.91	200.27	114,761,853.29
			Total scheme contribution	210.08	616.21	671,441,524.28
	Unspecified (U)	1,834	Total cost	321.36	694.47	589,378.67
			Total patient contribution	41.41	53.13	75,952.02
			Total scheme contribution	279.95	685.44	513,426.65
	Total for 2007	8,015,538	Total cost	241.17	601.64	1,933,070,365.79
			Total patient contribution	38.07	171.88	305,162,514.96
			Total scheme contribution	203.09	565.94	1,627,907,850.83

Table A.6 : Cost analysis of all prescriptions according to age groups for the study period 2005 to 2007

Study period	Age group	Number of prescriptions	Contribution (R)	Average cost (R)	Standard deviation (R)	Total cost (R)
2005	≤ 5 years	391,847	Total cost	133.31	139.25	52,238,121.63
			Total patient contribution	12.56	44.02	4,920,632.96
			Total scheme contribution	120.76	131.79	47,317,488.67
	5< and ≤12 years	415,323	Total cost	148.01	153.84	61,472,357.05
			Total patient contribution	13.72	44.32	5,698,875.55
			Total scheme contribution	134.29	145.96	55,773,481.50
	12< and ≤18 years	364,879	Total cost	163.71	210.48	59,734,845.85
			Total patient contribution	17.43	54.85	6,359,256.25
			Total scheme contribution	146.28	200.17	53,375,589.60
	> 18 years	7,350,737	Total cost	226.81	367.36	1,667,217,371.91
			Total patient contribution	27.49	85.79	202,062,836.46
			Total scheme contribution	199.32	348.62	1,465,154,535.45
	Total for 2005	8,522,786	Total cost	215.97	347.98	1,840,662,696.44
			Total patient contribution	25.70	81.75	219,041,601.22
			Total scheme contribution	190.27	330.01	1,621,621,095.22
2006	≤ 5 years	405,018	Total cost	134.47	176.91	54,463,852.43
			Total patient contribution	16.79	57.10	6,799,679.98
			Total scheme contribution	117.68	166.54	47,664,172.45
	5< and ≤12 years	429,889	Total cost	149.82	163.03	64,407,414.65
			Total patient contribution	17.41	55.50	7,485,310.07
			Total scheme contribution	132.41	152.25	56,922,104.58
	12< and ≤18 years	385,402	Total cost	164.88	226.54	63,546,146.03
			Total patient contribution	20.09	61.17	7,743,548.13
			Total scheme contribution	144.79	216.74	55,802,597.90

Table A.6 : Cost analysis of all prescriptions according to age groups for the study period 2005 to 2007 (continue)

Study period	Age group	Number of prescriptions	Contribution (R)	Average cost (R)	Standard deviation (R)	Total cost (R)
2006	> 18 years	7,828,198	Total cost	230.27	424.34	1,802,630,331.65
			Total patient contribution	30.81	92.59	241,213,020.94
			Total scheme contribution	199.46	407.02	1,561,417,310.71
	Total for 2006	9,048,507	Total cost	219.38	401.76	1,985,047,744.76
			Total patient contribution	29.09	88.81	263,241,559.12
			Total scheme contribution	190.29	384.99	1,721,806,185.64
2007	≤ 5 years	324,946	Total cost	139.19	252.74	45,228,627.09
			Total patient contribution	24.10	182.76	7,831,910.87
			Total scheme contribution	115.09	164.23	37,396,716.22
	5< and ≤12 years	365,755	Total cost	158.50	188.70	57,973,545.10
			Total patient contribution	24.04	63.60	8,794,231.95
			Total scheme contribution	134.46	172.46	49,179,313.15
	12< and ≤18 years	337,548	Total cost	172.70	334.44	58,293,879.25
			Total patient contribution	27.75	114.01	9,368,436.03
			Total scheme contribution	144.94	308.53	48,925,443.22
	> 18 years	6,987,267	Total cost	253.54	635.44	1,771,572,605.87
			Total patient contribution	39.95	177.40	279,167,880.10
			Total scheme contribution	213.59	599.27	1,492,404,725.77
	Total for 2007	8,015,516	Total cost	241.17	601.64	1,933,068,657.31
			Total patient contribution	38.07	171.88	305,162,458.95
			Total scheme contribution	203.09	565.94	1,627,906,198.36

Table A.7 : Analysis of prescriptions containing methylphenidate and/or atomoxetine for study period 2005 to 2007

Study period	Number of prescriptions	Number of medicine items	Average number of items per prescription	Standard deviation
2005	27,680	29,424	1.06	0.24
2006	31,577	33,576	1.05	0.26
2007	32,647	34,850	1.04	0.18

Table A.8 : Analysis of prescriptions containing methylphenidate and/or atomoxetine according to gender for the study period 2005 to 2007

Study period	Gender	Number of prescriptions	Number of medicine items	Average number of items per prescription	Standard deviation (\pm)
2005	Female (F)	7,113	7,567	1.06	0.25
	Male (M)	20,511	21,798	1.06	0.25
	Unspecified (U)	56	59	1.05	0.23
	Total for 2005	27,680	29,424	1.06	0.24
2006	Female (F)	8,013	8,525	1.06	0.26
	Male (M)	23,505	24,990	1.06	0.26
	Unspecified (U)	59	61	1.03	0.26
	Total for 2006	31,577	33,576	1.05	0.26
2007	Female (F)	8,466	9,001	1.06	0.26
	Male (M)	24,165	25,833	1.07	0.27
	Unspecified (U)	16	16	1.00	0.00
	Total for 2007	32,647	34,850	1.04	0.18

Table A.9 : Analysis of prescriptions containing methylphenidate and/or atomoxetine according to age groups for 2005 to 2007

Study period	Age group	Number of prescriptions	Number of medicine items	Average number of items per prescription	Standard deviation (\pm)
2005	≤ 5 years	140	146	1.04	0.20
	5< and ≤ 12 years	16,151	16,936	1.05	0.23
	12< and ≤ 18 years	7,569	8,227	1.09	0.29
	> 18 years	3,820	4,115	1.08	0.27
	Total for 2005	27,680	29,424	1.06	0.25
2006	≤ 5 years	154	160	1.04	0.19
	5< and ≤ 12 years	17,995	18,936	1.05	0.23
	12< and ≤ 18 years	8,929	9,613	1.08	0.28
	> 18 years	4,499	4,867	1.08	0.29
	Total for 2006	31,577	33,576	1.06	0.26
2007	≤ 5 years	203	212	1.04	0.23
	5< and ≤ 12 years	17,902	18,988	1.06	0.25
	12< and ≤ 18 years	9,533	10,216	1.07	0.27
	> 18 years	5,009	5,434	1.08	0.30
	Total for 2007	32,647	34,850	1.07	0.27

Table A.10 : Cost analysis of prescriptions consisting of methylphenidate and/or atomoxetine containing products for 2005 to 2007

Study period	Number of prescriptions	Contribution (R)	Average cost (R)	Standard deviation (R)	Total cost (R)
2005	27,680	Total cost	318.29	162.09	8,810,130.56
		Total scheme amount	279.91	163.12	7,748,035.75
		Total patient levy	38.37	91.88	1,062,094.81
2006	31,577	Total cost	351.58	189.33	11,101,929.25
		Total scheme amount	294.91	193.51	9,312,405.44
		Total patient levy	56.67	120.24	1,789,523.81
2007	32,647	Total cost	358.91	208.10	11,717,340.70
		Total scheme amount	286.20	205.25	9,343,473.11
		Total patient levy	72.71	134.27	2,373,867.59

Appendix A

Table A.11 : Cost analysis of prescriptions consisting of methylphenidate and/or atomoxetine containing products according to gender for 2005 to 2007

Study period	Gender	Number of prescriptions	Contribution (R)	Average cost (R)	Standard deviation (R)	Total cost (R)
2005	Female (F)	7,113	Total cost	307.37	158.54	2,186,354.95
			Total scheme amount	267.22	158.90	1,900,721.05
			Total patient levy	40.16	93.98	285,633.90
	Male (M)	20,511	Total cost	322.05	163.13	6,605,662.72
			Total scheme amount	284.29	164.32	5,831,021.87
			Total patient levy	37.77	91.13	774,640.85
	Unspecified (U)	56	Total cost	323.44	169.24	18,112.89
			Total scheme amount	290.94	171.02	16,292.83
			Total patient levy	32.50	97.97	1,820.06
2006	Female (F)	8,013	Total cost	344.59	189.90	2,761,186.49
			Total scheme amount	286.16	192.55	2,292,963.40
			Total patient levy	58.43	122.21	468,223.09
	Male (M)	23,505	Total cost	353.79	189.07	8,315,888.20
			Total scheme amount	297.87	193.68	7,001,447.93
			Total patient levy	55.92	119.15	1,314,440.27
	Unspecified (U)	59	Total cost	421.26	185.59	24,854.56
			Total scheme amount	304.98	220.91	17,994.11
			Total patient levy	116.28	225.10	6,860.45
2007	Female (F)	8,466	Total cost	349.49	208.08	2,958,795.47
			Total scheme amount	275.09	202.35	2,328,912.45
			Total patient levy	74.40	137.65	629,883.02
	Male (M)	24,165	Total cost	362.12	208.01	8,750,509.01
			Total scheme amount	289.99	206.12	7,007,667.31
			Total patient levy	72.12	133.11	1,742,841.70
	Unspecified (U)	16	Total cost	502.26	153.13	8,036.22
			Total scheme amount	430.83	153.90	6,893.35
			Total patient levy	71.43	10.67	1,142.87

Table A.12 : Cost analysis of prescriptions with methylphenidate and/or atomoxetine containing products to age groups for 2005 to 2007

Study period	Age groups	Number of prescriptions	Contribution (R)	Average cost (R)	Standard deviation (R)	Total cost (R)
2005	≤ 5 years	140	Total cost	219.44	157.23	30,721.29
			Total scheme amount	193.59	160.73	27,102.49
			Total patient levy	25.85	64.25	3,618.80
	5< and ≤12 years	16,151	Total cost	294.10	145.96	4,750,026.83
			Total scheme amount	261.74	149.58	4,227,348.17
			Total patient levy	32.36	79.44	522,678.66
	12< and ≤18 years	7,569	Total cost	357.39	159.05	2,705,082.80
			Total scheme amount	315.27	164.76	2,386,247.67
			Total patient levy	42.12	100.25	318,835.13
	> 18 years	3,820	Total cost	346.68	206.48	1,324,299.64
			Total scheme amount	289.88	198.11	1,107,337.42
			Total patient levy	56.80	117.95	216,962.22
2006	≤ 5 years	154	Total cost	232.69	164.40	35,835.02
			Total scheme amount	179.18	162.01	27,593.55
			Total patient levy	53.52	104.76	8,241.47
	5< and ≤12 years	17,995	Total cost	327.77	175.00	5,898,701.75
			Total scheme amount	278.49	181.79	5,011,470.43
			Total patient levy	49.30	106.00	887,231.32
	12< and ≤18 years	8,929	Total cost	393.21	190.08	3,510,932.53
			Total scheme amount	334.79	199.78	2,989,350.20
			Total patient levy	58.41	125.22	521,582.33
	> 18 years	4,499	Total cost	368.18	223.67	1,656,459.95
			Total scheme amount	285.39	213.95	1,283,991.26
			Total patient levy	82.79	155.37	372,468.69

Table A.12 : Cost analysis of prescriptions with methylphenidate and/or atomoxetine containing products to age groups for 2005 to 2007 (continued)

Study period	Age groups	Number of prescriptions	Contribution (R)	Average cost (R)	Standard deviation (R)	Total cost (R)
2007	≤ 5 years	203	Total cost	313.58	251.07	63,656.22
			Total scheme amount	230.41	229.93	46,774.03
			Total patient levy	83.16	173.40	16,882.19
	5< and ≤12 years	17,902	Total cost	335.01	193.43	5,997,324.08
			Total scheme amount	270.19	192.08	4,836,999.77
			Total patient levy	64.82	119.08	1,160,324.31
	12< and ≤18 years	9,533	Total cost	394.12	203.62	3,757,107.43
			Total scheme amount	324.47	208.98	3,093,212.87
			Total patient levy	69.64	131.23	663,894.56
	> 18 years	5,009	Total cost	379.17	249.40	1,899,252.97
			Total scheme amount	272.81	231.26	1,366,486.44
			Total patient levy	106.36	177.41	532,766.53

Table A.13 : Cost analysis of all medicine items according to generic indicator for study period 2005 to 2007

Study period	Generic indicator	Contribution (R)	Number of medicine items	Average cost per medicine item (R)	Standard deviation (R)	Total cost (R)
2005	(M)	Total cost	136,878	86.70	86.46	11,865,747.79
		Medical scheme contribution		78.19	79.82	10,701,933.53
		Patient contribution		8.50	26.74	1,163,814.26
	No Generic (N)	Total cost	8,379,008	137.32	236.94	1,150,564,570.00
		Medical scheme contribution		122.26	228.73	1,024,440,091.00
		Patient contribution		15.05	59.08	126,124,479.00
	Original (O)	Total cost	2,693,298	99.81	138.25	268,817,308.00
		Medical scheme contribution		81.43	131.75	219,315,504.00
		Patient contribution		18.38	40.68	49,501,804.47
	Generic (Y)	Total cost	8,396,865	48.76	60.72	409,416,323.00
		Medical scheme contribution		43.73	57.63	367,164,819.00
		Patient contribution		5.03	16.16	42,251,503.55
Total for 2005	Total cost	19,606,049	93.88	173.01	1,840,663,949.00	
	Medical scheme contribution		82.71	165.92	1,621,622,348.00	
	Patient contribution		11.17	43.20	219,041,601.00	

Table A.13 : Cost analysis of all medicine items according to generic indicator for study period 2005 to 2007 (continued)

Study period	Generic indicator	Contribution (R)	Number of medicine items	Average cost per medicine item (R)	Standard deviation (R)	Total cost (R)
2006	(M)	Total cost	32,568	95.62	38.58	3,114,178.75
		Medical scheme contribution		82.47	43.43	2,685,995.32
		Patient contribution		13.15	26.15	428,183.43
	No Generic (N)	Total cost	8,026,995	141.36	299.36	1,134,714,729.00
		Medical scheme contribution		124.13	292.18	996,378,391.00
		Patient contribution		17.23	64.69	138,336,338.00
	Original (O)	Total cost	3,242,612	102.52	160.23	332,420,799.00
		Medical scheme contribution		81.97	153.00	265,789,590.00
		Patient contribution		20.55	46.01	66,631,209.32
	Generic (Y)	Total cost	9,916,846	51.91	68.57	514,799,522.00
		Medical scheme contribution		46.08	65.55	456,953,677.00
		Patient contribution		5.83	18.62	57,845,844.97
	Total for 2006	Total cost	21,219,021	93.55	204.23	1,985,049,229.00
		Medical scheme contribution		81.14	197.88	1,721,807,654.00
		Patient contribution		12.41	45.92	263,241,575.00

Table A.13 : Cost analysis of all medicine items according to generic indicator for study period 2005 to 2007 (continued)

Study period	Generic Indicator	Contribution (R)	Number of medicine items	Average cost per medicine item (R)	Standard deviation (R)	Total cost (R)
2007	(M)	Total cost	12,845	59.49	69.22	764,195.64
		Medical scheme contribution		40.71	67.40	522,858.78
		Patient contribution		18.79	35.04	241,336.86
	No Generic (N)	Total cost	7,026,146	154.40	518.90	1,084,858,340.00
		Medical scheme contribution		132.55	487.70	931,308,070.00
		Patient contribution		21.85	162.76	153,550,270.00
	Original (O)	Total cost	3,019,594	102.45	179.48	309,364,126.00
		Medical scheme contribution		76.27	168.60	230,300,693.00
		Patient contribution		26.18	53.18	79,063,432.74
	Generic (Y)	Total cost	9,087,571	59.21	79.67	538,083,704.00
		Medical scheme contribution		51.25	75.42	465,776,228.00
		Patient contribution		7.96	22.90	72,307,475.42
Total for 2007	Total cost	19,146,156	100.96	329.82	1,933,070,366.00	
	Medical scheme contribution		85.03	309.61	1,627,907,851.00	
	Patient contribution		15.94	102.35	305,162,515.00	

Table A.14 : Cost analysis of all medicine items according to gender and generic indicator for study period 2005 to 2007

Study period	Gender	Generic indicator	Contribution (R)	Number of medicine items	Average cost per medicine item (R)	Standard deviation (R)	Total cost (R)
2005	Female (F)	(M)	Total cost	83,078	87.29	84.67	7,251,801.88
			Medical scheme contribution		78.27	78.12	6,502,704.49
			Patient contribution		9.02	27.23	749,097.39
		No Generic (N)	Total cost	5,170,569	133.28	221.74	689,109,656.00
			Medical scheme contribution		117.79	213.42	609,050,823.00
			Patient contribution		15.48	56.80	80,058,833.52
		Original (O)	Total cost	1,591,602	100.96	142.38	160,686,606.00
			Medical scheme contribution		81.70	136.17	130,038,318.00
			Patient contribution		19.26	41.05	30,648,288.06
		Generic (Y)	Total cost	4,966,652	48.23	58.77	239,561,528.00
			Medical scheme contribution		42.90	55.56	213,092,491.00
			Patient contribution		5.33	16.09	26,469,036.79
		Total female 2005	Total cost	11,811,901	92.84	165.28	1,096,609,592.00
			Medical scheme contribution		81.16	158.05	958,684,337.00
			Patient contribution		11.68	42.24	137,925,256.00

Table A.14 : Cost analysis of all medicine items according to gender and generic indicator for study period 2005 to 2007 (continued)

Study period	Gender	Generic Indicator	Contribution (R)	Number of medicine items	Average cost per medicine item (R)	Standard deviation (R)	Total cost (R)
2005	Male (M)	(M)	Total cost	53,691	85.82	89.21	4,607,989.12
			Medical scheme contribution		78.10	82.44	4,193,462.15
			Patient contribution		7.72	25.96	414,526.97
		No Generic (N)	Total cost	3,202,623	143.78	258.68	460,472,382.00
			Medical scheme contribution		129.40	250.48	414,435,398.00
			Patient contribution		14.37	62.63	46,036,984.11
		Original (O)	Total cost	1,099,757	98.17	132.11	107,958,767.00
			Medical scheme contribution		81.06	125.16	89,143,431.79
			Patient contribution		17.11	40.12	18,815,335.35
		Generic (Y)	Total cost	3,421,914	49.54	63.46	169,537,385.00
			Medical scheme contribution		44.94	60.50	153,768,922.00
			Patient contribution		4.61	16.27	15,768,462.91
		Total male 2005	Total cost	7,777,985	95.47	183.68	742,576,524.00
			Medical scheme contribution		85.05	176.71	661,541,214.00
			Patient contribution		10.42	44.62	81,035,309.34
Unspecified (U)	(M)	Total cost	109	54.65	39.90	5,956.79	
		Medical scheme contribution		52.91	40.34	5,766.89	
		Patient contribution		1.74	10.77	189.90	

Table A.14 : Cost analysis of all medicine items according to gender and generic indicator for study period 2005 to 2007 (continued)

Study period	Gender	Generic indicator	Contribution (R)	Number of medicine items	Average cost per medicine item (R)	Standard deviation (R)	Total cost (R)
2005	Unspecified (U)	No Generic (N)	Total cost	5,816	168.94	534.50	982,531.20
			Medical scheme contribution		164.01	533.68	953,869.89
			Patient contribution		4.93	25.99	28,661.31
		Original (O)	Total cost	1,939	88.67	84.64	171,935.04
			Medical scheme contribution		68.98	71.01	133,753.98
			Patient contribution		19.69	37.63	38,181.06
		Generic (Y)	Total cost	8,299	38.25	55.82	317,409.66
			Medical scheme contribution		36.56	54.98	303,405.81
			Patient contribution		1.69	8.76	14,003.85
		Total unspecified 2005	Total cost	16,163	91.43	329.97	1,477,832.69
			Medical scheme contribution		86.42	328.83	1,396,796.57
			Patient contribution		5.01	22.01	81,036.12
		Total for all generic indicators 2005	Total cost*	19,606,049	93.88	173.01	1,840,663,949.00
			Medical scheme contribution*		82.71	165.92	1,621,622,348.00
			Patient contribution*		11.17	43.20	219,041,601.00

Table A.14 : Cost analysis of all medicine items according to gender and generic indicator for study period 2005 to 2007 (continued)

Study period	Gender	Generic indicator	Contribution (R)	Number of medicine items	Average cost per medicine item (R)	Standard deviation (R)	Total cost (R)
2006	Female (F)	Original (O)	Total cost	1,951,965	105.38	170.48	205,699,460.00
			Medical scheme contribution		83.99	163.48	163,946,616.00
			Patient contribution		21.39	47.39	41,752,844.15
		Generic (Y)	Total cost	5,844,476	51.37	68.42	300,217,520.00
			Medical scheme contribution		45.18	65.21	264,056,967.00
			Patient contribution		6.19	19.21	36,160,553.61
		Total female 2006	Total cost	12,764,246	92.18	195.39	1,176,562,838.00
			Medical scheme contribution		79.28	188.75	1,011,957,533.00
			Patient contribution		12.90	46.11	164,605,305.00
	Male (M)	(M)	Total cost	968	51.10	94.38	49,468.69
			Medical scheme contribution		42.84	91.14	41,467.16
			Patient contribution		8.27	33.52	8,001.53
	Male (M)	No Generic (N)	Total cost	3,087,130	151.10	328.80	466,457,757.00
			Medical scheme contribution		134.25	322.00	414,448,208.00
			Patient contribution		16.85	66.16	52,009,549.40
		Original (O)	Total cost	1,288,989	98.17	143.29	126,540,473.00
			Medical scheme contribution		78.90	135.61	101,698,633.00
			Patient contribution		19.27	43.82	24,841,840.31
		Generic (Y)	Total cost	4,067,073	52.69	68.78	214,305,265.00
			Medical scheme contribution		47.37	66.03	192,640,165.00
			Patient contribution		5.33	17.74	21,665,099.73
Total male 2006	Total cost	8,444,160	95.61	216.68	807,352,964.00		
	Medical scheme contribution		83.94	210.69	708,828,473.00		
	Patient contribution		11.67	45.64	98,524,490.97		

Table A.14 : Cost analysis of all medicine items according to gender and generic indicator for study period 2005 to 2007 (continued)

Study period	Gender	Generic indicator	Contribution (R)	Number of medicine items	Average cost per medicine item (R)	Standard deviation (R)	Total cost (R)
2006	Unspecified (U)	(M)	Total cost	17	121.64	10.74	2,067.92
			Medical scheme contribution		118.67	12.48	2,017.36
			Patient contribution		2.97	8.40	50.56
		No Generic (N)	Total cost	3,643	184.95	564.76	673,756.00
			Medical scheme contribution		169.84	564.23	618,743.34
			Patient contribution		15.10	45.84	55,012.66
		Original (O)	Total cost	1,658	109.09	94.78	180,865.30
			Medical scheme contribution		87.06	84.10	144,341.44
			Patient contribution		22.02	40.37	36,523.86
		Generic (Y)	Total cost	5,297	52.24	56.17	276,737.00
			Medical scheme contribution		48.43	53.75	256,545.37
			Patient contribution		3.81	11.53	20,191.63
		Total unspecified 2006	Total cost	10,615	106.78	340.59	1,133,426.22
			Medical scheme contribution		96.25	338.82	1,021,647.51
			Patient contribution		10.53	33.05	111,778.71
Total for all generic indicators 2006	Total cost*	21,219,021	93.55	204.23	1,985,049,229.00		
	Medical scheme contribution*		81.14	197.88	1,721,807,654.00		
	Patient contribution*		12.41	45.92	263,241,575.00		

Table A.14 : Cost analysis of all medicine items according to gender and generic indicator for study period 2005 to 2007 (continued)

Study period	Gender	Generic indicator	Contribution (R)	Number of medicine items	Average cost per medicine item (R)	Standard deviation (R)	Total cost (R)
2007	Female (F)	(M)	Total cost	12,118	60.00	61.08	727,122.28
			Medical scheme contribution		40.82	62.63	494,651.91
			Patient contribution		19.18	34.81	232,470.37
		No Generic (N)	Total cost	4,397,480	146.55	467.78	644,464,218.00
			Medical scheme contribution		124.65	446.59	548,165,010.00
			Patient contribution		21.90	131.06	96,299,207.50
		Original (O)	Total cost	1,756,460	105.09	187.20	184,577,683.00
			Medical scheme contribution		77.62	176.62	136,327,757.00
			Patient contribution		27.47	54.93	48,249,925.61
		Generic (Y)	Total cost	5,385,837	58.77	80.30	316,508,587.00
			Medical scheme contribution		50.31	76.06	270,965,480.00
			Patient contribution		8.46	23.07	45,543,106.17
		Total female 2007	Total cost	11,551,895	99.23	305.38	1,146,277,610.00
			Medical scheme contribution		82.75	290.74	955,952,900.00
			Patient contribution		16.48	85.48	190,324,710.00
Male (M)	(M)	Total cost	727	50.99	149.78	37,073.36	
		Medical scheme contribution		38.80	122.02	28,206.87	
		Patient contribution		12.20	38.09	8,866.49	

Table A.14 : Cost analysis of all medicine items according to gender and generic indicator for study period 2005 to 2007 (continued)

Study period	Gender	Generic indicator	Contribution (R)	Number of medicine items	Average cost per medicine item (R)	Standard deviation (R)	Total cost (R)
2007	Male (M)	No Generic (N)	Total cost	2,626,971	167.50	594.39	440,008,107.00
			Medical scheme contribution		145.72	549.31	382,789,877.00
			Patient contribution		21.78	205.17	57,218,229.61
		Original (O)	Total cost	1,262,346	98.78	168.13	124,695,036.00
			Medical scheme contribution		74.39	156.81	93,908,088.38
			Patient contribution		24.39	50.59	30,786,947.30
		Generic (Y)	Total cost	3,700,293	59.85	7.73	221,463,162.00
			Medical scheme contribution		52.62	74.45	194,715,352.00
			Patient contribution		7.23	22.63	26,747,809.89
	Total male 2007	Total cost	7,590,337	103.58	363.80	786,203,378.00	
		Medical scheme contribution		88.46	336.18	671,441,524.00	
		Patient contribution		15.12	123.71	114,761,853.00	
	Unspecified (U)	No Generic (N)	Total cost	1,695	227.74	661.60	386,015.17
			Medical scheme contribution		208.37	660.99	353,182.34
			Patient contribution		19.37	22.85	32,832.83
		Original (O)	Total cost	788	116.00	94.61	91,407.73
			Medical scheme contribution		82.29	72.40	64,847.90
			Patient contribution		33.71	43.50	26,559.83
Generic (Y)		Total cost	1,441	77.69	79.61	111,955.77	
	Medical scheme contribution	66.20		71.79	95,396.41		

Table A.14 : Cost analysis of all medicine items according to gender and generic indicator for study period 2005 to 2007 (continued)

Study period	Gender	Generic indicator	Contribution (R)	Number of medicine items	Average cost per medicine item (R)	Standard deviation (R)	Total cost (R)
2007	Unspecified (U)	Generic (Y)	Patient contribution	1,441	11.49	21.10	16,559.36
		Total unspecified 2007	Total cost	3,924	150.20	444.85	589,378.67
			Medical scheme contribution		130.84	442.96	513,426.65
			Patient contribution		19.36	28.86	75,952.02
	Total all generic indicators 2007	Total cost*	19,146,156	100.96	329.82	1,933,070,366.00	
		Medical scheme contribution*		85.03	309.61	1,627,907,851.00	
		Patient contribution*		15.94	102.35	305,162,515.00	

Table A.15 : Cost analysis of all medicine items according to age group and generic indicator for study period 2005 to 2007

Study period	Age group	Generic Indicator	Contribution (R)	Number of medicine items	Average cost (R)	Standard deviation (R)	Total cost (R)
2005	≤ 5 years	(M)	Total cost	12,013	44.36	10.72	532,878.31
			Medical scheme contribution		41.52	12.37	498,778.16
			Patient contribution		2.84	7.13	34,100.15
		No Generic (N)	Total cost	406,856	71.65	85.51	29,153,171.24
			Medical scheme contribution		65.98	80.12	26,846,212.30
			Patient contribution		5.67	30.37	2,306,958.94
		Original (O)	Total cost	147,341	76.95	68.05	11,337,962.38
			Medical scheme contribution		65.57	66.46	9,661,022.81
			Patient contribution		11.38	24.33	1,676,939.57
		Generic (Y)	Total cost	408,575	27.45	32.04	11,214,109.70
			Medical scheme contribution		25.24	30.68	10,311,475.40
			Patient contribution		2.21	8.68	902,634.30
		Total for ≤ 5 years	Total cost	974,785	53.59	68.48	52,238,121.63
			Medical scheme contribution		48.54	64.36	47,317,488.67
			Patient contribution		5.05	22.72	4,920,632.96
	5 < and ≤ 12 years	(M)	Total cost	7,484	47.48	21.10	355,319.28
			Medical scheme contribution		44.40	20.23	332,291.01
			Patient contribution		3.08	9.82	23,028.27
		No Generic (N)	Total cost	398,394	86.16	105.31	34,323,975.87
			Medical scheme contribution		79.74	100.07	31,766,786.21
			Patient contribution		6.42	30.66	2,557,189.66
Original (O)		Total cost	140,284	88.40	78.33	12,400,958.44	
		Medical scheme contribution		74.33	75.07	10,426,727.47	
		Patient contribution		14.07	29.32	1,974,230.97	

Table A.15 : Cost analysis of all medicine items according to age group and generic indicator for study period 2005 to 2007 (continued)

Study period	Age group	Generic indicator	Contribution (R)	Number of medicine items	Average cost (R)	Standard deviation (R)	Total cost (R)
2005	5 < and ≤ 12 years	Generic (Y)	Total cost	464,646	30.97	37.99	14,392,103.46
			Medical scheme contribution		28.51	35.94	13,247,676.81
			Patient contribution		2.46	10.70	1,144,426.65
		Total for 5 < and ≤ 12 years	Total cost	1,010,808	60.82	81.60	61,472,357.05
			Medical scheme contribution		55.18	77.08	55,773,481.50
			Patient contribution		5.64	23.62	5,698,875.55
	12 < and ≤ 18 years	(M)	Total cost	8,827	58.70	37.56	518,169.70
			Medical scheme contribution		54.07	37.24	477,299.67
			Patient contribution		4.63	13.88	40,870.03
		No Generic (N)	Total cost	319,115	105.09	156.77	33,536,030.36
			Medical scheme contribution		96.47	150.77	30,784,857.50
			Patient contribution		8.62	39.36	2,751,172.86
		Original (O)	Total cost	115,333	90.02	107.15	10,381,723.29
			Medical scheme contribution		72.78	96.21	8,393,857.02
			Patient contribution		17.24	40.17	1,987,866.27
		Generic (Y)	Total cost	391,231	39.10	56.42	15,298,922.50
			Medical scheme contribution		35.07	52.55	13,719,575.41
			Patient contribution		4.04	15.19	1,579,347.09
		Total for 12 < and ≤ 18 years	Total cost	834,506	71.58	116.04	59,734,845.85
			Medical scheme contribution		63.96	109.95	53,375,589.60
			Patient contribution		7.62	30.74	6,359,256.25
	> 18 years	(M)	Total cost	108,554	96.35	93.84	10,459,380.50
			Medical scheme contribution		86.53	86.79	9,393,564.69
			Patient contribution		9.82	29.41	1,065,815.81
		No Generic (N)	Total cost	7,254,628	145.22	249.50	1,053,550,457.00
			Medical scheme contribution		128.89	241.18	935,041,299.00
			Patient contribution		16.34	62.03	118,509,157.00

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Table A.15 : Cost analysis of all medicine items according to age group and generic indicator for study period 2005 to 2007
(continued)

Study period	Age group	Generic indicator	Contribution (R)	Number of medicine items	Average cost (R)	Standard deviation (R)	Total cost (R)
2005	> 18 years	Original (O)	Total cost	2,290,340	102.47	145.50	234,696,664.00
			Medical scheme contribution		83.32	138.89	190,833,896.00
			Patient contribution		19.15	42.06	43,862,767.66
		Generic (Y)	Total cost	7,132,407	51.67	62.88	368,510,871.00
			Medical scheme contribution		46.25	59.80	329,885,775.00
			Patient contribution		5.42	16.79	38,625,095.51
		Total for > 18 years	Total cost	16,785,929	99.32	182.77	1,667,217,372.00
			Medical scheme contribution		87.28	175.51	1,465,154,535.00
			Patient contribution		12.04	45.42	202,062,836.00
	Total for age groups 2005	Total cost	19,606,049	93.88	173.01	1,840,663,949.00	
		Medical scheme contribution		82.71	165.92	1,621,622,348.00	
		Patient contribution		11.17	43.20	219,041,601.00	
2006	≤ 5 years	(M)	Total cost	24	75.13	48.80	1,803.03
			Medical scheme contribution		60.48	46.98	1,451.51
			Patient contribution		14.65	37.99	351.52
		No Generic (N)	Total cost	401,518	74.05	132.80	29,731,838.47
			Medical scheme contribution		66.26	126.64	26,604,417.58
			Patient contribution		7.79	38.32	3,127,420.89
		Original (O)	Total cost	168,320	68.27	61.35	11,491,115.93
			Medical scheme contribution		53.85	55.71	9,064,170.30
			Patient contribution		14.42	28.07	2,426,945.63
		Generic (Y)	Total cost	454,061	29.16	35.28	13,239,095.00
			Medical scheme contribution		26.42	34.07	11,994,133.06
			Patient contribution		2.74	9.97	1,244,961.94
		Total for ≤ 5 years	Total cost	1,023,923	53.19	92.47	54,463,852.43
			Medical scheme contribution		46.55	87.49	47,664,172.45
			Patient contribution		6.64	27.69	6,799,679.98

Table A.15 : Cost analysis of all medicine items according to age group and generic indicator for study period 2005 to 2007 (continued)

Study period	Age group	Generic indicator	Contribution (R)	Number of medicine items	Average cost (R)	Standard deviation (R)	Total cost (R)
2006	5 < and ≤ 12 years	(M)	Total cost	60	68.16	62.04	4,089.31
			Medical scheme contribution		59.40	62.29	3,564.04
			Patient contribution		8.75	24.88	525.27
		No Generic (N)	Total cost	377,809	90.14	120.39	34,056,773.59
			Medical scheme contribution		81.67	111.95	30,854,476.77
			Patient contribution		8.48	42.91	3,202,296.82
		Original (O)	Total cost	166,113	80.16	75.37	13,316,068.86
			Medical scheme contribution		63.66	66.01	10,574,501.51
			Patient contribution		16.50	31.97	2,741,567.35
		Generic (Y)	Total cost	512,958	33.20	39.34	17,030,482.89
			Medical scheme contribution		30.20	37.97	15,489,562.26
			Patient contribution		3.00	10.80	1,540,920.63
		Total for 5 < and ≤ 12 years	Total cost	1,056,940	60.94	86.55	64,407,414.65
			Medical scheme contribution		53.86	80.18	56,922,104.58
			Patient contribution		7.08	29.97	7,485,310.07
	12 < and ≤ 18 years	(M)	Total cost	617	73.05	26.30	45,069.67
			Medical scheme contribution		58.68	36.41	36,206.99
			Patient contribution		14.36	30.71	8,862.68
		No Generic (N)	Total cost	316,789	106.70	180.53	33,800,027.52
			Medical scheme contribution		96.37	175.24	30,527,928.05
			Patient contribution		10.33	42.88	3,272,099.47
Original (O)		Total cost	129,306	88.95	97.61	11,501,990.77	
		Medical scheme contribution		69.15	83.67	8,941,341.27	

Table A.15 : Cost analysis of all medicine items according to age group and generic indicator for study period 2005 to 2007 (continued)

Study period	Age group	Generic indicator	Contribution (R)	Number of medicine items	Average cost (R)	Standard deviation (R)	Total cost (R)
2006	12 < and ≤ 18 years	Original (O)	Patient contribution		19.80	45.53	2,560,649.50
		Generic (Y)	Total cost	456,481	39.87	55.79	18,199,058.07
			Medical scheme contribution		35.70	52.27	16,297,121.59
			Patient contribution		4.17	17.17	1,901,936.48
		Total for 12 < and ≤ 18 years	Total cost	903,193	70.36	124.01	63,546,146.03
			Medical scheme contribution		61.78	118.01	55,802,597.90
	Patient contribution			8.57	33.47	7,743,548.13	
	> 18 years	(M)	Total cost	31,867	96.13	38.57	3,063,216.74
			Medical scheme contribution		82.99	43.36	2,644,772.78
			Patient contribution		13.13	26.05	418,443.96
		No Generic (N)	Total cost	6,930,845	149.64	316.16	1,037,124,677.00
			Medical scheme contribution		131.06	309.00	908,390,159.00
			Patient contribution		18.57	67.56	128,734,518.00
		Original (O)	Total cost	2,778,870	106.56	169.82	296,111,552.00
			Medical scheme contribution		85.36	162.64	237,209,519.00
			Patient contribution		21.20	47.56	58,902,033.25
		Generic (Y)	Total cost	8,493,346	54.91	71.39	466,330,886.00
			Medical scheme contribution		48.65	68.36	413,172,860.00
			Patient contribution		6.26	19.37	53,158,025.92
		Total for > 18 years	Total cost	18,234,928	98.86	215.99	1,802,630,332.00
			Medical scheme contribution		85.63	209.58	1,561,417,311.00
			Patient contribution		13.23	47.94	241,213,021.00
		Total for all age groups 2006	Total cost	21,219,021	93.55	204.23	1,985,049,229.00
			Medical scheme contribution		81.14	197.88	1,721,807,654.00
			Patient contribution		12.41	45.92	263,241,575.00

Table A.15 : Cost analysis of all medicine items according to age group and generic indicator for study period 2005 to 2007 (continued)

Study period	Age group	Generic indicator	Contribution (R)	Number of medicine items	Average cost (R)	Standard deviation (R)	Total cost (R)
2007	≤ 5 years	(M)	Total cost	12	53.81	47.24	645.67
			Medical scheme contribution		51.71	48.26	620.46
			Patient contribution		2.10	5.88	25.21
		No Generic (N)	Total cost	328,831	76.59	186.82	25,184,811.80
			Medical scheme contribution		64.51	120.28	21,214,471.63
			Patient contribution		12.07	138.74	3,970,340.17
		Original (O)	Total cost	138,844	65.48	60.41	9,091,983.19
			Medical scheme contribution		47.14	50.42	6,545,553.02
			Patient contribution		18.34	31.29	2,546,430.17
		Generic (Y)	Total cost	359,892	30.43	38.48	10,951,186.43
			Medical scheme contribution		26.77	36.25	9,636,071.11
			Patient contribution		3.65	11.75	1,315,115.32
		Total for ≤ 5 years	Total cost	827,579	54.65	124.86	45,228,627.09
			Medical scheme contribution		45.19	83.92	37,396,716.22
			Patient contribution		9.46	88.53	7,831,910.87
	5 < and ≤ 12 years	(M)	Total cost	35	64.29	61.73	2,250.24
			Medical scheme contribution		56.48	57.87	1,976.73
			Patient contribution		7.81	22.73	273.51
		No Generic (N)	Total cost	321,746	98.34	142.72	31,640,889.77
			Medical scheme contribution		85.35	131.55	27,460,983.26
			Patient contribution		12.99	49.01	4,179,906.51
Original (O)		Total cost	142,381	78.30	72.38	11,148,283.57	
		Medical scheme contribution		57.61	61.44	8,203,051.95	
		Patient contribution		20.69	35.09	2,945,231.62	

Table A.15 : Cost analysis of all medicine items according to age group and generic indicator for study period 2005 to 2007 (continued)

Study period	Age group	Generic indicator	Contribution (R)	Number of medicine items	Average cost (R)	Standard deviation (R)	Total cost (R)	
2007	5 < and ≤ 12 years	Generic (Y)	Total cost	431,462	35.19	43.70	15,182,121.52	
			Medical scheme contribution		31.32	41.31	13,513,301.21	
			Patient contribution		3.87	11.90	1,668,820.31	
		Total for 5 < and ≤ 12 years	Total cost	895,624	64.73	99.63	57,973,545.10	
			Medical scheme contribution		54.91	90.78	49,179,313.15	
			Patient contribution		9.82	34.15	8,794,231.95	
	12 < and ≤ 18 years	(M)	Total cost	603	63.37	37.57	38,212.81	
			Medical scheme contribution		43.64	42.01	26,317.62	
			Patient contribution		19.73	36.39	11,895.19	
		No Generic (N)	Total cost	276,887	113.37	313.33	31,390,140.82	
			Medical scheme contribution		98.14	289.38	27,173,260.58	
			Patient contribution		15.23	110.42	4,216,880.24	
		Original (O)	Total cost	111,643	90.60	106.95	10,114,584.70	
			Medical scheme contribution		65.00	87.08	7,257,151.72	
			Patient contribution		25.59	51.78	2,857,432.98	
		Generic (Y)	Total cost	399,208	41.96	61.65	16,750,940.92	
			Medical scheme contribution		36.24	56.33	14,468,713.30	
			Patient contribution		5.72	20.04	2,282,227.62	
		Total for 12 < and ≤ 18 years	Total cost	788,341	73.95	197.82	58,293,879.25	
			Medical scheme contribution		62.06	181.36	48,925,443.22	
			Patient contribution		11.88	70.12	9,368,436.03	
		> 18 years	(M)	Total cost	12,195	59.29	70.46	723,086.92
				Medical scheme contribution		40.50	68.45	493,943.97
				Patient contribution		18.79	35.01	229,142.95

Table A.15 : Cost analysis of all medicine items according to age group and generic indicator for study period 2005 to 2007 (continued)

Study period	Age group	Generic indicator	Contribution (R)	Number of medicine items	Average cost (R)	Standard deviation (R)	Total cost (R)
2007	> 18 years	No Generic (N)	Total cost	6,098,656	163.42	549.67	996,640,802.00
			Medical scheme contribution		140.27	517.74	855,457,707.00
			Patient contribution		23.15	169.69	141,183,095.00
		Original (O)	Total cost	2,626,726	106.22	189.59	279,009,275.00
			Medical scheme contribution		79.30	178.72	208,294,937.00
			Patient contribution		26.92	54.89	70,714,337.97
		Generic (Y)	Total cost	7,897,008	62.71	82.72	495,199,442.00
			Medical scheme contribution		54.22	78.50	428,158,138.00
			Patient contribution		8.49	23.81	67,041,304.17
		Total for > 18 years	Total cost	16,634,585	106.50	349.00	1,771,572,606.00
			Medical scheme contribution		89.72	328.33	1,492,404,726.00
			Patient contribution		16.78	106.62	279,167,880.00
	Total for all age groups 2007	Total cost	19,146,156	100.96	329.82	1,933,070,366.00	
		Medical scheme contribution		85.03	309.61	1,627,907,851.00	
		Patient contribution		15.94	102.35	305,162,515.00	

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Table A.16 Cost analysis of methylphenidate or atomoxetine containing medicine items for study period 2005 to 2007

Study period	Contribution (R)	Number of medicine items	Average cost (R)	Standard Deviation (R)	Total cost (R)
2005	Total cost	29,424	299.42	144.97	8,810,130.56
	Total scheme contribution		263.32	149.21	7,748,035.75
	Total patient contribution		36.10	84.71	1,062,094.81
2006	Total cost	33,576	330.65	173.83	11,101,929.25
	Total scheme contribution		277.35	180.57	9,312,405.44
	Total patient contribution		53.30	112.25	1,789,523.81
2007	Total cost	34,850	336.22	192.02	11,717,340.70
	Total scheme contribution		268.11	192.46	9,343,473.11
	Total patient contribution		68.12	125.18	2,373,867.59

Table A.17: Cost analysis of methylphenidate or atomoxetine containing medicine items according to gender for study period 2005 to 2007

Study period	Gender	Number of medicine items	Contribution (R)	Average cost (R)	Standard Deviation (R)	Total cost (R)
2005	Female (F)	7,567	Total cost	288.93	142.50	2,186,354.95
			Total scheme contribution	251.19	145.98	1,900,721.05
			Total patient contribution	37.75	87.02	285,633.90
	Male (M)	21,798	Total cost	303.04	145.65	6,605,662.72
			Total scheme contribution	267.50	150.09	5,831,021.87
			Total patient contribution	35.54	83.90	774,640.85
	Unspecified (U)	59	Total cost	307.00	141.78	18,112.89
			Total scheme contribution	276.15	152.24	16,292.83
			Total patient contribution	30.85	83.19	1,820.06
2006	Female (F)	8,525	Total cost	323.89	176.15	2,761,186.49
			Total scheme contribution	268.97	180.95	2,292,963.40
			Total patient contribution	54.92	114.18	468,223.09
	Male (M)	24,990	Total cost	332.77	172.92	8,315,888.20
			Total scheme contribution	280.17	180.28	7,001,447.90
			Total patient contribution	52.60	111.14	1,314,440.27
	Unspecified (U)	61	Total cost	407.45	182.46	24,854.56
			Total scheme contribution	294.99	210.84	17,994.11
			Total patient contribution	112.47	222.30	6,860.45
2007	Female (F)	9,001	Total cost	328.72	193.90	2,958,795.47
			Total scheme contribution	258.74	191.51	2,328,912.45
			Total patient contribution	69.98	128.59	629,883.02
	Male (M)	25,833	Total cost	338.73	191.28	8,750,509.01
			Total scheme contribution	271.27	192.67	7,007,667.31
			Total patient contribution	67.47	124.01	1,742,841.70
	Unspecified (U)	16	Total cost	502.26	153.13	8,036.22
			Total scheme contribution	430.83	153.90	6,893.35
			Total patient contribution	71.43	10.67	1,142.87

Table A.18: Cost analysis of methylphenidate or atomoxetine containing medicine items according to age groups for study period 2005 to 2007

Study period	Age group	Number of medicine items	Contribution (R)	Average cost (R)	Standard Deviation (R)	Total cost (R)
2005	≤ 5 years	146	Total cost	210.42	141.61	30,721.29
			Total scheme contribution	185.63	144.68	27,102.49
			Total patient contribution	24.79	62.99	3,618.80
	5< and ≤12 years	16,936	Total cost	280.47	132.31	4,750,026.83
			Total scheme contribution	249.61	138.04	4,227,348.17
			Total patient contribution	30.86	74.71	522,678.66
	12< and ≤18 years	8,227	Total cost	328.81	140.66	2,705,082.80
			Total scheme contribution	290.05	149.51	2,386,247.67
			Total patient contribution	38.75	90.62	318,835.13
	> 18 years	4,115	Total cost	321.82	184.35	1,324,299.64
			Total scheme contribution	269.10	181.41	1,107,337.42
			Total patient contribution	52.72	106.67	216,962.22
2006	≤ 5 years	160	Total cost	223.97	160.01	35,835.02
			Total scheme contribution	172.46	157.57	27,593.55
			Total patient contribution	51.51	101.98	8,241.47
	5< and ≤12 years	18,936	Total cost	311.51	163.72	5,898,701.75
			Total scheme contribution	264.65	171.62	5,011,470.43
			Total patient contribution	46.85	100.78	887,231.32
	12< and ≤18 years	9,613	Total cost	365.23	172.02	3,510,932.53
			Total scheme contribution	310.97	183.94	2,989,350.20
			Total patient contribution	54.26	115.93	521,582.33
	> 18 years	4,867	Total cost	340.35	201.64	1,656,459.95
			Total scheme contribution	263.82	198.28	1,283,991.26
			Total patient contribution	76.53	140.80	372,468.69

Table A.18: Cost of methylphenidate or atomoxetine containing medicine items according to age groups for study period 2005 to 2007 (continued)

Study period	Age group	Number of medicine items	Contribution (R)	Average cost (R)	Standard Deviation (R)	Total cost (R)
2007	≤ 5 years	212	Total cost	300.27	222.09	63,656.22
			Total scheme contribution	220.63	207.77	46,774.03
			Total patient contribution	79.63	160.28	16,882.19
	5< and ≤12 years	18,988	Total cost	315.85	181.63	5,997,324.08
			Total scheme contribution	254.74	182.16	4,836,999.77
			Total patient contribution	61.11	112.63	1,160,324.31
	12< and ≤18 years	10,216	Total cost	367.77	189.22	3,757,107.43
			Total scheme contribution	302.78	196.36	3,093,212.87
			Total patient contribution	64.99	122.72	663,894.56
	> 18 years	5,434	Total cost	349.51	220.06	1,899,252.97
			Total scheme contribution	251.47	210.25	1,366,486.44
			Total patient contribution	98.04	160.53	532,766.53

Table A.19: Cost analysis of methylphenidate or atomoxetine containing medicine items according to generic indicator for study period 2005 to 2007

Study period	Generic Indicator	Contribution (R)	Number of medicine items	Average cost (R)	Standard Deviation (R)	Total cost (R)
2005	No Generic (N)	Total cost	18,230	363.27	119.53	6,622,400.44
		Total scheme contribution		324.12	135.04	5,908,629.08
		Total patient contribution		39.15	95.98	713,771.36
	Original (O)	Total cost	8,643	215.85	125.05	1,865,631.46
		Total scheme contribution		178.50	121.04	1,542,785.78
		Total patient contribution		37.35	66.94	322,845.68
	Generic (Y)	Total cost	2,551	126.26	67.48	322,098.66
		Total scheme contribution		116.28	66.64	296,620.89
		Total patient contribution		9.99	31.76	25,477.77
2006	No Generic (N)	Total cost	22,816	397.28	153.43	9,064,346.86
		Total scheme contribution		340.56	171.75	7,770,264.66
		Total patient contribution		56.72	127.04	1,294,082.20
	Original (O)	Total cost	7,893	221.36	128.37	1,668,229.49
		Total scheme contribution		153.00	122.47	1,207,641.42
		Total patient contribution		58.35	75.73	460,588.07
	Generic (Y)	Total cost	2,867	128.83	77.04	369,352.90
		Total scheme contribution		116.67	75.16	334,499.36
		Total patient contribution		12.16	38.34	34,853.54
2007	No Generic (N)	Total cost	25,871	393.77	177.76	10,187,189.25
		Total scheme contribution		321.95	187.51	8,329,290.52
		Total patient contribution		71.81	137.78	1,857,898.73
	Original (O)	Total cost	6,638	184.20	128.74	1,222,735.47
		Total scheme contribution		113.65	104.97	754,421.39
		Total patient contribution		70.55	80.07	468,314.08
	Generic (Y)	Total cost	2,341	131.32	92.65	307,415.98
		Total scheme contribution		110.96	85.21	259,761.20
		Total patient contribution		20.36	53.50	47,654.78

Table A.20 : Cost analysis of methylphenidate or atomoxetine containing medicine items according to generic indicator and active ingredient during 2005

Study period	Generic Indicator	Active ingredient	Trade name	Number of medicine items	Contribution (R)	Average cost (R)	Standard Deviation (R)	Total cost (R)
2005	No Generic (N)	Atomoxetine	Strattera 10mg Cap®	169	Total cost	382.05	264.90	64,565.83
					Total scheme contribution	325.24	260.15	54,964.94
					Total patient contribution	56.81	127.65	9,600.89
			Strattera 18mg Cap®	249	Total cost	376.20	225.02	93,673.70
					Total scheme contribution	322.65	221.83	80,339.44
					Total patient contribution	53.55	131.54	13,334.26
			Strattera 25mg Cap®	364	Total cost	501.27	203.20	182,463.66
					Total scheme contribution	425.34	239.89	154,822.22
					Total patient contribution	75.94	158.80	27,641.44
			Strattera 40mg Cap®	401	Total cost	600.91	161.03	240,965.61
					Total scheme contribution	502.02	224.78	201,310.20
					Total patient contribution	98.89	196.87	39,655.41
		Strattera 60mg Cap®	196	Total cost	581.53	82.63	113,980.71	
				Total scheme contribution	470.79	208.85	92,275.43	
				Total patient contribution	110.74	200.27	21,705.28	
		Methylphenidate	Adaphen 5mg Tab®	20	Total cost	65.79	28.95	1,315.73
					Total scheme contribution	63.31	30.69	1,266.28
					Total patient contribution	2.47	4.39	49.45
Concerta 18mg Oros®	1,233		Total cost	361.26	90.28	445,436.79		
			Total scheme contribution	319.60	122.93	394,065.49		
			Total patient contribution	41.66	95.26	51,371.30		

Table A.20 : Cost analysis of methylphenidate or atomoxetine containing medicine items according to generic indicator and active ingredient during 2005 (continued)

Study period	Generic Indicator	Active ingredient	Trade name	Number of medicine items	Contribution (R)	Average cost (R)	Standard Deviation (R)	Total cost (R)
2005	No Generic (N)	Methylphenidate	Concerta 36mg Oros®	1,969	Total cost	400.09	67.36	787,783.76
					Total scheme contribution	345.32	120.81	679,937.61
					Total patient contribution	54.77	107.01	107,846.15
			Concerta 54mg Oros®	297	Total cost	460.30	68.75	136,710.44
					Total scheme contribution	381.72	158.73	113,369.89
					Total patient contribution	78.59	149.99	23,340.55
			Ritalin LA 20mg Cap®	8,707	Total cost	301.41	55.95	2,624,389.50
					Total scheme contribution	276.43	79.73	2,406,879.64
					Total patient contribution	24.98	61.53	217,509.86
			Ritalin LA 30mg Cap®	2,667	Total cost	430.51	92.32	1,148,171.63
					Total scheme contribution	386.96	125.60	1,032,022.58
					Total patient contribution	43.55	97.50	116,149.05
			Ritalin LA 40mg Cap®	734	Total cost	547.26	103.70	401,690.50
					Total scheme contribution	471.38	177.04	345,995.10
					Total patient contribution	75.88	161.15	55,695.40
	Ritalin SR 20mg Tab®	1,224	Total cost	311.48	96.49	381,252.58		
			Total scheme contribution	287.08	100.02	351,380.26		
			Total patient contribution	24.41	54.48	29,872.32		
	Original (O)	Methylphenidate	Ritalin 10mg Tab®	8,173	Total cost	210.21	122.61	1,718,024.48
					Total scheme contribution	173.73	118.57	1,419,926.27
					Total patient contribution	36.47	65.67	298,098.21
Ritalin SR 20mg Tab®			470	Total cost	314.06	126.29	147,606.98	
				Total scheme contribution	261.40	133.15	122,859.51	
				Total patient contribution	52.65	84.67	24,747.47	

Table A.20 : Cost analysis of methylphenidate or atomoxetine containing medicine items according to generic indicator and active ingredient during 2005 (continued)

Study period	Generic Indicator	Active ingredient	Trade name	Number of medicine items	Contribution (R)	Average cost (R)	Standard Deviation (R)	Total cost (R)
2005	Generic (Y)	Methylphenidate	Adaphen 10mg Tab®	1,133	Total cost	122.32	65.57	138,583.12
					Total scheme contribution	112.21	64.61	127,136.34
					Total patient contribution	10.10	30.12	11,446.78
			Adaphen XL 20mg Tab®	12	Total cost	217.99	90.73	2,615.84
					Total scheme contribution	195.28	111.48	2,343.31
					Total patient contribution	22.71	60.35	272.53
			Methylphenidate HCL-Douglas®	1,406	Total cost	128.66	68.17	180,899.70
					Total scheme contribution	118.88	67.28	167,141.24
					Total patient contribution	9.79	32.71	13,758.46

Table A.21 : Cost analysis of methylphenidate or atomoxetine containing medicine items according to generic indicator and active ingredient during 2006

Study period	Generic Indicator	Active Ingredient	Trade name	Number of medicine items	Contribution (R)	Average cost (R)	Standard Deviation (R)	Total cost (R)
2006	No Generic (N)	Atomoxetine	Strattera 10mg Cap®	306	Total cost	455.82	300.60	139,481.58
					Total scheme contribution	392.38	294.39	120,068.34
					Total patient contribution	63.44	125.81	19,413.24
			Strattera 18mg Cap®	503	Total cost	444.32	243.37	223,493.87
					Total scheme contribution	377.05	242.64	189,658.27
					Total patient contribution	67.27	154.59	33,835.60
			Strattera 25mg Cap®	1,015	Total cost	551.25	188.31	559,519.94
					Total scheme contribution	464.85	234.55	471,821.83
					Total patient contribution	86.40	165.52	87,698.11
			Strattera 40mg Cap®	1,743	Total cost	598.27	192.57	1,042,789.67
					Total scheme contribution	475.61	252.70	828,992.39
					Total patient contribution	122.66	215.98	213,797.28
		Strattera 60mg Cap®	769	Total cost	572.14	102.68	439,975.40	
				Total scheme contribution	462.69	200.65	355,806.07	
				Total patient contribution	109.45	188.70	84,169.33	
		Methylphenidate	Adaphen 5mg Tab®	5	Total cost	47.57	14.66	237.87
					Total scheme contribution	47.57	14.66	237.87
					Total patient contribution	0.00	0.00	0.00
			Concerta 18mg Oros®	2,399	Total cost	360.18	94.87	864,077.83
					Total scheme contribution	308.50	130.97	740,097.98
					Total patient contribution	51.68	105.68	123,979.85

Table A.21 : Cost analysis of methylphenidate or atomoxetine containing medicine items according to generic indicator and active ingredient during 2006 (continued)

Study period	Generic Indicator	Active Ingredient	Trade name	Number of medicine items	Contribution (R)	Average cost (R)	Standard Deviation (R)	Total cost (R)
2006	No Generic (N)	Methylphenidate	Concerta 36mg Oros®	4,104	Total cost	398.12	88.07	1,633,882.70
					Total scheme contribution	344.49	131.95	1,413,781.93
					Total patient contribution	53.63	109.87	220,100.77
			Concerta 54mg Oros®	1,111	Total cost	446.78	99.78	496,371.59
					Total scheme contribution	381.03	158.39	423,329.64
					Total patient contribution	65.74	133.38	73,041.95
			Ritalin LA 20mg Cap®	7,592	Total cost	291.44	76.17	2,212,592.13
					Total scheme contribution	261.47	98.19	1,985,076.60
					Total patient contribution	29.97	73.65	227,515.53
			Ritalin LA 30mg Cap®	2,523	Total cost	419.52	104.82	1,058,449.61
					Total scheme contribution	361.36	147.66	911,720.16
					Total patient contribution	58.16	122.64	146,729.45
	Ritalin LA 40mg Cap®	746	Total cost	527.45	111.28	393,474.67		
			Final scheme amount	441.92	197.20	329,673.58		
			Final levy	85.52	175.39	63,801.09		
	Original (O)	Methylphenidate	Ritalin 10mg Tab®	6,828	Total cost	197.29	125.19	1,347,103.52
					Final scheme amount	138.38	116.71	944,859.10
					Final levy	58.91	73.87	402,244.42
Ritalin SR 20mg Tab®			1,065	Total cost	301.53	110.75	321,125.97	
				Final scheme amount	246.74	116.99	262,782.32	
				Final levy	54.78	86.67	58,343.65	

Table A.21 : Cost analysis of methylphenidate or atomoxetine containing medicine items according to generic indicator and active ingredient during 2006 (continued)

Study period	Generic Indicator	Active ingredient	Trade name	Number of medicine items	Contribution (R)	Average cost (R)	Standard Deviation (R)	Total cost (R)
2006	Generic (Y)	Methylphenidate	Adaphen 10mg Tab®	1,078	Total cost	123.49	76.82	133,117.16
					Final scheme amount	111.24	73.30	119,920.98
					Final levy	12.24	41.46	13,196.18
			Adaphen XL 20mg Tab®	125	Total cost	235.10	88.99	29,386.96
					Final scheme amount	220.46	90.62	27,557.11
					Final levy	14.64	46.93	1,829.85
			Methylphenidate HCL-Douglas®	1,664	Total cost	124.31	70.20	206,848.78
					Final scheme amount	112.39	69.26	187,021.27
					Final levy	11.92	35.44	19,827.51

Table A.22 : Cost analysis of methylphenidate or atomoxetine containing medicine items according to generic indicator and active ingredient during 2007

Study period	Generic Indicator	Active ingredient	Trade name	Number of medicine items	Contribution (R)	Average cost (R)	Standard Deviation (R)	Total cost (R)
2007	No Generic (N)	Atomoxetine	Strattera 10mg Cap®	253	Total cost	448.36	285.51	113,434.08
					Total scheme contribution	330.28	247.50	83,559.92
					Total patient contribution	118.08	231.93	29,874.16
			Strattera 18mg Cap®	436	Total cost	485.37	273.43	211,620.15
					Total scheme contribution	385.83	276.27	168,220.36
					Total patient contribution	99.54	201.91	43,399.79
			Strattera 25mg Cap®	878	Total cost	524.02	221.22	460,085.69
					Total scheme contribution	411.47	249.13	361,269.84
					Total patient contribution	112.55	185.32	98,815.85
			Strattera 40mg Cap®	1,804	Total cost	586.78	230.89	1,058,552.34
					Total scheme contribution	458.32	263.24	826,809.80
					Total patient contribution	128.46	209.70	231,742.54
		Strattera 60mg Cap®	929	Total cost	555.39	148.87	515,955.06	
				Total scheme contribution	441.60	222.46	410,250.18	
				Total patient contribution	113.78	190.18	105,704.88	
		Methylphenidate	Adaphen 5mg Tab®	4	Total cost	54.85	28.81	219.40
					Total scheme contribution	54.85	28.81	219.40
					Total patient contribution	0.00	0.00	-
			Concerta 18mg Oros®	3,193	Total cost	349.66	141.03	1,116,455.73
					Total scheme contribution	284.14	156.46	907,273.60
					Total patient contribution	65.51	117.38	209,182.13
			Concerta 36mg Oros®	5,682	Total cost	402.07	135.19	2,284,550.61
					Total scheme contribution	331.05	161.53	1,881,039.60
					Total patient contribution	71.02	126.77	403,511.01

Table A.22 : Cost analysis of methylphenidate or atomoxetine containing medicine items according to generic indicator and active ingredient during 2007 (continue)

Study period	Generic Indicator	Active Ingredient	Trade name	Number of medicine items	Contribution (R)	Average cost (R)	Standard Deviation (R)	Total cost (R)
2007	No Generic (N)	Methylphenidate	Concerta 54mg Oros®	1,923	Total cost	452.91	134.88	870,942.56
					Total scheme contribution	368.00	182.34	707,672.45
					Total patient contribution	84.90	144.93	163,270.11
			Ritalin LA 20mg Cap®	7,374	Total cost	283.05	109.65	2,087,175.47
					Total scheme contribution	239.06	120.30	1,762,844.35
					Total patient contribution	43.98	86.54	324,331.12
			Ritalin LA 30mg Cap®	2,663	Total cost	403.86	152.66	1,075,488.27
					Total scheme contribution	339.24	169.88	903,396.93
					Total patient contribution	64.62	129.17	172,091.34
			Ritalin LA 40mg Cap®	732	Total cost	536.49	172.22	392,709.89
					Total scheme contribution	432.70	222.84	316,734.09
					Total patient contribution	103.79	183.82	75,975.80

Table A.22 : Cost analysis of methylphenidate or atomoxetine containing medicine items according to generic indicator and active ingredient during 2007 (continue)

Study period	Generic Indicator	Active Ingredient	Trade name	Number of medicine items	Contribution (R)	Average cost (R)	Standard Deviation (R)	Total cost (R)
2007	Original (O)	Methylphenidate	Ritalin 10mg Tab®	6,261	Total cost	179.36	126.29	1,122,970.43
					Total scheme contribution	107.14	99.52	670,793.04
					Total patient contribution	72.22	80.86	452,177.39
			Ritalin SR 20mg Tab®	377	Total cost	264.63	141.90	99,765.04
					Total scheme contribution	221.83	131.09	83,628.35
					Total patient contribution	42.80	59.19	16,136.69
	Generic (Y)	Methylphenidate	Adaphen 10mg Tab®	1,007	Total cost	135.48	104.97	136,428.31
					Total scheme contribution	111.05	91.52	111,822.64
					Total patient contribution	24.43	62.44	24,605.67
			Adaphen XL 20mg Tab®	71	Total cost	215.62	95.33	15,308.89
					Total scheme contribution	199.81	91.85	14,186.84
					Total patient contribution	15.80	18.87	1,122.05
Methylphenidate HCL-Douglas®	1,263	Total cost	123.26	78.43	155,678.78			
		Total scheme contribution	105.90	76.47	133,751.78			
		Total patient contribution	17.36	46.44	21,927.06			

Table A.23 : Number of methylphenidate or atomoxetine containing items according to gender for study period 2005 to 2007

Study period	Member gender	Frequency (N)	Percent (%)
2005	Male (M)	21,798	74.08
	Female (F)	7,567	25.72
	Unspecified (U)	59	0.20
	Total	29,424	100.00
2006	Male (M)	24,990	74.43
	Female (F)	8,525	25.39
	Unspecified (U)	61	0.18
	Total	33,576	100.00
2007	Male (M)	25,833	74.13
	Female (F)	9,001	25.83
	Unspecified (U)	16	0.05
	Total	34,850	100.00

Table A.24 : Number of methylphenidate or atomoxetine containing products according to gender and active ingredient for 2005

Study period	Gender	Active ingredient	Trade name	Generic indicator	Number of medicine items	Percent (%)
2005	Female (F)	Atomoxetine	Strattera 40mg Cap®	No generic (N)	103	32.39
			Strattera 25mg Cap®	No generic (N)	65	20.44
			Strattera 60mg Cap®	No generic (N)	56	17.61
			Strattera 18mg Cap®	No generic (N)	53	16.67
			Strattera 10mg Cap®	No generic (N)	41	12.89
		Total atomoxetine		318	4.20	
		Methylphenidate	Ritalin 10mg Tab®	Original (O)	2,289	31.58
			Ritalin LA 20mg Cap®	No generic (N)	2,173	29.98
			Concerta 36mg Oros®	No generic (N)	536	7.39
			Ritalin LA 30 Cap®	No generic (N)	486	6.70
			Methylphenidate HCl-Douglas®	Generic (Y)	391	5.39
			Ritalin SR 20mg Tab®	No generic (N)	288	5.34
				Original (O)	99	
			Concerta 18mg Oros®	No generic (N)	369	5.09
			Adaphen 10mg Tab®	Generic (Y)	367	5.06
	Ritalin LA 40mg Cap®		No generic (N)	185	2.55	
	Concerta 54mg Oros®	No generic (N)	54	0.74		
	Adaphen 5mg Tab®	No generic (N)	9	0.12		
	Adaphen XL 20mg Tab®	Generic (Y)	3	0.04		
	Total methylphenidate		7,249	95.80		
	Male (M)	Atomoxetine	Strattera 25mg Cap®	No generic (N)	299	28.29
			Strattera 40mg Cap®	No generic (N)	296	28.00
			Strattera 18mg Cap®	No generic (N)	194	18.35
Strattera 60mg Cap®			No generic (N)	140	13.25	
Strattera 10mg Cap®			No generic (N)	128	12.11	
Total atomoxetine			1,057	4.85		

Table A.24 : Number of methylphenidate or atomoxetine containing products according to gender and active ingredient for 2005 (continued)

Study period	Gender	Active ingredient	Trade name	Generic indicator	Number of medicine items	Percent (%)
2005	Male (M)	Methylphenidate	Ritalin LA 20mg Cap®	No generic (N)	6,515	31.41
			Ritalin 10mg Tab®	Original (O)	5,874	28.32
			Ritalin LA 30 Cap®	No generic (N)	2,169	10.46
			Concerta 36mg Oros®	No generic (N)	1,429	6.89
			Ritalin SR 20mg Tab®	No generic (N)	935	6.30
				Original (O)	371	
			Methylphenidate HCl-Douglas®	Generic (Y)	1,011	4.87
			Concerta 18mg Oros®	No generic (N)	864	4.17
			Adaphen 10mg Tab®	Generic (Y)	764	3.68
			Ritalin LA 40mg Cap®	No generic (N)	546	2.63
			Concerta 54mg Oros®	No generic (N)	243	1.17
			Adaphen 5mg Tab®	No generic (N)	11	0.05
			Adaphen XL 20mg Tab®	Generic (Y)	9	0.04
	Total methylphenidate				20,741	95.15
	Unspecified (U)	Atomoxetine	Strattera 18mg Cap®	No generic (N)	2	50.00
			Strattera 40mg Cap®	No generic (N)	2	50.00
		Total atomoxetine			4	6.78
		Methylphenidate	Ritalin LA 20mg Cap®	No generic (N)	19	34.55
			Ritalin LA 30 Cap®	No generic (N)	12	21.82
			Ritalin 10mg Tab®	Original (O)	10	18.18
Concerta 36mg Oros®			No generic (N)	4	7.27	
Methylphenidate HCl-Douglas®			Generic (Y)	4	7.27	
Ritalin LA 40mg Cap®			No generic (N)	3	5.45	
Adaphen 10mg Tab®			Generic (Y)	2	3.64	
Ritalin SR 20mg Tab®	No generic (N)	1	1.82			
Total methylphenidate				55	93.22	

Appendix A

Table A.25 : Number of methylphenidate or atomoxetine containing products according to gender and active ingredient for 2006

Study period	Gender	Active ingredient	Trade name	Generic indicator	Number of medicine items	Percent (%)
2006	Female (F)	Atomoxetine	Strattera 40mg Cap®	No generic (N)	453	40.23
			Strattera 25mg Cap®	No generic (N)	232	20.60
			Strattera 60mg Cap®	No generic (N)	109	18.56
			Strattera 18mg Cap®	No generic (N)	132	11.72
			Strattera 10mg Cap®	No generic (N)	100	8.88
		Total atomoxetine			1,126	13.21
		Methylphenidate	Ritalin 10mg Tab®	Original (O)	1,939	26.21
			Ritalin LA 20mg Cap®	No generic (N)	1,833	24.77
			Concerta 36mg Oros®	No generic (N)	1,037	14.02
			Concerta 18mg Oros®	No generic (N)	653	8.83
			Ritalin LA 30 Cap®	No generic (N)	533	7.20
			Methylphenidate HCl-Douglas®	Generic (Y)	425	5.74
			Adaphen 10mg Tab®	Generic (Y)	340	4.60
			Concerta 54mg Oros®	No generic (N)	238	3.22
			Ritalin SR 20mg Tab®	Original (O)	230	3.11
	Ritalin LA 40mg Cap®		No generic (N)	129	1.74	
	Adaphen XL 20mg Tab®	Generic (Y)	40	0.54		
	Adaphen 5mg Tab®	No generic (N)	2	0.03		
	Total methylphenidate			7,399	86.79	
	Male (M)	Atomoxetine	Strattera 40mg Cap®	No generic (N)	1,276	40.09
Strattera 25mg Cap®			No generic (N)	782	24.57	
Strattera 60mg Cap®			No generic (N)	548	17.22	
Strattera 18mg Cap®			No generic (N)	371	11.66	
Strattera 10mg Cap®			No generic (N)	206	6.47	
Total atomoxetine				3,183	12.74	

Table A.25 : Number of methylphenidate or atomoxetine containing products according to gender and active ingredient for 2006 (continued)

Study period	Gender	Active ingredient	Trade name	Generic indicator	Number of medicine items	Percent (%)	
2006	Male (M)	Methylphenidate	Ritalin LA 20mg Cap®	No generic (N)	5,753	26.38	
			Ritalin 10mg Tab®	Original (O)	4,885	22.40	
			Concerta 36mg Oros®	No generic (N)	3,052	14.00	
			Ritalin LA 30 Cap®	No generic (N)	1,988	9.12	
			Concerta 18mg Oros®	No generic (N)	1,746	8.01	
			Methylphenidate HCl-Douglas®	Generic (Y)	1,233	5.65	
			Concerta 54mg Oros®	No generic (N)	873	4.00	
			Ritalin SR 20mg Tab®	Original (O)	835	3.83	
			Adaphen 10mg Tab®	Generic (Y)	737	3.38	
			Ritalin LA 40mg Cap®	No generic (N)	617	2.83	
			Adaphen XL 20mg Tab®	Generic (Y)	85	0.39	
			Adaphen 5mg Tab®	No generic (N)	3	0.01	
	Total methylphenidate				21,807	87.26	
	Unspecified (U)	Atomoxetine	Strattera 40mg Cap®	No generic (N)	14	51.85	
			Strattera 60mg Cap®	No generic (N)	12	44.44	
			Strattera 25mg Cap®	No generic (N)	1	3.70	
		Total atomoxetine				27	44.26
		Methylphenidate	Concerta 36mg Oros®	No generic (N)	15	44.12	
			Methylphenidate HCl-Douglas®	Generic (Y)	6	17.65	
			Ritalin LA 20mg Cap®	No generic (N)	6	17.65	
Ritalin 10mg Tab®			Original (O)	4	11.76		
Ritalin LA 30 Cap®			No generic (N)	2	5.88		
Adaphen 10mg Tab®		Generic (Y)	1	2.94			
Total methylphenidate				34	55.74		

Table A.26 : Number of methylphenidate or atomoxetine containing products according to gender and active ingredient for 2007

Study period	Gender	Active ingredient	Trade name	Generic indicator	Number of medicine items	Percent (%)
2007	Female (F)	Atomoxetine	Strattera 40mg Cap®	No generic (N)	471	39.71
			Strattera 25mg Cap®	No generic (N)	271	22.85
			Strattera 60mg Cap®	No generic (N)	258	21.75
			Strattera 18mg Cap®	No generic (N)	113	9.53
			Strattera 10mg Cap®	No generic (N)	73	6.16
		Total atomoxetine			1,186	13.18
		Methylphenidate	Ritalin LA 20mg Cap®	No generic (N)	1,827	23.38
			Ritalin 10mg Tab®	Original (O)	1,788	22.88
			Concerta 36mg Oros®	No generic (N)	1,465	18.75
			Concerta 18mg Oros®	No generic (N)	798	10.21
			Ritalin LA 30 Cap®	No generic (N)	522	6.68
			Concerta 54mg Oros®	No generic (N)	470	6.01
			Methylphenidate HCl-Douglas®	Generic (Y)	353	4.52
			Adaphen 10mg Tab®	Generic (Y)	326	4.17
			Ritalin LA 40mg Cap®	No generic (N)	150	1.92
	Ritalin SR 20mg Tab®		Original (O)	101	1.29	
	Adaphen XL 20mg Tab®	Generic (Y)	14	0.18		
	Adaphen 5mg Tab®	No generic (N)	1	0.01		
	Total methylphenidate			7,815	86.82	
	Male (M)	Atomoxetine	Strattera 40mg Cap®	No generic (N)	1,326	42.71
Strattera 60mg Cap®			No generic (N)	669	21.55	
Strattera 25mg Cap®			No generic (N)	607	19.55	
Strattera 18mg Cap®			No generic (N)	323	10.40	
Strattera 10mg Cap®			No generic (N)	180	5.80	
Total atomoxetine				3,105	12.02	

Table A.26 : Number of methylphenidate or atomoxetine containing products according to gender and active ingredient for 2007 (continued)

Study period	Gender	Active ingredient	Trade name	Generic indicator	Number of medicine items	Percent (%)
2007	Male (M)	Methylphenidate	Ritalin 10mg Tab®	Original (O)	4,471	19.67
			Concerta 36mg Oros®	No generic (N)	4,217	18.55
			Concerta 18mg Oros®	No generic (N)	2,394	10.53
			Ritalin LA 30 Cap®	No generic (N)	2,141	9.42
			Concerta 54mg Oros®	No generic (N)	1,449	6.38
			Methylphenidate HCl-Douglas®	Generic (Y)	910	4.00
			Adaphen 10mg Tab®	Generic (Y)	681	3.00
			Ritalin LA 40mg Cap®	No generic (N)	582	2.56
			Ritalin SR 20mg Tab®	Original (O)	276	1.21
			Adaphen XL 20mg Tab®	Generic (Y)	57	0.25
			Adaphen 5mg Tab®	No generic (N)	3	0.01
	Total methylphenidate				22,728	87.98
	Unspecified (U)	Atomoxetine	Strattera 40mg Cap®	No generic (N)	7	77.78
			Strattera 60mg Cap®	No generic (N)	2	22.22
		Total atomoxetine			9	56.25
		Methylphenidate	Concerta 54mg Oros®	No generic (N)	4	57.14
			Ritalin 10mg Tab®	Original (O)	2	28.57
			Concerta 18mg Oros®	No generic (N)	1	14.29
	Total methylphenidate			7	43.75	

Table A.27 : Number of methylphenidate or atomoxetine containing items according to age groups for study period 2005 to 2007

Study period	Age group	Number of Items	Percent (%)
2005	≤ 5 years	146	0.50
	5< and ≤12 years	16,936	57.56
	12< and ≤18 years	8,227	27.96
	> 18 years	4,115	13.99
	Total for 2005	29,424	100.01
2006	≤ 5 years	160	0.48
	5< and ≤12 years	18,936	56.40
	12< and ≤18 years	9,613	28.63
	> 18 years	4,867	14.50
	Total for 2006	33,576	100.01
2007	≤ 5 years	212	0.61
	5< and ≤12 years	18,988	54.48
	12< and ≤18 years	10,216	29.31
	> 18 years	5,434	15.59
	Total for 2007	34,850	99.99

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Table A.28 : Number of methylphenidate or atomoxetine containing products according to prescriber during 2005

Study period	Prescriber	Active Ingredient	Trade name	Generic Indicator	Number of medicine items	Percent (%)
2005	General medical practioner (GP)	Atomoxetine	Strattera 40mg Cap®	No generic (N)	129	29.52
			Strattera 18mg Cap®	No generic (N)	96	21.97
			Strattera 25mg Cap®	No generic (N)	95	21.74
			Strattera 60mg Cap®	No generic (N)	66	15.10
			Strattera 10mg Cap®	No generic (N)	51	11.67
		Total atomoxetine			437	3.05
		Methylphenidate	Ritalin LA 20mg Cap®	No generic (N)	4,466	32.2
			Ritalin 10mg Tab®	Original (O)	4,127	29.76
			Ritalin LA 30mg Cap®	No generic (N)	1,210	8.72
			Ritalin SR 20mg Tab®	No generic (N)	804	8.02
				Original (O)	308	
			Adaphen 10mg Tab®	Generic (Y)	804	5.80
			Methylphenidate HCl-Douglas®	Generic (Y)	726	5.23
			Concerta 36mg Oros®	No generic (N)	583	4.20
			Concerta 18mg Oros®	No generic (N)	413	2.98
	Ritalin LA 40mg Cap®		No generic (N)	324	2.34	
	Concerta 54mg Oros®	No generic (N)	75	0.54		
	Adaphen 5mg Tab®	No generic (N)	19	0.14		
	Adaphen XL 20mg Tab®	Generic (Y)	10	0.07		
	Total methylphenidate			13,869	96.95	
	Paediatrician	Atomoxetine	Strattera 40mg Cap®	No generic (N)	135	29.87
			Strattera 25mg Cap®	No generic (N)	129	28.54
			Strattera 18mg Cap®	No generic (N)	89	19.69
Strattera 10mg Cap®			No generic (N)	59	13.05	
Strattera 60mg Cap®			No generic (N)	40	8.85	
Total atomoxetine				452	4.65	

Table A.28 : Number of methylphenidate or atomoxetine containing products according to prescriber during 2005
(continued)

Study period	Prescriber	Active ingredient	Trade name	Generic indicator	Number of medicine items	Percent (%)	
2005	Paediatrician	Methylphenidate	Ritalin LA 20mg Cap®	No generic (N)	2,908	31.39	
			Ritalin 10mg Tab®	Original (O)	2,861	30.88	
			Ritalin LA 30mg Cap®	No generic (N)	1,049	11.32	
			Concerta 36mg Oros®	No generic (N)	751	8.11	
			Methylphenidate HCl-Douglas®	Generic (Y)	479	5.17	
			Concerta 18mg Oros®	No generic (N)	454	4.90	
			Ritalin SR 20mg Tab®	No generic (N)	200	2.96	
				Original (O)	74		
			Adaphen 10mg Tab®	Generic (Y)	197	2.13	
			Ritalin LA 40mg Cap®	No generic (N)	194	2.09	
			Concerta 54mg Oros®	No generic (N)	95	1.03	
			Adaphen XL 20mg Tab®	Generic (Y)	2	0.02	
			Adaphen 5mg Tab®	No generic (N)	1	0.01	
				Total methylphenidate			9,265
	Psychiatrist	Atomoxetine		Strattera 40mg Cap®	No generic (N)	89	29.47
				Strattera 25mg Cap®	No generic (N)	79	26.16
				Strattera 60mg Cap®	No generic (N)	67	22.19
				Strattera 18mg Cap®	No generic (N)	36	11.92
				Strattera 10mg Cap®	No generic (N)	31	10.26
			Total atomoxetine			302	10.71
		Methylphenidate		Ritalin LA 20mg Cap®	No generic (N)	668	26.54
				Ritalin 10mg Tab®	Original (O)	548	21.77
Concerta 36mg Oros®				No generic (N)	385	15.30	
Ritalin LA 30mg Cap®				No generic (N)	222	8.82	
Concerta 18mg Oros®	No generic (N)			201	7.99		
		Ritalin LA 40mg Cap®	No generic (N)	147	5.84		

Table A.28 : Number of methylphenidate or atomoxetine containing products according to prescriber during 2005
(continued)

Study period	Prescriber	Active ingredient	Trade name	Generic indicator	Number of medicine items	Percent (%)
2005	Psychiatrist	Methylphenidate	Ritalin SR 20mg Tab®	No generic (N)	100	5.44
				Original (O)	37	
			Methylphenidate HCl-Douglas®	Generic (Y)	88	3.50
			Concerta 54mg Oros®	No generic (N)	70	2.78
			Adaphen 10mg Tab®	Generic (Y)	51	2.03
		Total methylphenidate			2,517	89.29
	Neurologist	Atomoxetine	Strattera 25mg Cap®	No generic (N)	37	32.17
			Strattera 40mg Cap®	No generic (N)	21	18.26
			Strattera 60mg Cap®	No generic (N)	21	18.26
			Strattera 10mg Cap®	No generic (N)	20	17.39
			Strattera 18mg Cap®	No generic (N)	16	13.91
		Total atomoxetine			115	9.03
		Methylphenidate	Ritalin LA 20mg Cap®	No generic (N)	286	24.70
			Ritalin 10mg Tab®	Original (O)	235	20.29
			Concerta 36mg Oros®	No generic (N)	190	16.41
			Concerta 18mg Oros®	No generic (N)	116	10.02
			Ritalin LA 30mg Cap®	No generic (N)	86	7.43
			Ritalin SR 20mg Tab®	No generic (N)	57	6.91
				Original (O)	23	
			Methylphenidate HCl-Douglas®	Generic (Y)	48	4.15
Concerta 54mg Oros®	No generic (N)		42	3.63		
Ritalin LA 40mg Cap®	No generic (N)		41	3.54		
Adaphen 10mg Tab®	Generic (Y)	34	2.94			
Total methylphenidate			1,158	90.97		

Table A.28 : Number of methylphenidate or atomoxetine containing products according to prescriber during 2005
(continued)

Study period	Prescriber	Active ingredient	Trade name	Generic indicator	Number of medicine items	Percent (%)	
2005	Other	Atomoxetine	Strattera 40mg Cap®	No generic (N)	27	36.99	
			Strattera 25mg Cap®	No generic (N)	24	32.88	
			Strattera 18mg Cap®	No generic (N)	12	16.44	
			Strattera 10mg Cap®	No generic (N)	8	10.96	
			Strattera 60mg Cap®	No generic (N)	2	2.74	
		Total atomoxetine				73	5.6
		Methylphenidate	Ritalin 10mg Tab®	Original (O)	401	32.52	
			Ritalin LA 20mg Cap®	No generic (N)	379	30.49	
			Ritalin LA 30mg Cap®	No generic (N)	100	8.13	
			Ritalin SR 20mg Tab®	No generic (N)	63	7.4	
				Original (O)	28		
			Methylphenidate HCl-Douglas®	Generic (Y)	65	5.28	
			Concerta 36mg Oros®	No generic (N)	60	4.88	
			Concerta 18mg Oros®	No generic (N)	49	3.98	
			Adaphen 10mg Tab®	Generic (Y)	47	3.82	
			Ritalin LA 40mg Cap®	No generic (N)	28	2.28	
		Concerta 54mg Oros®	No generic (N)	15	1.22		
		Total methylphenidate				1,235	94.40

Table A.29 : Number of methylphenidate or atomoxetine containing products according to prescriber during 2006

Study period	Prescriber	Active ingredient	Trade name	Generic indicator	Number of medicine items	Percent (%)
2006	General medical practitioner (GP)	Atomoxetine	Strattera 40mg Cap®	No generic (N)	559	35.49
			Strattera 25mg Cap®	No generic (N)	371	23.56
			Strattera 60mg Cap®	No generic (N)	276	17.52
			Strattera 18mg Cap®	No generic (N)	244	15.49
			Strattera 10mg Cap®	No generic (N)	125	7.94
		Total atomoxetine			1,575	10.02
		Methylphenidate	Ritalin LA 20mg Cap®	No generic (N)	3,931	27.79
			Ritalin 10mg Tab®	Original (O)	3,276	23.16
			Concerta 36mg Oros®	No generic (N)	1,548	10.94
			Ritalin LA 30mg Cap®	No generic (N)	1,153	8.15
			Concerta 18mg Oros®	No generic (N)	955	6.75
			Methylphenidate HCl-Douglas®	Generic (Y)	934	6.60
			Adaphen 10mg Tab®	Generic (Y)	795	5.62
			Ritalin SR 20mg Tab®	Original (O)	750	5.30
	Concerta 54mg Oros®		No generic (N)	363	2.57	
	Ritalin LA 40mg Cap®	No generic (N)	351	2.48		
	Adaphen XL 20mg Tab®	Generic (Y)	86	0.61		
	Adaphen 5mg Tab®	No generic (N)	5	0.04		
	Total methylphenidate			14,147	89.98	
	Paediatrician	Atomoxetine	Strattera 40mg Cap®	No generic (N)	475	38.12
Strattera 25mg Cap®			No generic (N)	346	27.77	
Strattera 60mg Cap®			No generic (N)	191	15.33	
Strattera 18mg Cap®			No generic (N)	140	11.24	
Strattera 10mg Cap®			No generic (N)	94	7.54	
Total atomoxetine				1,246	11.19	

Table A.29 : Number of methylphenidate or atomoxetine containing products according to prescriber during 2006
(continued)

Study period	Prescriber	Active ingredient	Trade name	Generic indicator	Number of medicine items	Percent (%)	
2006	Paediatrician	Methylphenidate	Ritalin 10mg Tab®	Original (O)	2,517	25.45	
			Ritalin LA 20mg Cap®	No generic (N)	2,514	25.42	
			Concerta 36mg Oros®	No generic (N)	1,494	15.10	
			Ritalin LA 30mg Cap®	No generic (N)	979	9.90	
			Concerta 18mg Oros®	No generic (N)	928	9.38	
			Methylphenidate HCl-Douglas®	Generic (Y)	534	5.40	
			Concerta 54mg Oros®	No generic (N)	418	4.23	
			Ritalin LA 40mg Cap®	No generic (N)	189	1.91	
			Adaphen 10mg Tab®	Generic (Y)	151	1.53	
			Ritalin SR 20mg Tab®	Original (O)	143	1.45	
			Adaphen XL 20mg Tab®	Generic (Y)	24	0.24	
			Total methylphenidate				9,891
	Psychiatrist	Atomoxetine		Strattera 40mg Cap®	No generic (N)	462	49.46
				Strattera 60mg Cap®	No generic (N)	209	22.38
				Strattera 25mg Cap®	No generic (N)	161	17.24
				Strattera 18mg Cap®	No generic (N)	63	6.75
				Strattera 10mg Cap®	No generic (N)	39	4.18
		Total atomoxetine				934	24.19
		Methylphenidate		Ritalin LA 20mg Cap®	No generic (N)	653	22.31
				Concerta 36mg Oros®	No generic (N)	640	21.87
Ritalin 10mg Tab®				Original (O)	563	19.23	
Concerta 18mg Oros®				No generic (N)	268	9.16	
Concerta 54mg Oros®				No generic (N)	224	7.65	
Ritalin LA 30mg Cap®				No generic (N)	214	7.31	
Ritalin LA 40mg Cap®	No generic (N)			136	4.65		
Methylphenidate HCl-Douglas®	Generic (Y)	105	3.59				

Table A.29 : Number of methylphenidate or atomoxetine containing products according to prescriber during 2006
(continued)

Study period	Prescriber	Active ingredient	Trade name	Generic indicator	Number of medicine items	Percent (%)
2006	Psychiatrist	Methylphenidate	Ritalin SR 20mg Tab®	Original (O)	63	2.15
			Adaphen 10mg Tab®	Generic (Y)	50	1.71
			Adaphen XL 20mg Tab®	Generic (Y)	11	0.38
		Total methylphenidate			2,927	75.81
	Neurologist	Atomoxetine	Strattera 40mg Cap®	No generic (N)	166	44.5
			Strattera 25mg Cap®	No generic (N)	81	21.72
			Strattera 60mg Cap®	No generic (N)	62	16.62
			Strattera 18mg Cap®	No generic (N)	34	9.12
			Strattera 10mg Cap®	No generic (N)	30	8.04
		Total atomoxetine			373	24.03
		Methylphenidate	Concerta 36mg Oros®	No generic (N)	269	22.82
			Ritalin LA 20mg Cap®	No generic (N)	242	20.53
			Ritalin 10mg Tab®	Original (O)	202	17.13
			Concerta 18mg Oros®	No generic (N)	148	12.55
	Ritalin LA 30mg Cap®		No generic (N)	78	6.62	
	Ritalin SR 20mg Tab®		Original (O)	61	5.17	
	Concerta 54mg Oros®		No generic (N)	52	4.41	
	Adaphen 10mg Tab®		Generic (Y)	45	3.82	
	Ritalin LA 40mg Cap®		No generic (N)	45	3.82	
Total methylphenidate			1,179	75.97		
		Methylphenidate HCl-Douglas®	Generic (Y)	37	3.14	

Table A.29 : Number of methylphenidate or atomoxetine containing products according to prescriber during 2006
(continued)

Study period	Prescriber	Active Ingredient	Trade name	Generic Indicator	Number of medicine items	Percent (%)
2006	Other	Atomoxetine	Strattera 40mg Cap®	No generic (N)	81	38.94
			Strattera 25mg Cap®	No generic (N)	56	26.92
			Strattera 60mg Cap®	No generic (N)	31	14.90
			Strattera 18mg Cap®	No generic (N)	22	10.58
			Strattera 10mg Cap®	No generic (N)	18	8.65
		Total atomoxetine			208	15.99
		Methylphenidate	Ritalin 10mg Tab®	Original (O)	270	24.7
			Ritalin LA 20mg Cap®	No generic (N)	249	22.78
			Concerta 36mg Oros®	No generic (N)	153	14.00
			Concerta 18mg Oros®	No generic (N)	100	9.15
			Ritalin LA 30mg Cap®	No generic (N)	99	9.06
			Concerta 54mg Oros®	No generic (N)	54	4.94
			Methylphenidate HCl-Douglas®	Generic (Y)	54	4.94
			Ritalin SR 20mg Tab®	Original (O)	48	4.39
			Adaphen 10mg Tab®	Generic (Y)	37	3.39
			Ritalin LA 40mg Cap®	No generic (N)	25	2.29
			Adaphen XL 20mg Tab®	Generic (Y)	4	0.37
Total methylphenidate			1,093	84.01		

Table A.30 : Number of methylphenidate or atomoxetine containing products according to prescriber during 2007

Study period	Prescriber	Active ingredient	Trade name	Generic indicator	Number of medicine items	Percent (%)
2007	General medical practitioner (GP)	Atomoxetine	Strattera 40mg Cap®	No generic (N)	560	40.03
			Strattera 60mg Cap®	No generic (N)	324	23.16
			Strattera 25mg Cap®	No generic (N)	264	18.87
			Strattera 18mg Cap®	No generic (N)	166	11.87
			Strattera 10mg Cap®	No generic (N)	85	6.08
		Total atomoxetine		1,399	8.63	
		Methylphenidate	Ritalin LA 20mg Cap®	No generic (N)	4,010	27.08
			Ritalin 10mg Tab®	Original (O)	2,887	19.49
			Concerta 36mg Oros®	No generic (N)	2,442	16.49
			Concerta 18mg Oros®	No generic (N)	1,344	9.08
			Ritalin LA 30mg Cap®	No generic (N)	1,333	9.00
			Concerta 54mg Oros®	No generic (N)	764	5.16
			Adaphen 10mg Tab®	Generic (Y)	697	4.71
			Methylphenidate HCl-Douglas®	Generic (Y)	647	4.37
	Ritalin LA 40mg Cap®		No generic (N)	355	2.40	
	Ritalin SR 20mg Tab®		Original (O)	279	1.88	
	Adaphen XL 20mg Tab®	Generic (Y)	49	0.33		
	Adaphen 5mg Tab®	No generic (N)	2	0.01		
	Total methylphenidate		14,809	91.37		
	Paediatrician	Atomoxetine	Strattera 40mg Cap®	No generic (N)	607	45.23
Strattera 25mg Cap®			No generic (N)	312	23.25	
Strattera 60mg Cap®			No generic (N)	189	14.08	
Strattera 18mg Cap®			No generic (N)	144	10.73	
Strattera 10mg Cap®			No generic (N)	90	6.71	
Total atomoxetine			1,342	11.77		

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Table A.30 : Number of methylphenidate or atomoxetine containing products according to prescriber during 2007
(continued)

Study period	Prescriber	Active ingredient	Trade name	Generic indicator	Number of medicine items	Percent (%)	
2007	Paediatrician	Methylphenidate	Ritalin LA 20mg Cap®	No generic (N)	2,364	23.50	
			Ritalin 10mg Tab®	Original (O)	2,338	23.24	
			Concerta 36mg Oros®	No generic (N)	1,913	19.02	
			Concerta 18mg Oros®	No generic (N)	1,151	11.44	
			Ritalin LA 30mg Cap®	No generic (N)	877	8.72	
			Concerta 54mg Oros®	No generic (N)	619	6.15	
			Methylphenidate HCl-Douglas®	Generic (Y)	421	4.19	
			Ritalin LA 40mg Cap®	No generic (N)	180	1.79	
			Adaphen 10mg Tab®	Generic (Y)	150	1.49	
			Ritalin SR 20mg Tab®	Original (O)	35	0.35	
			Adaphen XL 20mg Tab®	Generic (Y)	10	0.10	
			Adaphen 5mg Tab®	No generic (N)	1	0.01	
			Total methylphenidate				10,059
	Psychiatrist	Atomoxetine	Strattera 40mg Cap®	No generic (N)	442	44.87	
			Strattera 60mg Cap®	No generic (N)	278	28.22	
			Strattera 25mg Cap®	No generic (N)	152	15.43	
			Strattera 18mg Cap®	No generic (N)	68	6.90	
			Strattera 10mg Cap®	No generic (N)	45	4.57	
		Total atomoxetine				985	22.85
		Methylphenidate	Concerta 36mg Oros®	No generic (N)	843	25.35	
Ritalin 10mg Tab®			Original (O)	594	17.86		
Ritalin LA 20mg Cap®			No generic (N)	553	16.63		
Concerta 54mg Oros®			No generic (N)	399	12.00		
Concerta 18mg Oros®			No generic (N)	332	9.98		
Ritalin LA 30mg Cap®			No generic (N)	288	8.66		
Ritalin LA 40mg Cap®	No generic (N)		107	3.22			

Table A.30 : Number of methylphenidate or atomoxetine containing products according to prescriber during 2007
(continued)

Study period	Prescriber	Active ingredient	Trade name	Generic indicator	Number of medicine items	Percent (%)
2007	Psychiatrist	Methylphenidate	Methylphenidate HCl-Douglas®	Generic (Y)	104	3.13
			Adaphen 10mg Tab®	Generic (Y)	75	2.25
			Ritalin SR 20mg Tab®	Original (O)	22	0.66
			Adaphen XL 20mg Tab®	Generic (Y)	8	0.24
			Adaphen 5mg Tab®	No generic (N)	1	0.03
		Total methylphenidate			3,326	77.15
	Neurologist	Atomoxetine	Strattera 40mg Cap®	No generic (N)	126	34.15
			Strattera 25mg Cap®	No generic (N)	103	27.91
			Strattera 60mg Cap®	No generic (N)	81	21.95
			Strattera 18mg Cap®	No generic (N)	39	10.57
			Strattera 10mg Cap®	No generic (N)	20	5.42
		Total atomoxetine			369	21.87
		Methylphenidate	Concerta 36mg Oros®	No generic (N)	325	24.66
			Concerta 18mg Oros®	No generic (N)	241	18.29
			Ritalin LA 20mg Cap®	No generic (N)	224	17.00
			Ritalin 10mg Tab®	Original (O)	200	15.17
			Ritalin LA 30mg Cap®	No generic (N)	85	6.45
			Concerta 54mg Oros®	No generic (N)	74	5.61
			Ritalin LA 40mg Cap®	No generic (N)	56	4.25
			Methylphenidate HCl-Douglas®	Generic (Y)	52	3.95
Adaphen 10mg Tab®	Generic (Y)		38	2.88		
Total methylphenidate			1,318	78.13		

Table A.30 : Number of methylphenidate or atomoxetine containing products according to prescriber during 2007
(continued)

Study period	Prescriber	Active ingredient	Trade name	Generic Indicator	Number of medicine items	Percent (%)
2007	Other	Atomoxetine	Strattera 40mg Cap®	No generic (N)	69	33.66
			Strattera 60mg Cap®	No generic (N)	57	27.80
			Strattera 25mg Cap®	No generic (N)	47	22.93
			Strattera 18mg Cap®	No generic (N)	19	9.27
			Strattera 10mg Cap®	No generic (N)	13	6.34
		Total atomoxetine		205	16.61	
		Methylphenidate	Ritalin 10mg Tab®	Original (O)	241	23.42
			Ritalin LA 20mg Cap®	No generic (N)	219	21.28
			Concerta 36mg Oros®	No generic (N)	159	15.45
			Concerta 18mg Oros®	No generic (N)	125	12.15
			Ritalin LA 30mg Cap®	No generic (N)	77	7.48
			Concerta 54mg Oros®	No generic (N)	67	6.51
			Adaphen 10mg Tab®	Generic (Y)	47	4.57
			Methylphenidate HCl-Douglas®	Generic (Y)	38	3.69
			Ritalin LA 40mg Cap®	No generic (N)	34	3.30
			Ritalin SR 20mg Tab®	Original (O)	19	1.85
			Adaphen XL 20mg Tab®	Generic (Y)	3	0.29
Total methylphenidate		1,029	83.39			

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Table A.31 : Prescribed daily dose according to trade name for, 2005

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2005	Adaphen 10mg Tab®	1< dose <5	3	0.27	27.25	44.83
		dose = 5	25	2.21		
		5< dose <10	2	0.18		
		dose = 10	436	38.48		
		10< dose <15	7	0.63		
		dose = 15	95	8.38		
		15< dose <20	5	0.45		
		dose = 20	328	28.95		
		20< dose <25	5	0.45		
		dose = 25	23	2.03		
		dose = 30	56	4.94		
		30< dose <40	5	0.44		
		dose = 40	48	4.24		
		40< dose <150	32	2.83		
		dose = 150	47	4.15		
		150< dose <600	15	1.32		
	dose = 600	1	0.09			
	Total		1,133	100.04		
	Adaphen 5mg Tab®	dose = 5	12	60	10.75	15.50
dose = 10		5	25			
dose = 15		2	10			
dose = 75		1	5			
Total		20	100			

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Table A.31 : Prescribed daily dose according to trade name for 2005 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2005	Adaphen XL 20mg Tab®	dose = 10	1	8.33	44.5	80.74
		dose = 20	8	66.67		
		20 < dose < 300	2	16.66		
		dose = 300	1	8.33		
	Total		12	99.99		
	Concerta 18mg Oros®	3 < dose < 18	6	0.48	22.56	36.33
		dose = 18	1,172	95.05		
		18 < dose < 36	9	0.72		
		dose = 36	15	1.22		
		36 < dose < 270	16	1.29		
		dose = 270	12	0.97		
		dose = 540	3	0.24		
	Total		1,233	99.97		
	Concerta 36mg Oros®	9.6 < dose < 36	6	0.3	46.72	73.53
		dose = 36	1,911	97.05		
		36 < dose < 72	5	0.25		
		dose = 72	3	0.15		
		72 < dose < 540	6	0.3		
		dose = 540	37	1.88		
		dose = 1080	1	0.05		
Total		1,969	99.98			
Concerta 54mg Oros®	dose = 18	1	0.34	66.61	97.46	
	dose = 54	291	97.98			
	dose = 810	5	1.68			
Total		297	100			

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Table A.31 : Prescribed daily dose according to trade name for 2005 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)	
2005	Methylphenidate HCl-Douglas®	dose = 5	34	2.42	22.97	35.19	
		5< dose <10	6	0.42			
		dose = 10	550	39.12			
		10< dose <15	14	0.99			
		dose = 15	127	9.03			
		15< dose <20	7	0.49			
		dose = 20	338	24.04			
		20< dose <30	37	2.63			
		dose = 30	137	9.74			
		30< dose <40	27	1.92			
		dose = 40	57	4.05			
		40< dose <60	20	1.41			
		dose = 60	19	1.35			
		dose = 75	1	0.07			
		dose = 150	12	0.85			
		dose = 225	12	0.85			
		dose =300	7	0.5			
	dose = 600	1	0.07				
		Total		1,406	99.95		
		Ritalin 10mg Tab®	0< dose < 5	15	0.16	21.45	44.36
	dose = 5		222	2.72			
	5< dose <10		51	0.56			
	dose = 10		4,307	52.7			
	10< dose <15		82	0.99			
	dose = 15		692	8.47			
	15< dose <20		42	0.48			

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Table A.31 : Prescribed daily dose according to trade name for 2005 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2005	Ritalin 10mg Tab®	dose = 20	1,497	18.32	21.45	44.36
		20< dose <25	26	0.31		
		dose = 25	104	1.27		
		25< dose <30	7	0.08		
		dose = 30	484	5.92		
		30< dose <40	55	0.68		
		dose = 40	162	1.98		
		40< dose <60	84	1		
		dose = 60	111	1.36		
		60< dose <150	28	0.34		
		dose = 150	126	1.54		
		150< dose <1200	77	0.93		
		dose = 1200	1	0.01		
	Total		8,173	99.82		
	Ritalin LA 20mg Cap®	1< dose <20	27	0.29	28.17	49.79
dose = 20		8,111	93.15			
20< dose <40		82	0.93			
dose = 40		239	2.74			
40< dose <300		45	0.5			
dose = 300		180	2.07			
dose = 600		23	0.26			
	8,707	99.94				

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Table A.31 : Prescribed daily dose according to trade name for 2005 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2005	Ritalin LA 30mg Cap®	4 < dose < 30	14	0.29	40.22	63.51
		dose = 30	2,489	93.33		
		30 < dose < 60	25	0.94		
		dose = 60	74	2.77		
		60 < dose < 450	11	0.41		
		dose = 450	52	1.95		
		dose = 900	2	0.07		
	Total		2,667	99.76		
	Ritalin LA 40mg Cap®	1 < dose < 40	10	1.37	47.58	62.64
		dose = 40	701	95.5		
		40 < dose < 600	14	1.92		
		dose = 600	9	1.23		
	Total		734	100.02		
	Ritalin SR 20mg Tab®	8 < dose < 20	17	1	32.43	69.71
		dose = 20	1,509	89.08		
		20 < dose < 40	15	0.89		
		dose = 40	74	4.37		
		40 < dose < 300	31	1.83		
		dose = 300	36	2.13		
		300 < dose < 1200	11	0.65		
		dose = 1200	1	0.06		
Total		1,694	100.01			

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Table A.31 : Prescribed daily dose according to trade name for 2005 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2005	Strattera 10mg Tab®	2< dose <10	8	4.73	12.86	15.21
		dose = 10	140	82.84		
		10< dose <20	5	2.95		
		dose = 20	10	5.92		
		20< dose < 140	4	2.36		
		dose = 140	2	1.18		
	Total		169	99.98		
	Strattera 18mg Cap®	4< dose <18	8	3.2	21.07	19.87
		dose = 18	223	89.56		
		18< dose <36	6	2.4		
		dose = 36	6	2.41		
		36< dose <252	5	2		
		dose = 252	1	0.4		
	Total		249	99.97		
	Strattera 25mg Cap®	12< dose <25	13	3.57	32.55	41.25
		dose = 25	311	85.44		
		25< dose <50	17	4.65		
		dose = 50	10	2.75		
		50< dose <375	11	3		
		dose = 375	2	0.55		
Total		364	99.96			
Strattera 40mg Cap®	20< dose <40	11	2.74	46.96	47.68	
	dose = 40	360	89.78			
	40< dose <80	7	1.75			
	dose = 80	16	3.99			
	80< dose <560	4	1			
	dose = 560	3	0.75			
Total		401	100.01			

Table A.31 : Prescribed daily dose according to trade name for 2005 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2005	Strattera 60mg Cap®	dose = 56	11	5.61	64.22	55.78
		dose = 60	179	91.33		
		60 < dose < 840	5	2.55		
		dose = 840	1	0.51		
	Total		196	100		

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Table A.32 : Prescribed daily dose according to trade name for 2006

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2006	Adaphen 10mg Tab®	dose = 2.67	1	0.09	23.15	27.20
		dose = 5	28	2.6		
		5 < dose < 10	5	0.46		
		dose = 10	452	41.93		
		10 < dose < 15	3	0.27		
		dose = 15	50	4.64		
		15 < dose < 20	2	0.18		
		dose = 20	309	28.66		
		20 < dose < 25	3	0.27		
		dose = 25	19	1.76		
		dose = 26.09	1	0.09		
		dose = 30	55	5.1		
		30 < dose < 40	5	0.46		
		dose = 40	29	2.69		
		40 < dose < 60	16	1.48		
		dose = 60	70	6.49		
		dose = 100	2	0.19		
	dose = 150	26	2.41			
	dose = 300	2	0.19			
	Total		1,078	100		
	Adaphen 5mg Tab®	dose = 2.5	1	20	4.50	1.12
		dose = 5	4	80		
Total		5	100			

Table A.32 : Prescribed daily dose according to trade name for 2006 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2006	Adaphen XL 20mg Tab®	dose = 20	106	84.8	25.76	26.37
		20 < dose < 300	18	14.4		
		dose = 300	1	0.80		
	Total		125	100.00		
	Concerta 18mg Oros®	5.4 < dose < 18	8	0.32	19.82	16.22
		dose = 18	2,298	95.79		
		18 < dose < 36	10	0.42		
		dose = 36	33	1.38		
		36 < dose < 54	2	0.08		
		dose = 54	38	1.58		
		dose = 90	1	0.04		
	dose = 270	9	0.38			
	Total		2,399	100.00		
	Concerta 36mg Oros®	6 < dose < 36	9	0.20	38.02	29.67
		dose = 36	4,044	98.55		
		36 < dose < 72	2	0.05		
		dose = 72	33	0.80		
72 < dose < 540		2	0.05			
dose = 540	14	0.35				
Total		4,104	100.00			
Concerta 54mg Oros®	27 < dose < 54	9	0.81	55.40	32.21	
	dose = 54	1,097	98.74			
	dose = 108	3	0.27			
	dose = 810	2	0.18			
Total		1,111	100			

Table A.32 : Prescribed daily dose according to trade name for 2006 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2006	Merthylphenidate HCl-Douglas®	2.67 < dose < 10	42	2.52	18.40	12.89
		dose = 10	718	43.15		
		10 < dose < 15	5	0.30		
		dose = 15	140	8.41		
		15 < dose < 20	1	0.06		
		dose = 20	409	24.58		
		20 < dose < 25	6	0.37		
		dose = 25	69	4.15		
		25 < dose < 30	5	0.30		
		dose = 30	130	7.81		
		30 < dose < 40	19	1.14		
		dose = 40	55	3.31		
		40 < dose < 60	15	0.90		
		dose = 60	45	2.70		
		dose = 75	1	0.06		
		dose = 150	4	0.24		
		Total		1,664	100.00	
	Ritalin 10mg Tab®	1.33 < dose < 5	10	0.15	17.79	31.23
		dose = 5	233	3.43		
		5 < dose < 10	39	0.57		
		dose = 10	3,680	53.90		

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Table A.32 : Prescribed daily dose according to trade name for 2006 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2006	Ritalin 10mg Tab®	10< dose <15	53	0.77	17.79	31.23
		dose = 15	544	7.98		
		15< dose <20	28	0.39		
		dose = 20	1,317	19.29		
		20< dose <25	17	0.25		
		dose = 25	108	1.58		
		25< dose <30	5	0.07		
		dose = 30	327	4.79		
		30< dose <40	32	0.46		
		dose = 40	99	1.45		
		40< dose <50	25	0.37		
		dose = 50	67	0.98		
		50< dose <60	18	0.24		
		dose = 60	166	2.43		
		60< dose <150	17	0.25		
		dose = 150	24	0.35		
		150< dose <450	8	0.12		
		dose = 450	8	0.12		
		dose = 750	1	0.02		
dose = 1200	2	0.04				
	Total		6,828	100.00		

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Table A.32 : Prescribed daily dose according to trade name for 2006 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2006	Ritalin LA 20mg Cap®	0.67 < dose < 20	15	0.22	23.67	25.44
		dose = 20	7,100	93.52		
		20 < dose < 40	43	0.55		
		dose = 40	174	2.29		
		dose = 42.86	1	0.01		
		dose = 60	195	2.57		
		60 < dose < 300	10	0.13		
		dose = 300	53	0.70		
	dose = 450	1	0.01			
	Total		7,592	100.00		
	Ritalin LA 30mg Cap®	4 < dose < 30	6	0.24	35.0998245	35.2350141
		dose = 30	2,338	92.67	35.0998245	35.2350141
		30 < dose < 60	18	0.72		
		dose = 60	131	5.19	35.0998245	35.2350141
		60 < dose < 300	9	0.35		
		dose = 300	8	0.31		
		dose = 450	13	0.52		
	Total		2,523	100.00		
	Ritalin LA 40mg Cap®	5.33 < dose < 40	2	0.26	44.2469041	64.1616555
		dose = 40	738	98.93		
		40 < dose < 1200	4	0.53		
		dose = 1200	2	0.28		
	Total		746	100.00		

Table A.32 : Prescribed daily dose according to trade name for 2006 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2006	Rialin SR 20mg Tab®	6.67 < dose <20	10	0.94	24.7806841	28.8004502
		dose = 20	942	88.45		
		20 < dose <40	12	1.12		
		dose = 40	53	4.99		
		dose = 50	1	0.09		
		dose = 60	34	3.20		
		dose = 80	6	0.56		
		dose = 300	6	0.56		
	dose = 600	1	0.09			
	Total		1,065	100.00		
	Strattera 10mg Cap®	1.67 < dose <10	16	5.23	13.2483477	12.861731
		dose = 10	234	76.47		
		10 < dose <20	12	3.92		
		dose = 20	28	9.15		
		20 < dose <140	14	4.59		
		dose = 140	2	0.64		
	Total		306	100.00		
	Strattera 18mg Cap®	4.2 < dose <18	21	4.17	19.5987078	6.3589042
		dose = 18	439	87.28		
		18 < dose <36	4	0.78		
		dose = 36	28	5.57		
36 < dose <72		10	2.00	19.5987078	6.3589042	
dose = 72		1	0.20			
Total		503	100.00			

Table A.32 : Prescribed daily dose according to trade name for 2006 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2006	Strattera 25mg Cap®	2.5< dose <25	60	5.90	29.3099669	27.4533326
		dose = 25	866	85.32		
		25< dose <50	22	2.18		
		dose = 50	41	4.04		
	Strattera 25mg Cap®	50< dose <350	20	1.97	29.3099669	27.4533326
		dose = 350	6	0.59		
	Total		1,015	100.00		
	Strattera 40mg Cap®	2.67< dose <40	77	4.41	45.4742016	35.6126045
		dose = 40	1,499	86.00		
		40< dose <80	32	1.84		
		dose = 80	109	6.25		
		80< dose <112	7	0.41		
		dose = 112	9	0.52		
		112< dose <560	3	0.17		
		dose = 560	5	0.29		
		dose = 600	2	0.11		
	Total		1,743	100.00		
	Strattera 60mg Cap®	46.67< dose <60	39	5.07	67.2360375	69.1329793
		dose = 60	703	91.42		
		60< dose <120	7	0.91		
dose = 120		14	1.82			
dose = 840		6	0.78			
Total		769	100.00			

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Table A.33 : Prescribed daily dose according to trade name for 2007

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2007	Adaphen 10mg Tab®	3.33< dose <10	16	1.59	25.07	18.72
		dose = 10	368	36.54		
		10< dose <20	44	4.37		
		dose = 20	255	25.32		
		20< dose <30	11	1.09		
		dose = 30	82	8.14		
		30< dose <40	2	0.20		
		dose = 40	42	4.17		
		40< dose <60	21	2.09		
		dose = 60	153	15.19		
		dose = 80	12	1.19		
		dose = 90	1	0.10		
	Total		1,007	99.99		
	Adaphen 5mg Tab®	dose = 5	1	25.00	31.25	22.50
		dose = 20	1	25.00		
dose = 50		2	50.00			
Total		4	100			
Adaphen XL 20mg Tab®	dose = 20	63	88.73	23.38	10.13	
	dose = 40	4	5.63			
	dose = 60	4	5.63			
Total		71	99.99			

Table A.33 : Prescribed daily dose according to trade name for 2007 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2007	Concerta 18mg Oros®	10.8< dose <18	3	0.09	19.11	5.48
		dose = 18	3,029	94.86		
		18< dose <36	29	0.91		
		dose = 36	69	2.16		
		36< dose <54	8	0.25		
		dose = 54	55	1.72		
	Total		3,193	99.99		
	Concerta 36mg Oros®	12< dose <36	9	0.16	37.14	6.36
		dose = 36	5,475	96.36		
		36< dose <72	22	0.38		
		dose = 72	175	3.08		
		dose = 108	1	0.02		
	Total		5,682	100		
	Concerta 54mg Oros®	27< dose <54	2	0.10	54.16	3.08
		dose = 54	1,913	99.48		
dose = 57.86		2	0.10			
dose = 108		6	0.31			
Total		1,923	99.99			

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Table A.33 : Prescribed daily dose according to trade name for 2007 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2007	Methylphenidate HCl-Douglas®	dose = 5	20	1.58	17.84	11.12
		5 < dose < 10	7	0.56		
		dose = 10	535	42.36		
		10 < dose < 15	13	1.03		
		dose = 15	149	11.80		
		15 < dose < 20	2	0.16		
		dose = 20	322	25.49		
		dose = 25	26	2.06		
		dose = 30	85	6.73		
		30 < dose < 40	3	0.23		
		dose = 40	52	4.12		
		dose = 45	4	0.32		
		dose = 50	10	0.79		
		dose = 60	35	2.77		
			Total			
2007	Ritalin 10mg Tab®	2.33 < dose < 5	7	0.11	16.11	11.39
		dose = 5	239	3.82		
		5 < dose < 10	19	0.30		
		dose = 10	3,416	54.56		
		10 < dose < 15	59	0.94		
		dose = 15	467	7.46		
		15 < dose < 20	17	0.28		
		dose = 20	1,240	19.81		
		20 < dose < 30	62	0.99		
		dose = 30	330	5.27		
		30 < dose < 40	15	0.24		
		dose = 40	113	1.80		
		40 < dose < 60	86	1.37		

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Table A.33 : Prescribed daily dose according to trade name for 2007 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2007	Ritalin 10mg Tab®	dose = 60	184	2.94	16.11	11.39
		60< dose <110	6	0.09		
		dose = 110	1	0.02		
	Total		6,261	100.00		
	Ritalin LA 20mg Cap®	1.33< dose <20	17	0.23	21.81	7.57
		dose = 20	6,860	93.03		
		20< dose <40	51	0.69		
		dose = 40	229	3.11		
		40< dose <60	6	0.08		
		dose = 60	210	2.85		
		dose = 120	1	0.01		
	Total		7,374	100.00		
	Ritalin LA 30mg Cap®	2< dose <30	33	1.24	31.68	10.99
		dose = 30	2,481	93.17		
		30< dose <60	18	0.68		
		dose = 60	121	4.54		
		dose = 120	8	0.30		
		dose = 300	2	0.08		
	Total		2,663	100.01		
	Ritalin LA 40mg Cap®	13.33< dose <40	3	0.41	40.59	5.23
dose = 40		716	97.81			
dose = 42.86		1	0.14			
dose = 80		12	1.64			
Total		732	100.00			

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Table A.33 : Prescribed daily dose according to trade name for 2007 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2007	Ritalin SR 20mg Tab®	7.33< dose <20	4	1.06	22.67	9.13
		dose = 20	335	88.86		
		dose = 26.09	2	0.53		
		dose = 40	20	5.31		
		dose = 58.33	1	0.27		
		dose = 60	15	3.98		
	Total		377	100.01		
	Strattera 10mg Cap®	5< dose <10	7	2.77	12.89	9.63
		dose = 10	210	83.00		
		10< dose <20	8	3.16		
		dose = 20	12	4.74		
		dose = 30	1	0.40		
		dose = 40	13	5.14		
		dose = 70	1	0.40		
		dose = 100	1	0.40		
	Total		253	100.01		
	Strattera 18mg Cap®	4.5< dose <18	14	3.21	20.29	10.52
		dose = 18	379	86.93		
		18< dose <36	8	1.83		
		dose = 36	26	5.96		
36< dose <126		6	1.37			
dose = 126		3	0.69			
Total		436	99.99			

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Table A.33 : Prescribed daily dose according to trade name for 2007 (continued)

Study period	Trade name	Daily dosage (mg)	Number of prescriptions	Percent (%)	Average dosage (mg)	Standard deviation (mg)
2007	Strattera 25mg Cap®	dose = 23.33	51	5.81	26.99	8.70
		dose = 25	752	85.65		
		25< dose <50	23	2.62		
		dose = 50	37	4.21		
		50< dose <116.67	13	1.48		
		dose = 116.67	2	0.23		
	Total		878	100.00		
	Strattera 40mg Cap®	13.33< dose <40	93	5.16	43.98	12.90
		dose = 40	1,513	83.87		
		40< dose <80	42	2.33		
		dose = 80	135	7.48		
		80< dose <112	9	0.49		
		dose = 112	10	0.55		
		dose = 120	2	0.11		
	Total		1,804	99.99		
	Strattera 60mg Cap®	dose = 30	1	0.11	61.78	10.73
		dose = 56	46	4.95		
		dose = 60	844	90.85		
		60< dose <120	11	1.18		
dose = 120		27	2.91			
Total		929	100.00			

Table A.34 : Prescribed daily dose according to trade name and age groups for 2005

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Adaphen 5mg Tab®	≤ 5 years	dose = 10	1	100.00	10.00	0.00
	Total			1	100.00		
	Adaphen 5mg Tab®	5< and ≤12 years	dose = 5	6	66.67	6.67	2.50
			dose = 10	3	33.33		
	Total			9	100.00		
	Adaphen 5mg Tab®	12< and ≤18 years	dose = 5	1	100.00	5.00	0.00
	Total			1	100.00		
	Adaphen 5mg Tab®	18≤ age	dose = 5	5	55.56	15.56	22.70
			dose = 10	1	11.11		
			dose = 15	2	22.22		
	dose = 75		1	11.11			
Total			9	100.00			
2005	Adaphen 10mg Tab®	≤ 5 years	dose = 10	7	77.78	11.11	2.20
			dose = 15	2	22.22		
	Total			9	100.00		
	Adaphen 10mg Tab®	5< and ≤12 years	2.33< dose <10	15	2.50	21.03	35.05
			dose = 10	274	45.59		
			10< dose <15	5	0.85		
			dose = 15	72	11.98		
			15< dose <20	2	0.34		
			dose = 20	149	24.79		
			20< dose <25	3	0.50		
			dose = 25	20	3.33		
			25< dose <40	22	3.66		
			dose = 40	19	3.16		
			40< dose <300	14	2.32		
		dose = 300	6	1.00			
Total			601	100.02			

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Table A.34 : Prescribed daily dose according to trade name and age groups for 2005 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Adaphen 10mg Tab®	12< and ≤18 years	dose = 5	4	1.72	22.37	35.53
			dose = 10	90	38.79		
			10< dose <15	2	0.86		
			dose = 15	19	8.19		
			dose = 20	86	37.07		
			dose = 25	2	0.86		
			dose = 30	12	5.17		
			30< dose<150	11	4.74		
			dose = 150	2	0.86		
			dose = 225	2	0.86		
	dose = 300	2	0.86				
	Total			232	99.98		
	Adaphen 10mg Tab®	18≤ age	1.33< dose <10	11	3.78	44.49	62.38
			dose = 10	65	22.34		
			10< dose <20	5	1.72		
			dose = 20	93	31.96		
			20< dose <30	3	1.03		
	Adaphen 10mg Tab®	18≤ age	dose = 30	23	7.90	44.49	62.38
			30< dose <40	4	1.37		
			dose = 40	21	7.22		
			40< dose <60	10	3.43		
dose = 60			14	4.81			
dose = 100			1	0.34			
dose = 150			37	12.71			
150< dose <600			3	1.03			
dose = 600	1	0.34					
Total			291	99.98			

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Table A.34 : Prescribed daily dose according to trade name and age groups for 2005 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Adaphen XL 20mg Tab®	5< and ≤12 years	dose = 20	1	50.00	22.00	2.83
			dose = 24	1	50.00		
	Total			2	100.00		
	Adaphen XL 20mg Tab®	12< and ≤18 years	dose = 10	1	16.67	18.33	4.08
			dose = 20	5	83.33		
	Total			6	100.00		
	Adaphen XL 20mg Tab®	18≤ age	dose = 20	2	50.00	95.00	136.99
			dose = 40	1	25.00		
			dose = 300	1	25.00		
	Total			4	100.00		
	Concerta 18mg Oros®	≤ 5 years	dose = 18	10	100.00	18.00	0.00
	Total			10	100.00		
	Concerta 18mg Oros®	5< and ≤12 years	3< dose <18	4	0.44	21.90	34.18
			dose = 18	850	95.83		
			18< dose <36	8	0.89		
dose = 36			7	0.79			
36< dose <540			16	1.79			
dose = 540			2	0.23			
Total			887	99.97			
Concerta 18mg Oros®	12< and ≤18 years	dose = 18	187	94.44	26.64	51.31	
		18< dose <270	6	3.05			
		dose = 270	4	2.02			
		dose = 540	1	0.51			
Total			198	100.02			

Table A.34 : Prescribed daily dose according to trade name and age groups for 2005 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Concerta 18mg Oros®	18≤ age	8.4< dose <18	2	1.44	21.33	22.34
			dose = 18	125	90.58		
			18< dose <270	10	7.23		
			dose = 270	1	0.72		
	Total			138	99.97		
	Concerta 36mg Oros®	≤ 5 years	dose = 36	4	100.00	36.00	0.00
	Total			4	100.00		
	Concerta 36mg Oros®	5< and ≤12 years	9.6< dose <36	2	0.20	42.08	58.95
			dose = 36	982	98.30		
			36< dose <540	5	0.50		
			dose = 540	9	0.90		
			dose = 1080	1	0.10		
	Total			999	100.00		
	Concerta 36mg Oros®	12< and ≤18 years	dose = 31.2	1	0.15	50.02	81.92
dose = 36			665	96.52			
36< dose <540			5	0.74			
dose = 540			18	2.61			
Total			689	100.02			
Concerta 36mg Oros®	18≤ age	16.8< dose <36	3	1.08	55.41	95.26	
		dose = 36	260	93.86			
		36< dose <540	4	1.44			
		dose = 540	10	3.61			
Total			277	99.99			
Concerta 54mg Oros®	5< and ≤12 years	dose = 54	102	99.03	61.40	74.49	
		dose = 810	1	0.97			
Total			103	100.00			
Concerta 54mg Oros®	12< and ≤18 years	dose = 18	1	0.71	59.14	63.99	
		dose = 54	138	98.57			

Table A.34 : Prescribed daily dose according to trade name and age groups for 2005 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005			dose = 810	1	0.71		
	Total			140	99.99		
	Concerta 54mg Oros®	18≤ age	dose = 54	51	94.44	96.00	174.80
			dose = 810	3	5.56		
	Total			54	100.00		
	Methylphenidate HCl-Douglas®	≤ 5 years	dose = 5	2	8.70	19.13	1.19
			dose = 10	5	21.74		
			dose = 15	6	26.09		
			15< dose <35	6	26.08		
			dose = 35	4	17.39		
	Total			23	100.00		
	Methylphenidate HCl-Douglas®	5< and ≤12 years	5< dose <10	35	3.92	22.19	35.28
			dose = 10	373	41.82		
			10< dose <15	6	0.67		
			dose = 15	98	10.99		
			15< dose <20	6	0.66		
			dose = 20	204	22.87		
			20< dose <30	32	3.58		
			dose = 30	62	6.95		
			30< dose <40	21	2.35		
	dose = 40		17	1.91			
	40< dose <150		12	1.34			
	dose = 150		11	1.23			
	dose = 225		9	1.01			
	dose = 300	6	0.67				
Total			892	99.97			

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	Methylphenidate HCl- Douglas®	12< and ≤18 years	dose = 10	118	42.75	19.00	20.76
			10< dose <15	5	1.81		
			dose = 15	21	7.61	19.00	20.76
			dose = 16.67	1	0.36		
			dose = 20	78	28.26		

Table A.34 : Prescribed daily dose according to trade name and age groups for 2005 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Methylphenidate HCl- Douglas®		20< dose <30	5	1.81		
			dose = 30	35	12.68		
			30< dose <300	12	4.33		
			dose = 300	1	0.36		
	Total			276	99.97		
	Methylphenidate HCl- Douglas®	18≤ age	dose = 5	3	1.40	31.70	47.80
			dose = 10	54	25.12		
			10< dose <20	5	2.33		
			dose = 20	53	24.65		
			dose = 30	37	17.21		
			dose = 40	35	16.28		
			40< dose <60	8	3.72		
			dose = 60	16	7.44		
			dose = 225	3	1.40		
	dose = 600	1	0.47				
	Total			215	100.02		
	Ritalin 10mg Tab®	≤ 5 years	5< dose <10	14	18.42	11.86	5.86
			dose = 10	42	55.26		
			10< dose <30	17	22.37		
			dose = 30	3	3.95		
Total			76	100.00			
Ritalin 10mg Tab®	5< and ≤12 years	0.33< dose <5	10	0.19	17.67	25.81	
		dose = 5	179	3.36			
		5< dose <10	42	0.81			

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	dose = 10	2,932	55.08
	10 < dose < 15	69	1.32
	dose = 15	554	10.41
	15 < dose < 20	27	0.53
	dose = 20	905	17.00
	20 < dose < 30	84	1.57
	dose = 30	236	4.43

Table A.34 : Prescribed daily dose according to trade name and age groups for 2005 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Ritalin 10mg Tab®	5 < and ≤ 12 years	30 < dose < 40	43	0.82	17.67	25.81
			dose = 40	69	1.30		
			40 < dose < 60	29	0.55		
			dose = 60	37	0.70		
			60 < dose < 150	9	0.17		
			dose = 150	73	1.37		
			dose = 210	1	0.02		
			dose = 225	6	0.11		
			dose = 300	17	0.32		
	dose = 450	1	0.02				
	Total			5,323	100.08		
	Ritalin 10mg Tab®	12 < and ≤ 18 years	2 < dose < 10	29	1.92	23.50	53.81
			dose = 10	779	51.02		
			10 < dose < 15	9	0.60		
			dose = 15	88	5.76		
			15 < dose < 20	13	0.87		
			dose = 20	318	20.83		
			20 < dose < 30	36	2.37		
			dose = 30	128	8.38		
30 < dose < 40			5	0.33			
dose = 40			50	3.27			
40 < dose < 150	27	1.77					

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	dose = 150	27	1.77
	dose = 225	4	0.26
	dose = 300	7	0.46
	dose = 450	2	0.13
	dose = 600	4	0.26
	dose = 1200	1	0.07

Table A.34 : Prescribed daily dose according to trade name and age groups for 2005 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Total			1,527	100.07		
	Ritalin 10mg Tab®	18≤ age	4< dose <10	14	1.12	35.66	78.97
			dose = 10	554	44.43		
			10< dose <20	51	4.08		
			dose = 20	262	21.01		
			20< dose <30	17	1.36		
	Ritalin 10mg Tab®	18≤ age	dose = 30	117	9.38	35.66	78.97
			30< dose <40	7	0.56		
			dose = 40	43	3.45		
			40< dose <50	11	0.88		
			dose = 50	30	2.41		
			dose = 56,25	1	0.08		
			dose = 60	61	4.89		
			60< dose <150	18	1.44		
			dose = 150	26	2.09		
			dose = 300	7	0.56		
			dose = 450	25	2.00		
			dose = 600	1	0.08		
			dose = 900	1	0.08		
dose = 1050	1	0.08					

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	Total		1,247	99.98			
	Ritalin LA 20mg Cap®	≤ 5 years	dose = 20	8	80.00	50.00	88.07
			dose = 40	1	10.00		
			dose = 300	1	10.00		
Total		10	100.00				

Table A.34 : Prescribed daily dose according to trade name and age groups for 2005 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Ritalin LA 20mg Cap®	5< and ≤12 years	1.6< dose <20	20	0.38	27.43	48.74
			dose = 20	4,999	95.20		
			20< dose <40	46	0.87		
			dose = 40	51	0.97		
			40< dose <300	16	0.31		
			dose = 300	106	2.02		
			dose = 600	13	0.25		
	Total		5,251	100.00			
	Ritalin LA 20mg Cap®	12< and ≤18 years	3.33< dose <20	5	0.20	28.69	50.43
			dose = 20	2,364	92.52		
			20< dose <40	28	1.10		
			dose = 40	78	3.05		
			40< dose <300	16	0.63		
			dose = 300	58	2.27		
			dose = 600	6	0.23		
	Total		2,555	100.00			
	Ritalin LA 20mg Cap®	18≤ age	dose = 13.33	2	0.22	30.77	53.27
dose = 20			740	83.05			

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		20 < dose < 40	8	0.89		
		dose = 40	109	12.23		
		40 < dose < 300	13	1.46		
		dose = 300	15	1.68		
		dose = 600	4	0.45		
	Total		891	99.98		
	Ritalin LA 30mg Cap®	≤ 5 years	dose = 30	1	100.00	30.00 0.00
	Total		1	100.00		

Table A.34 : Prescribed daily dose according to trade name and age groups for 2005 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Ritalin LA 30mg Cap®	5 < and ≤ 12 years	4 < dose < 30	12	1.08	39.12	58.19
			dose = 30	1,031	93.56		
			30 < dose < 60	6	0.54		
			dose = 60	27	2.45		
			60 < dose < 450	5	0.45		
			dose = 450	21	1.91		
	Total			1,102	99.99		
	Ritalin LA 30mg Cap®	12 < and ≤ 18 years	21.43 < dose < 30	2	0.16	40.80	66.00
			dose = 30	1,163	93.87		
			30 < dose < 60	17	1.36		
			dose = 60	27	2.18		
			60 < dose < 450	3	0.32		
			dose = 450	26	2.10		
		dose = 900	1	0.08			
Total			1,239	100.07			
Ritalin LA 30mg Cap®	18 ≤ age	dose = 30	294	90.46	41.76	70.97	

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		dose = 36	2	0.62		
		dose = 60	20	6.15		
		60< dose <450	3	0.93		
		dose = 450	5	1.54		
		dose = 900	1	0.31		
	Total		325	100.01		
	Ritalin LA 40mg Cap®	5< and ≤12 years	13.33< dose <40	2	1.16	46.78
	Ritalin LA 40mg Cap®	5< and ≤12 years	dose = 40	165	95.93	46.78
			40< dose <600	3	1.74	
			dose = 600	2	1.16	
	Total			172	99.99	

Table A.34 : Prescribed daily dose according to trade name and age groups for 2005 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)	
2005	Ritalin LA 40mg Cap®	12< and ≤18 years	1.33< dose <40	8	2.01	46.13	57.74	
			dose = 40	383	96.47			
			40< dose <600	2	0.50			
			dose = 600	4	1.01			
		Total			397	99.99		
	Ritalin LA 40mg Cap®	18≤ age	dose = 40	153	92.73	51.91	75.25	
			40< dose <600	9	5.45			
			dose = 600	3	1.82			
		Total			165	100.00		
	Ritalin SR 20mg Tab®	5< and ≤12 years	10< dose <20	6	0.83	27.49	46.53	
dose = 20			682	94.07				
20< dose <300			20	2.77				
dose = 300			16	2.21				
dose = 600			1	0.14				

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	Total		725	100.02			
	Ritalin SR 20mg Tab®	12< and ≤18 years	8< dose <20	9	1.49	29.51	52.77
			dose = 20	538	89.07		
			20< dose <40	6	1.00		
			dose = 40	28	4.64		
			40< dose <300	8	1.33		
			dose = 300	13	2.15		
			dose = 600	2	0.33		
	Total		604	100.01			

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Table A.34 : Prescribed daily dose according to trade name and age groups for 2005 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Ritalin SR 20mg Tab®	18 ≤ age	10 < dose < 20	2	0.54	47.06	115.78
			dose = 20	289	79.18		
			20 < dose < 40	2	0.54		
			dose = 40	35	9.59		
			dose = 60	10	2.74		
			dose = 80	10	2.74		
			80 < dose < 1200	16	4.38		
	Ritalin SR 20mg Tab®	18 ≤ age	dose = 1200	1	0.27	47.06	115.78
	Total			365	99.98		
	Strattera 10mg Cap®	≤ 5 years	dose = 9.33	1	20.00	11.87	4.56
			dose = 10	3	60.00		
			dose = 20	1	20.00		
	Total			5	100.00		
	Strattera 10mg Cap®	5 < and ≤ 12 years	2.33 < dose < 10	7	5.18	12.11	12.66
			dose = 10	114	84.44		
			10 < dose < 20	3	2.22		
			dose = 20	7	5.19		
20 < dose < 140			3	2.22			
dose = 140			1	0.74			
Total			135	99.99			
Strattera 10mg Cap®	12 < and ≤ 18 years	dose = 10	10	71.43	20.63	34.48	
		10 < dose < 140	3	21.42			
		dose = 140	1	7.14			
Total			14	99.99			

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Table A.34 : Prescribed daily dose according to trade name and age groups for 2005 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Strattera 10mg Cap®	18≤ age	dose = 10	13	86.67	12.67	7.99
			dose = 20	1	6.67		
			dose = 40	1	6.67		
	Total			15	100.01		
	Strattera 18mg Cap®	≤ 5 years	dose = 18	1	100.00	18.00	0.00
	Total			1	100.00		
	Strattera 18mg Cap®	5< and ≤12 years	4.2< dose <18	6	3.25	21.70	22.79
			dose = 18	164	89.13		
			18< dose <36	5	2.71		
			dose = 36	4	2.17		
			36< dose <252	4	2.17		
			dose = 252	1	0.54		
	Total			184	99.97		
	Strattera 18mg Cap®	12< and ≤18 years	dose = 16.8	2	4.26	18.46	2.77
			dose = 18	43	91.49		
dose = 24			1	2.13			
dose = 36			1	2.13			
Total			47	100.01			
Strattera 18mg Cap®	18≤ age	dose = 18	15	88.24	21.71	11.50	
		dose = 36	1	5.88			
		dose = 63	1	5.88			
Total			17	100.00			
Strattera 25mg Cap®	≤ 5 years	dose = 25	5	100.00	25.00	0.00	
Total			5	100.00			

Table A.34 : Prescribed daily dose according to trade name and age groups for 2005 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Strattera 25mg Cap®	5< and ≤12 years	12.5< dose <25	12	4.92	35.05	49.73
			dose = 25	204	83.61		
			25< dose <50	11	4.51		
			dose = 50	6	2.46		
			50< dose <350	6	2.46		
			dose = 350	3	1.23		
			dose = 375	2	0.82		
	Total			244	100.01		
	Strattera 25mg Cap®	12< and ≤18 years	dose = 23.33	1	1.12	27.10	8.40
			dose = 25	79	88.76		
			25< dose <50	5	5.60		
			dose = 50	3	3.37		
			dose = 87.5	1	1.12		
	Total			89	99.97		
Strattera 25mg Cap®	18≤ age	dose = 25	23	88.46	29.23	15.34	
		25< dose <100	2	7.70			
		dose = 100	1	3.85			
Total			26	100.01			
Strattera 40mg Cap®	≤ 5 years	dose = 40	1	100.00	40.00	0.00	
Total			1	100.00			
Strattera 40mg Cap®	5< and ≤12 years	20< dose <40	8	2.91	45.24	47.51	
		dose = 40	262	95.27			
		40< dose <560	3	1.08			
		dose = 560	2	0.73			
Total			275	99.99			

Table A.34 : Prescribed daily dose according to trade name and age groups for 2005 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Strattera 40mg Cap®	12< and ≤18 years	dose = 37.33	2	2.30	44.94	13.47
			dose = 40	74	85.06		
	Strattera 40mg Cap®	12< and ≤18 years	dose = 60	1	1.15	44.94	13.47
			dose = 80	8	9.20		
			dose = 85.71	1	1.15		
			dose = 89.33	1	1.15		
	Total			87	100.01		
	Strattera 40mg Cap®	18≤ age	dose = 37.33	1	2.63	64.25	84.25
			dose = 40	23	60.53		
			40< dose <80	6	15.78		
			dose = 80	7	18.42		
			dose = 560	1	2.63		
	Total			38	99.99		
	Strattera 60mg Cap®	5< and ≤12 years	dose = 56	2	6.25	59.75	0.98
			dose = 60	30	93.75		
Total			32	100.00			
Strattera 60mg Cap®	12< and ≤18 years	dose = 56	9	7.14	66.62	69.55	
		dose = 60	111	88.10			
		60< dose <80	2	1.58			
		dose = 80	3	2.38			
		dose = 840	1	0.79			
Total			126	99.99			
Strattera 60mg Cap®	18≤ age	dose = 60	38	100.00	60.00	0.00	
Total			38	100.00			

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Table A.35 : Prescribed daily dose according to trade name and age groups for 2006

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Adaphen 10mg Tab®	≤ 5 years	dose = 5	1	33.33	15.00	13.23
			dose = 10	1	33.33		
			dose = 30	1	33.33		
	Total			3	99.99		
	Adaphen 10mg Tab®	5< and ≤12 years	2.67< dose <10	21	3.68	15.84	11.46
			dose = 10	290	50.79		
			10< dose <20	42	7.35		
			dose = 20	157	27.50		
			20< dose <30	18	3.15		
			dose = 30	27	4.73		
			30< dose <150	14	2.54		
	dose = 150	2	0.35				
	Total			571	100.09		
	Adaphen 10mg Tab®	12< and ≤18 years	dose = 5	6	3.17	20.22	30.74
			dose = 10	81	42.86		
			10< dose <20	12	6.35		
			dose = 20	62	32.80		
20< dose <30			5	2.64			
dose = 30			10	5.29			
30< dose <300			11	5.82			
dose = 300	2	1.06					
Total			189	99.99			

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Table A.35 : Prescribed daily dose according to trade name and age groups for 2006 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Adaphen 10mg Tab®	18≤ age	dose = 5	6	1.90	38.24	37.43
			dose = 10	80	25.40		
			dose = 18.33	1	0.32		
			dose = 20	90	28.57		
			20< dose <40	22	6.98		
			dose = 40	21	6.67		
			40< dose <60	6	1.91		
			dose = 60	63	20.00		
			dose = 100	2	0.63		
			dose = 150	24	7.62		
	Total			315	100.00		
	Adaphen 5mg Tab®	5< and ≤12 years	dose = 2.5	1	25.00	4.38	1.25
			dose = 5	3	75.00		
	Total			4	100.00		
	Adaphen 5mg Tab®	18≤ age	dose = 5	1	100.00	5.00	0.00
	Total			1	100.00		
	Adaphen XL 20mg Tab®	5< and ≤12 years	dose = 20	62	96.88	20.63	3.51
			dose = 40	2	3.13		
	Total			64	100.01		
	Adaphen XL 20mg Tab®	12< and ≤18 years	dose = 20	20	83.33	26.67	15.23
dose = 60			4	16.67			
Total			24	100.00			
Adaphen XL 20mg Tab®	18≤ age	dose = 20	24	64.86	34.05	45.91	
		dose = 40	12	32.43			
		dose = 300	1	2.70			
Total			37	99.99			

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Table A.35 : Prescribed daily dose according to trade name and age groups for 2006 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Concerta 18mg Oros	≤ 5 years	dose = 18	12	100.00	18.00	0.00
	Total			12	100.00		
	Concerta 18mg Oros®	5< and ≤12 years	5.4< dose <18	4	0.22	19.76	16.38
			dose = 18	1732	96.22		
			18< dose <36	8	0.45		
			dose = 36	20	1.11		
			dose = 38.57	1	0.06		
			dose = 54	28	1.56		
	Total			1800	100.01		
	Concerta 18mg Oros®	12< and ≤18 years	dose = 13.8	1	0.27	18.86	4.68
			dose = 18	351	95.90		
			18< dose <54	10	2.74		
			dose = 54	4	1.09		
	Total			366	100.00		
	Concerta 18mg Oros®	18≤ age	9< dose <18	3	1.36	21.96	25.12
			dose = 18	203	91.86		
			18< dose <270	13	5.89		
dose = 270			2	0.90			
Total			221	100.01			
Concerta 36mg Oros®	≤ 5 years	dose = 36	2	100.00	36.00	0.00	
Total			2	100.00			
Concerta 36mg Oros®	5< and ≤12 years	6< dose <36	6	0.28	36.91	21.99	
		dose = 36	2096	99.48			
		dose = 72	1	0.05			
		dose = 540	4	0.19			
Total			2107	100.00			

Table A.35 : Prescribed daily dose according to trade name and age groups for 2006 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Concerta 36mg Oros®	12< and ≤18 years	9.6< dose <36	3	0.20	39.34	36.89
			dose = 36	1484	97.38		
			dose = 39.6	1	0.07		
			dose = 72	27	1.77		
			dose = 180	1	0.07		
			dose = 540	8	0.52		
	Total			1524	100.01		
	Concerta 36mg Oros®	18≤ age	dose = 36	462	98.09	38.71	33.15
			36< dose <540	7	1.50		
			dose = 540	2	0.42		
	Total			471	100.01		
	Concerta 54mg Oros®	5< and ≤12 years	dose = 45	2	0.64	53.93	0.75
			dose = 50.4	1	0.32		
			dose = 54	309	99.04		
	Total			312	100.00		
Concerta 54mg Oros®	12< and ≤18 years	27< dose <54	6	1.03	53.83	1.91	
		dose = 54	574	98.97			
Total			580	100.00			
Concerta 54mg Oros®	18≤ age	dose = 54	214	97.72	61.64	72.28	
		dose = 108	3	1.37			
		dose = 810	2	0.91			
Total			219	100.00			
Methylphenidate HCl-Douglas®	≤ 5 years	dose = 5	3	27.27	9.55	4.16	
		dose = 10	7	63.64			
		dose = 20	1	9.09			
Total			11	100.00			

Table A.35 : Prescribed daily dose according to trade name and age groups for 2006 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Methylphenidate HCl-Douglas®	5< and ≤12 years	2.66< dose <10	38	3.57	16.17	8.99
			dose = 10	495	46.48		
			10< dose <15	2	0.18		
			dose = 15	118	11.08		
			dose = 15.71	1	0.09		
			dose = 20	250	23.47		
			20< dose <25	6	0.57		
			dose = 25	48	4.51		
			25< dose <30	2	0.18		
			dose = 30	53	4.98		
			dose = 35	15	1.41		
			dose = 40	21	1.97		
			40< dose <60	7	0.65		
			dose = 60	8	0.75		
			dose = 75	1	0.09		
	Total			1065	99.98		
	Methylphenidate HCl-Douglas®	12< and ≤18 years	dose = 10	122	42.51	20.23	17.54
			10< dose <20	19	6.62		
			dose = 20	81	28.22		
			dose = 25	8	2.79		
			dose = 30	34	11.85		
			30< dose <60	10	3.48		
			dose = 60	10	3.48		
			dose = 150	3	1.05		
	Total			287	100.00		

Table A.35 : Prescribed daily dose according to trade name and age groups for 2006 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Methylphenidate HCl-Douglas®	18 ≤ age	dose = 5	1	0.33	24.88	16.56
			dose = 10	94	31.23		
			dose = 15	6	1.99		
			dose = 20	77	25.58		
			20 < dose < 30	16	5.31		
			dose = 30	43	14.29		
			30 < dose < 40	2	0.66		
			dose = 40	32	10.63		
			40 < dose < 60	2	0.66		
			dose = 60	27	8.97		
	dose = 150	1	0.33				
	Total			301	99.98		
		Ritalin 10mg Tab®	≤ 5 years	dose = 5	11	12.94	11.43
dose = 6.67				1	1.18		
dose = 10				57	67.06		
10 < dose < 30				11	12.94		
dose = 30				5	5.88		
Total			85	100.00			

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Table A.35 : Prescribed daily dose according to trade name and age groups for 2006 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Ritalin 10mg Tab®	5< and ≤12 years	3.33< dose <5	7	0.16	15.13	14.49
			dose = 5	166	3.80		
			5< dose <10	34	0.78		
			dose = 10	2,457	56.29		
			10< dose <15	41	0.94		
			dose = 15	451	10.33		
			15< dose = 20	16	0.37		
			dose = 20	800	18.33		
			20< dose <30	103	2.36		
			dose = 30	138	3.16		
			30< dose <40	14	0.37		
			dose = 40	28	0.64		
			40< dose <50	8	0.18		
			dose = 50	35	0.80		
			50< dose <60	7	0.16		
			dose = 60	39	0.89		
			60< dose <150	2	0.04		
	dose = 150	14	0.32				
	150< dose <320	4	0.09				
	dose = 320	1	0.02				
	Total			4,365	100.03		
	Ritalin 10mg Tab®	12< and ≤18 years	3.33< dose <10	40	3.34	18.78	39.75
dose = 10			650	54.30			
10< dose <20			67	5.60			
dose = 20			237	19.80			

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Table A.35 : Prescribed daily dose according to trade name and age groups for 2006 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Ritalin 10mg Tab®	12< and ≤18 years	20< dose <30	12	1.00	18.78	39.75
			dose = 30	95	7.94		
			dose = 35	13	1.09		
			dose = 40	24	2.01		
			40< dose <60	23	1.92		
			dose = 60	27	2.26		
			60< dose <1200	8	0.67		
			dose = 1200	1	0.08		
	Total			1,197	100.01		
	Ritalin 10mg Tab®	18≤ age	1.33< dose <10	23	1.95	27.07	56.10
			dose = 10	516	43.69		
			10< dose <20	44	3.72		
			dose = 20	275	23.29		
			20< dose <30	15	1.27		
			dose = 30	89	7.54		
			30< dose <60	89	7.54		
			dose = 60	100	8.47		
			60< dose <150	13	1.10		
			dose = 150	6	0.51		
			150< dose <450	2	0.17		
			dose = 450	7	0.59		
			dose = 750	1	0.08		
			dose = 1200	1	0.08		
Total			1,181	100.00			
Ritalin LA 20mg Cap®	≤ 5 years	dose = 20	28	96.55	21.38	7.43	
		dose = 60	1	3.45			
Total			29	100.00			

Table A.35 : Prescribed daily dose according to trade name and age groups for 2006 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Ritalin LA 20mg Cap®	5< and ≤12 years	0.67< dose <20	11	0.25	22.89	23.53
			dose = 20	4237	95.75		
			20< dose <40	19	0.43		
			dose = 40	36	0.81		
			dose = 60	91	2.06		
			60< dose <300	2	0.04		
			dose = 300	29	0.66		
	Total			4425	100.00		
	Ritalin LA 20mg Cap®	12< and ≤18 years	0.67< dose <20	3	0.13	24.73	30.03
			dose = 20	2082	92.21		
			20< dose <40	22	0.97		
			dose = 40	50	2.21		
			dose = 42.86	1	0.04		
			dose = 60	74	3.28		
			60< dose <300	5	0.22		
dose = 300			20	0.89			
dose = 600	1	0.04					
Total			2258	99.99			

Table A.35 : Prescribed daily dose according to trade name and age groups for 2006 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Ritalin LA 20mg Cap®	18≤ age	dose = 9.33	1	0.11	24.98	21.83
			dose = 20	753	85.57		
			20< dose <40	2	0.23		
			dose = 40	88	10.00		
			dose = 60	29	3.30		
			60< dose <300	3	0.35		
			dose = 300	4	0.45		
	Total			880	100.01		
	Ritalin LA 30mg Cap®	5< and ≤12 years	15< dose <30	2	0.20	34.64	36.43
			dose = 30	915	93.75		
			30< dose <60	5	0.52		
			dose = 60	46	4.71		
			dose = 225	1	0.10		
			dose = 450	7	0.72		
	Total			976	100.00		
	Ritalin LA 30mg Cap®	12< and ≤18 years	20< dose <30	3	0.26	33.38	29.33
			dose = 30	1082	94.25		
30< dose <60			10	0.87			
dose = 60			46	4.01			
dose = 225			2	0.17			
dose = 450			5	0.44			
Total			1148	100.00			
	Ritalin LA 30mg Cap®	18≤ age	dose = 4	1	0.25	41.16	45.72

Table A.35 : Prescribed daily dose according to trade name and age groups for 2006 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Ritalin LA 30mg Cap®	18≤ age	dose = 30	341	85.46	41.16	45.72
			30< dose <60	3	0.76		
			dose = 60	39	9.77		
			dose = 150	6	1.50		
			dose = 300	8	2.01		
			dose = 450	1	0.25		
	Total			399	100.00		
	Ritalin LA 40mg Cap®	≤ 5 years	dose = 40	1	100.00	40.00	0.00
	Total			1	100.00		
	Ritalin LA 40mg Cap®	5< and ≤12 years	dose = 40	168	99.41	46.86	89.23
			dose = 1200	1	0.59		
	Total			169	100.00		
	Ritalin LA 40mg Cap®	12< and ≤18 years	5.33< dose <40	2	0.49	43.56	59.13
			dose = 40	401	98.77		
40< dose <1200			2	0.49			
dose = 1200			1	0.25			
Total			406	100.00			
Ritalin LA 40mg Cap®	18≤ age	dose = 40	168	98.82	43.31	42.95	
		dose = 42.86	1	0.59			
		dose = 600	1	0.59			
Total			170	100.00			
Ritalin SR 20mg Tab®	≤ 5 years	dose = 20	1	100.00	20.00	0.00	
Total			1	100.00			

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Table A.35 : Prescribed daily dose according to trade name and age groups for 2006 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Ritalin SR 20mg Tab®	5< and ≤12 years	10< dose <20	8	1.76	22.76	19.87
			dose = 20	414	91.19		
			20< dose <60	17	3.75		
			dose = 60	13	2.86		
			dose = 300	2	0.44		
	Total			454	100.00		
	Ritalin SR 20mg Tab®	12< and ≤18 years	6.67< dose <20	2	0.56	24.18	29.76
			dose = 20	334	93.04		
			dose = 30	3	0.84		
			dose = 40	13	3.62		
			40< dose <300	3	0.84		
			dose = 300	4	1.11		
	Total			359	100.01		
	Ritalin SR 20mg Tab®	18≤ age	dose = 20	193	76.89	29.32	38.96
dose = 40			32	12.75			
dose = 60			19	7.57			
dose = 80			6	2.39			
dose = 600			1	0.40			
Total			251	100.00			
	Strattera 10mg Cap®	≤ 5 years	dose = 10	4	100.00	10.00	0.00
Total				4	100.00		

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Table A.35 : Prescribed daily dose according to trade name and age groups for 2006 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Strattera 10mg Cap®	5< and ≤12 years	2.33< dose <10	15	6.41	11.95	6.32
			dose = 10	185	79.06		
			10< dose <20	7	2.99		
			dose = 20	18	7.69		
			20< dose = 40	6	2.57		
			dose = 46.67	3	1.28		
	Total			234	100.00		
	Strattera 10mg Cap®	12< and ≤18 years	dose = 1.67	1	2.22	17.81	27.17
			dose = 10	33	73.33		
			10< dose <140	9	20.00		
			dose = 140	2	4.44		
	Total			45	99.99		
	Strattera 10mg Cap®	18≤ age	dose = 10	12	52.17	18.05	17.53
			10< dose <20	3	13.05		
			dose = 20	5	21.74		
			20< dose <93.33	2	8.70		
			dose = 93.33	1	4.35		
Total			23	100.01			
Strattera 18mg Cap®	≤ 5 years	dose = 16.8	3	60.00	17.28	0.66	
		dose = 18	2	40.00			
Total			5	100.00			
Strattera 18mg Cap®	5< and ≤12 years	4.2< dose <18	15	3.88	19.36	6.25	
		dose = 18	345	89.15			
		18< dose <36	4	1.04			
		dose = 36	16	4.13			
		36< dose <72	6	1.55			

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Table A.35 : Prescribed daily dose according to trade name and age groups for 2006 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Strattera 18mg Cap®	5< and ≤12 years	dose = 72	1	0.26	19.36	6.25
	Total			387	100.01		
	Strattera 18mg Cap®	12< and ≤18 years	4.2< dose <18	3	3.41	21.00	7.32
			dose = 18	70	79.55		
			dose = 36	11	12.50		
			dose = 38.57	4	4.55		
	Total			88	100.01		
	Strattera 18mg Cap®	18≤ age	dose = 18	22	95.65	18.78	3.75
			dose = 36	1	4.35		
	Total			23	100.00		
	Strattera 25mg Cap®	≤ 5 years	dose = 25	2	100.00	25.00	0.00
	Total			2	100.00		
	Strattera 25mg Cap®	5< and ≤12 years	11.67< dose <23.33	4	0.51	28.98	28.22
			dose = 23.33	44	5.66		
			dose = 25	678	87.26		
25< dose <50			15	1.93			
dose = 50			16	2.06			
50< dose <350			15	1.93			
dose = 350			5	0.64			
Total			777	99.99			
Strattera 25mg Cap®	12< and ≤18 years	4.167< dose <25	9	4.62	30.75	26.68	
		dose = 25	155	79.49			
		25< dose <50	6	3.08			
		dose = 50	20	10.26			
		50< dose <350	4	2.05			
		dose = 350	1	0.51			
Total			195	100.01			

Table A.35 : Prescribed daily dose according to trade name and age groups for 2006 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Strattera 25mg Cap®	18≤ age	2.5< dose <25	3	7.32	28.89	13.94
			dose = 25	31	75.61		
			dose = 43.75	1	2.44		
			dose = 50	5	12.20		
			dose = 87.5	1	2.44		
	Total			41	100.01		
	Strattera 40mg Cap®	≤ 5 years	dose = 37.33	2	50.00	56.85	37.27
			dose = 40	1	25.00		
			dose = 112.73	1	25.00		
	Total			4	100.00		
	Strattera 40mg Cap®	5< and ≤12 years	2.67< dose <37.33	5	0.47	41.44	23.28
			dose = 37.33	48	4.48		
			dose = 40	993	92.63		
			40< dose <80	11	1.03		
			dose = 80	8	0.75		
			dose = 112	5	0.47		
	dose = 560	2	0.19				
	Total			1072	100.02		
	Strattera 40mg Cap®	12< and ≤18 years	5.71< dose <40	19	3.96	50.56	55.91
			dose = 40	396	82.50		
40< dose <80			10	2.08			
dose = 80			41	8.54			
80< dose <600			12	2.50			
dose = 600	2	0.42					
Total			480	100.00			

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Table A.35 : Prescribed daily dose according to trade name and age groups for 2006 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Strattera 40mg Cap®	18≤ age	4.29< dose <40	3	1.60	55.30	20.61
			dose = 40	109	58.29		
			40< dose <80	11	5.89		
			dose = 80	60	32.09		
			dose = 89.33	2	1.07		
			dose = 112	2	1.07		
	Total			187	100.01		
	Strattera 60mg Cap®	≤ 5 years	dose = 60	1	100.00	60.00	0.00
	Total			1	100.00		
	Strattera 60mg Cap®	5< and ≤12 years	dose = 56	13	8.44	59.66	1.12
			dose = 60	141	91.56		
	Total			154	100.00		
	Strattera 60mg Cap®	12< and ≤18 years	46.67< dose <60	20	4.28	71.56	88.30
			dose = 60	425	91.01		
			60< dose <120	6	1.28		
dose = 120			10	2.14			
dose = 840			6	1.28			
Total			467	99.99			
Strattera 60mg Cap®	18≤ age	54< dose <60	6	4.08	61.47	9.88	
		dose = 60	136	92.52			
		dose = 64.62	1	0.68			
		dose = 120	4	2.72			
Total			147	100.00			

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Table A.36 : Prescribed daily dose according to trade name and age groups for 2007

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Adaphen 10mg Tab®	≤ 5 years	5< dose <60	3	42.86	42.14	24.81
			dose = 60	4	57.14		
	Total			7	100.00		
	Adaphen 10mg Tab®	5< and ≤12 years	5< dose <10	11	2.57	15.92	9.13
			dose = 10	220	51.40		
			10< dose <20	32	7.48		
			dose = 20	113	26.40		
			20< dose <30	5	1.17		
			dose = 30	31	7.24		
			30< dose <60	10	2.34		
	dose = 60	6	1.40				
	Total			428	100.00		
	Adaphen 10mg Tab®	12< and ≤18 years	dose = 3.33	1	0.61	20.94	14.97
			dose = 10	68	41.46		
			10< dose <20	10	6.10		
			dose = 20	49	29.88		
			20< dose <50	15	9.15		
dose = 50			9	5.49			
dose = 60	12	7.32					
Total			164	100.01			

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Table A.36 : Prescribed daily dose according to trade name and age groups for 2007 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Adaphen 10mg Tab®	18 ≤ age	dose = 5	3	0.74	36.04	21.43
			dose = 10	79	19.36		
			dose = 15	2	0.49		
			dose = 20	93	22.79		
			20 < dose < 30	4	0.98		
			dose = 30	40	9.80		
			30 < dose < 40	2	0.49		
			dose = 40	31	7.60		
			40 < dose < 60	10	2.46		
			dose = 60	131	32.11		
			dose = 80	12	2.94		
	dose = 90	1	0.25				
	Total			408	100.01		
	Adaphen 5mg Tab®	5 < and ≤ 12 years	dose = 5	1	50.00	12.50	10.61
			dose = 20	1	50.00		
	Total			2	100.00		
	Adaphen 5mg Tab®	18 ≤ age	dose = 50	2	100.00	50.00	0.00
	Total			2	100.00		
	Adaphen XL 20mg Tab®	≤ 5 years	dose = 20	1	100.00	20.00	0.00
Total			1	100.00			
Adaphen XL 20mg Tab®	5 < and ≤ 12 years	dose = 20	45	97.83	20.43	2.95	
		dose = 40	1	2.17			
Total			46	100.00			
Adaphen XL 20mg Tab®	12 < and ≤ 18 years	dose = 20	9	90.00	24.00	12.65	
		dose = 60	1	10.00			
Total			10	100.00			

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Table A.36 : Prescribed daily dose according to trade name and age groups for 2007 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Adaphen XL 20mg Tab®	18≤ age	dose = 20	8	57.14	32.86	16.84
			dose = 40	3	21.43		
			dose = 60	3	21.43		
	Total			14	100.00		
	Concerta 18mg Oros®	≤ 5 years	dose = 18	32	78.05	22.39	8.80
			dose = 36	8	19.51		
			dose = 54	1	2.44		
	Total			41	100.00		
	Concerta 18mg Oros®	5< and ≤12 years	10.8< dose <18	3	0.13	18.87	4.89
			dose = 18	2196	95.77		
			18< dose <36	22	0.96		
			dose = 36	37	1.61		
			dose = 37.8	2	0.09		
			dose = 54	33	1.44		
Total			2293	100.00			
Concerta 18mg Oros®	12< and ≤18 years	dose = 18	517	93.83	19.43	6.26	
		18< dose <36	6	1.09			
		dose = 36	12	2.18			
		36< dose <54	4	0.72			
		dose = 54	12	2.18			
Total			551	100.00			
Concerta 18mg Oros®	18≤ age	dose = 18	284	92.21	19.95	7.17	
		18< dose <54	15	4.87			
		dose = 54	9	2.92			
Total			308	100.00			

Table A.36 : Prescribed daily dose according to trade name and age groups for 2007 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Concerta 36mg Oros	≤ 5 years	dose = 36	19	90.48	39.43	10.83
			dose = 72	2	9.52		
	Total			21	100.00		
	Concerta 36mg Oros®	5< and ≤12 years	12< dose <36	4	0.14	36.30	3.33
			dose = 36	2822	98.74		
			36< dose <72	9	0.32		
			dose = 72	23	0.80		
	Total			2858	100.00		
	Cocnerta 36mg Oros®	12< and ≤18 years	12< dose <36	4	0.20	37.75	7.79
			dose = 36	1915	94.43		
			36< dose <72	11	0.54		
			dose = 72	98	4.83		
	Total			2028	100.00		
	Concerta 36mg Oros®	18≤ age	dose = 31.2	1	0.13	38.56	9.41
			dose = 36	719	92.77		
36< dose <72			2	0.26			
dose = 72			52	6.71			
dose = 108			1	0.13			
Total			775	100.00			
Concerta 54mg Oros®	≤ 5 years	dose = 54	3	100.00	54.00	0.00	
Total			3	100.00			
Concerta 54mg Oros®	5< and ≤12 years	dose = 48.6	1	0.18	54.29	3.96	
		dose = 54	554	98.93			
		dose = 57.86	2	0.36			
		dose = 108	3	0.54			
Total			560	100.01			

Table A.36 : Prescribed daily dose according to trade name and age groups for 2007 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Concerta 54mg Oros®	18≤ age	dose = 27	1	0.22	54.29	4.51
			dose = 54	461	99.14		
			dose = 108	3	0.65		
	Total			465	100.01		
	Methylphenidate HCl-Douglas®	≤ 5 years	dose = 10	6	75.00	11.88	3.72
			dose = 15	1	12.50		
			dose = 20	1	12.50		
	Total			8	100.00		
	Methylphenidate HCl-Douglas®	5< and ≤12 years	5< dose <10	22	2.83	15.60	8.58
			dose = 10	351	45.12		
			10< dose <15	12	1.55		
			dose = 15	134	17.22		
			dose = 16.67	1	0.13		
			dose = 20	184	23.65		
			dose = 25	16	2.06		
dose = 30			31	3.98			
30< dose <60			16	2.06			
dose = 60	11	1.41					
Total			778	100.01			

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Table A.36 : Prescribed daily dose according to trade name and age groups for 2007 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Methylphenidate HCl-Douglas®	12< and ≤18 years	dose = 5	2	0.90	18.39	11.11
			dose = 10	103	46.40		
			dose = 15	13	5.86		
			dose = 20	57	25.68		
			20< dose <40	23	10.36		
			dose = 40	18	8.11		
			dose = 45	2	0.90		
			dose = 60	4	1.80		
	Total			222	100.01		
	Methylphenidate HCl-Douglas®	18≤ age	5< dose <10	3	1.18	24.42	14.86
			dose = 10	75	29.41		
			10< dose <20	3	1.18		
			dose = 20	80	31.37		
			dose = 25	2	0.78		
			dose = 30	40	15.69		
dose = 36			1	0.39			
dose = 40			22	8.63			
40< dose <60			9	3.53			
dose = 60	20	7.84					
Total			255	100.00			
Ritalin 10mg Tab®	≤ 5 years	4.67 < dose <10	10	15.15	13.51	10.31	
		dose = 10	37	56.06			
		10< dose <60	17	25.76			
		dose = 60	2	3.03			
Total			66	100.00			

Table A.36 : Prescribed daily dose according to trade name and age groups for 2007 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Ritalin 10mg Tab®	5< and ≤12 years	3.33< dose <5	2	0.05	14.60	9.38
			dose = 5	194	4.79		
			5< dose <10	16	0.40		
			dose = 10	2321	57.32		
			10< dose <15	34	0.84		
			dose = 15	374	9.24		
			15< dose <20	10	0.24		
			dose = 20	742	18.33		
			20< dose <30	43	1.06		
			dose = 30	169	4.17		
			30< dose <40	5	0.13		
			dose = 40	26	0.64		
			dose = 45	1	0.02		
			dose = 50	33	0.82		
			50< dose <60	6	0.15		
dose = 60	73	1.80					
Total				4049	100.00		
2007	Ritalin 10mg Tab®	12< and ≤18 years	2.33< dose <10	30	2.64	17.07	12.40
			dose = 10	617	54.31		
			10< dose <15	17	1.50		
			dose = 15	59	5.19		
			15< dose <20	3	0.27		
			dose = 20	222	19.54		
			20< dose <30	11	0.97		
			dose = 30	84	7.39		
dose = 35	4	0.35					

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Table A.36 : Prescribed daily dose according to trade name and age groups for 2007 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Ritalin 10mg Tab®	12< and ≤18 years	dose = 40	42	3.70	17.07	12.40
			40< dose <60	16	1.41		
			dose = 60	24	2.11		
			60< dose <110	6	0.53		
			dose = 110	1	0.09		
	Total			1136	100.00		
	Ritalin 10mg Tab®	18≤ age	3.33< dose <10	13	1.29	15.34	
			dose = 10	441	43.66		
			10< dose <20	40	3.96		
			dose = 20	269	26.63		
			20< dose <30	8	0.80		
			dose = 30	73	7.23		
			30< dose <40	6	0.60		
			dose = 40	45	4.46		
			40< dose <60	30	2.97		
Total			1010	100.02			
Ritalin LA 20mg Cap®	≤ 5 years	dose = 20	21	100.00		0.00	
Total			21	100.00			
Ritalin LA 20mg Cap®	5< and ≤12 years	1.33< dose <20	10	0.24	6.69		
		dose = 20	3972	94.91			
		20< dose <40	25	0.60			
		dose = 40	75	1.79			
		40< dose <60	3	0.07			
Total			4185	100.00			

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Table A.36 : Prescribed daily dose according to trade name and age groups for 2007 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Ritalin LA 20mg Cap®	12< and ≤18 years	2.67< dose <20	5	0.23	21.62	7.43
			dose = 20	2065	93.61		
			20< dose <40	23	1.05		
			dose = 40	51	2.31		
			40< dose <60	2	0.09		
			dose = 60	59	2.67		
			dose = 120	1	0.05		
	Total			2206	100.01		
	Ritalin LA 20mg Cap®	18≤ age	9.33< dose <20	2	0.21	24.30	10.52
			dose = 20	802	83.37		
			20< dose <40	3	0.31		
			dose = 40	103	10.71		
			dose = 50	1	0.10		
			dose = 60	51	5.30		
	Total			962	100.00		
	Ritalin LA 30mg Cap®	5< and ≤12 years	7< dose <30	28	2.70	30.46	5.66
			dose = 30	978	94.22		
			30< dose <60	3	0.29		
			dose = 60	29	2.79		
	Total			1038	100.00		
Ritalin LA 30mg Cap®	12< and ≤18 years	dose = 20	2	0.16	31.59	6.72	
		dose = 30	1138	93.66			
		30< dose <60	11	0.90			
		dose = 60	64	5.27			
Total			1215	99.99			

Table A.36 : Prescribed daily dose according to trade name and age groups for 2007 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Ritalin LA 30mg Cap®	18≤ age	2< dose <30	3	0.73	35.02	23.56
			dose = 30	365	89.02		
			30< dose <60	4	0.97		
			dose = 60	28	6.83		
			dose = 120	8	1.95		
			dose = 300	2	0.49		
	Total			410	99.99		
	Ritalin LA 40mg Cap®	≤ 5 years	dose = 40	1	100.00	40.00	0.00
	Total			1	100.00		
	Ritalin LA 40mg Cap®	5< and ≤12 years	dose = 40	134	99.26	40.30	3.44
			dose = 80	1	0.74		
	Total			135	100.00		
	Ritalin LA 40mg Cap®	12< and ≤18 years	dose = 26.67	2	0.51	39.93	0.95
			dose = 40	392	99.49		
	Total			394	100.00		
	Ritalin LA 40mg Cap®	18≤ age	dose = 13.33	1	0.50	42.06	9.32
			dose = 40	189	93.56		
dose = 42.86			1	0.50			
dose = 80			11	5.45			
Total			202	100.01			
Ritalin SR 20mg Tab®	≤ 5 years	dose = 20	2	100.00	20.00	0.00	
Total			2	100.00			
Ritalin SR 20mg Tab®	5< and ≤12 years	dose = 10	3	2.10	21.47	7.87	
		dose = 20	133	93.01			
		dose = 40	2	1.40			
		dose = 60	5	3.50			
Total			143	100.01			

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Table A.36 : Prescribed daily dose according to trade name and age groups for 2007 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Ritalin SR 20mg Tab®	12< and ≤18 years	dose = 20	117	94.35	21.39	6.65
			20< dose <60	4	3.23		
			dose = 60	3	2.42		
	Total			124	100.00		
	Ritalin SR 20mg Tab®	18≤ age	dose = 7.33	1	0.93	25.79	12.08
			dose = 20	83	76.85		
			dose = 40	16	14.81		
			dose = 58.33	1	0.93		
			dose = 60	7	6.48		
	Total			108	100.00		
	Strattera 10mg Cap®	≤ 5 years	dose = 10	10	83.33	15.00	11.68
			dose = 40	2	16.67		
	Total			12	100.00		
	Strattera 10mg Cap®	5< and ≤12 years	5< dose <10	7	3.50	12.70	8.25
			dose = 10	163	81.50		
10< dose <20			8	4.00			
dose = 20			10	5.00			
dose = 40			11	5.50			
dose = 70			1	0.50			
Total			200	100.00			
Strattera 10mg Cap	12< and ≤18 years	dose = 10	27	100.00	10.00	0.00	
Total			27	100.00			
Strattera 10mg Cap®	18≤ age	dose = 10	10	71.43	19.29	24.01	
		dose = 20	2	14.29			
		dose = 30	1	7.14			
		dose = 100	1	7.14			
Total			14	100.00			

Table A.36 : Prescribed daily dose according to trade name and age groups for 2007 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Strattera 18mg Cap®	≤ 5 years	dose = 18	18	100.00	18.00	0.00
	Total			18	100.00		
	Strattera 18mg Cap®	5< and ≤12 years	6< dose <18	13	3.88	19.32	5.37
			dose = 18	295	88.06		
			18< dose <36	5	1.49		
			dose = 36	21	6.27		
			dose = 72	1	0.30		
	Total			335	100.00		
	Strattera 18mg Cap®	12< and ≤18 years	dose = 4.5	1	1.72	24.15	20.65
			dose = 18	47	81.03		
			18< dose <126	8	13.79		
			dose = 126	2	3.45		
	Total			58	99.99		
	Strattera 18mg Cap®	18≤ age	dose = 18	19	76.00	25.92	22.52
			18< dose <126	5	20.00		
			dose = 126	1	4.00		
	Total			25	100.00		
Strattera 25mg Cap®	≤ 5 years	dose = 25	11	100.00	25.00	0.00	
Total			11	100.00			
Strattera 25mg Cap®	5< and ≤12 years	dose = 23.33	45	6.51	26.87	8.13	
		dose = 25	585	84.66			
		dose = 26.79	14	2.03			
		26.79< dose <50	7	1.01			
		dose = 50	29	4.20			
		dose = 70	10	1.45			
		dose = 116.67	1	0.14			
Total			691	100.00			

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Table A.36 : Prescribed daily dose according to trade name and age groups for 2007 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Strattera 25mg Cap®	12< and ≤18 years	dose = 23.33	6	4.88	28.31	12.56
			dose = 25	105	85.37		
			25< dose <116.67	11	8.95		
			dose = 116.67	1	0.81		
	Total			123	100.01		
	Strattera 25mg Cap®	18≤ age	dose = 25	51	96.23	25.94	4.81
			dose = 50	2	3.77		
	Total			53	100.00		
	Strattera 40mg Cap®	5< and ≤12 years	13.33< dose <37.33	4	0.36	40.03	3.09
			dose = 37.33	47	4.26		
			dose = 40	1037	94.02		
			40< dose <80	10	0.91		
			dose = 80	5	0.45		
	Total			1103	100.00		
Strattera 40mg Cap®	12< and ≤18 years	18.67< dose <40	39	8.37	47.09	17.20	
		dose = 40	347	74.46			
		40< dose <80	12	2.58			
		dose = 80	54	11.59			
		80< dose <112	4	0.85			
		dose = 112	9	1.93			
		dose = 120	1	0.21			
Total			466	99.99			

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Table A.36 : Prescribed daily dose according to trade name and age groups for 2007 (continued)

Study period	Trade name	Age group	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Strattera 40mg Cap®	18≤ age	dose = 37.33	3	1.28	56.37	20.05
			dose = 40	129	54.89		
			40< dose <80	20	8.51		
			dose = 80	76	32.34		
			80< dose <120	6	2.55		
			dose = 120	1	0.43		
	Total			235	100.00		
	Strattera 60mg Cap®	5< and ≤12 years	dose = 56	25	17.36	59.31	1.52
			dose = 60	119	82.64		
	Total			144	100.00		
	Strattera 60mg Cap®	12< and ≤18 years	dose = 56	17	2.85	61.58	9.74
			dose = 60	559	93.63		
			60< dose <120	8	1.34		
dose = 120			13	2.18			
Total			597	100.00			
Strattera 60mg Cap®	18≤ age	30< dose <60	5	2.66	64.29	16.01	
		dose = 60	166	88.30			
		60< dose <120	3	1.59			
		dose = 120	14	7.45			
Total			188	100.00			

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Table A.37 : Prescribed daily dose according to trade name and gender for 2005

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Adaphen 10mg Tab®	Female (F)	1< dose <10	19	5.17	28.53	50.87
			dose = 10	120	32.70		
			10< dose <20	33	8.98		
			dose = 20	122	33.24		
			20< dose <40	28	7.63		
			dose = 40	13	3.54		
			40< dose <150	9	2.44		
			dose = 150	19	5.18		
			150< dose <600	3	0.81		
		dose = 600	1	0.27			
		Total		367	99.96		
		Male (M)	2< dose <10	11	1.44	26.60	41.68
			dose = 10	316	41.36		
			10< dose <15	5	0.65		
			dose = 15	66	8.64		
			15< dose <20	3	0.39		
			dose = 20	205	26.83		
			20< dose <30	24	3.14		
			dose = 30	37	4.84		
			dose = 40	35	4.58		
			40< dose <150	22	2.87		
			dose = 150	28	3.66		
dose = 225	4		0.52				
dose = 300	8		1.05				
Total		764	99.97				

Table A.37 : Prescribed daily dose according to trade name and gender for 2005 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Adaphen 10mg Tab	Unspecified (U)	dose = 20	1	50.00	40.00	28.28
			dose = 60	1	50.00		
		Total		2	100.00		
	Adaphen 5mg Tab®	Female (F)	dose = 5	2	22.22	17.22	21.95
			dose = 10	4	44.44		
			dose = 15	2	22.22		
			dose = 75	1	11.11		
		Total		9	99.99		
		Male (M)	dose = 5	10	90.91	5.45	1.51
			dose = 10	1	9.09		
	Total		11	100.00			
	Adaphen XL 20mg Tab®	Female (F)	dose = 20	2	66.67	113.33	161.66
			dose = 300	1	33.33		
		Total		3	100.00		
		Male (M)	dose = 10	1	11.11	21.56	7.86
			dose = 20	6	66.67		
			dose = 24	1	11.11		
			dose = 40	1	11.11		
	Total		9	100.00			
	Concerta 18mg Oros®	Female (F)	3< dose <18	3	0.81	22.61	31.42
dose = 18			349	94.58			
18< dose <36			2	0.54			
dose = 36			5	1.36			
36< dose <270			5	1.35			
dose = 270			5	1.36			
Total			369	100.00			

Table A.37 : Prescribed daily dose according to trade name and gender for 2005 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Concerta 18mg Oros®	Male (M)	9< dose < 18	3	0.35	22.54	38.26
			dose = 18	823	95.25		
			18< dose <36	7	0.83		
			dose = 36	10	1.16		
			36< dose <540	18	2.09		
			dose = 540	3	0.35		
	Total		864	100.03			
	Concerta 36mg Tab®	Female (F)	16< dose <36	4	0.75	56.52	98.87
			dose = 36	509	94.96		
			36< dose <540	2	0.38		
			dose = 540	21	3.92		
		Total		536	100.01		
		Male (M)	9< dose <36	2	0.14	43.08	61.15
			dose = 36	1398	97.83		
			36< dose <540	12	0.84		
			dose = 540	16	1.12		
			dose = 1080	1	0.07		
	Total		1429	100.00			
	Unspecified (U)	dose = 36	4	100.00	36.00	0.00	
	Total		4	100.00			
Concerta 54mg Oros®	Female (F)	dose = 54	52	96.30	82.00	144.11	
		dose = 810	2	3.70			
	Total		54	100.00			
	Male (M)	dose = 18	1	0.41	63.19	83.70	
		dose = 54	239	98.35			
		dose = 810	3	1.23			
Total		243	99.99				

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Table A.37 : Prescribed daily dose according to trade name and gender for 2005 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Methylphenidate HCl-Douglas®	Female (F)	5 < dose < 10	10	2.55	25.81	37.45
			dose = 10	148	37.85		
			10 < dose < 15	10	2.56		
			dose = 15	39	9.97		
			15 < dose < 20	2	0.52		
			dose = 20	89	22.76		
			20 < dose < 30	8	2.04		
			dose = 30	28	7.16		
			dose = 40	26	6.65		
			40 < dose < 300	30	7.67		
			dose = 300	1	0.26		
		Total		391	99.99		
		Male (M)	5 < dose < 10	30	2.97	21.92	34.30
			dose = 10	398	39.37		
			10 < dose < 20	97	9.60		
			dose = 20	249	24.63		
			20 < dose < 30	29	2.87		
			dose = 30	109	10.78		
			30 < dose < 40	27	2.67		
			dose = 40	31	3.07		
			40 < dose < 60	9	0.90		
			dose = 60	17	1.68		
			60 < dose < 600	14	1.38		
dose = 600	1		0.10				
Total		1011	100.02				
Unspecified (U)	dose = 10	4	100.00	10.00	0.00		
Total		4	100.00				

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Table A.37 : Prescribed daily dose according to trade name and gender for 2005 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Ritalin 10mg Tab®	Female (F)	0< dose <5	4	0.17	23.29	54.80
			dose = 5	64	2.80		
			5< dose <10	20	0.86		
			dose = 10	1237	54.04		
			10< dose <15	29	1.25		
			dose = 15	157	6.86		
			15< dose <20	13	0.55		
			dose = 20	440	19.22		
			20< dose <30	20	0.87		
			dose = 30	115	5.02		
			30< dose <40	13	0.56		
			dose = 40	40	1.75		
			40< dose <50	16	0.69		
			dose = 50	16	0.70		
			dose = 60	26	1.14		
			60< dose <150	9	0.39		
			dose = 150	37	1.62		
		150< dose <1200	32	1.39			
dose = 1200	1	0.04					
	Total			2288	99.88		

Table A.37 : Prescribed daily dose according to trade name and gender for 2005 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)		
2005	Ritalin 10mg Tab®	Male (M)	0.33< dose <5	11	0.21	20.74	39.57		
			dose = 5	158	2.69				
			5< dose <10	31	0.53				
			dose = 10	3063	52.15				
			10< dose <15	53	0.91				
			dose = 15	535	9.11				
			15< dose <20	29	0.47				
			dose = 20	1056	17.98				
			20< dose <30	117	2.01				
			dose = 30	369	6.28				
			30< dose <40	42	0.70				
			dose = 40	120	2.04				
			40< dose <60	52	0.88				
			dose = 60	85	1.45				
			60< dose <150	19	0.32				
			dose = 150	89	1.52				
		150< dose <1050	44	0.76					
		dose = 1050	1	0.02					
			Total			5874	100.03		
			Unspecified (U)	dose = 10	7	70.00	17.00	12.52	
	dose = 20	1		10.00					
	dose = 40	2		20.00					
	Total			10	100.00				

Table A.37 : Prescribed daily dose according to trade name and gender for 2005 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Ritalin LA 20mg Cap®	Female (F)	1< dose <20	6	0.28	29.11	54.00
			dose = 20	2019	92.91		
			20< dose <40	27	1.24		
			dose = 40	55	2.53		
			40< dose <300	10	0.46		
			dose = 300	48	2.21		
			dose = 600	8	0.37		
		Total		2173	100.00		
		Male (M)	3.33< dose <20	21	0.34	27.87	48.37
			dose = 20	6074	93.23		
			20< dose <40	55	0.86		
			dose = 40	183	2.81		
			40< dose <300	35	0.55		
			dose = 300	132	2.03		
		dose = 600	15	0.23			
		Total		6515	100.05		
		Unspecified (U)	dose = 20	18	94.74	21.05	4.59
dose = 40	1		5.26				
Total		19	100.00				

Table A.37 : Prescribed daily dose according to trade name and gender for 2005 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Ritalin LA 30mg Cap®	Female (F)	6< dose <30	2	0.42	42.13	66.40
			dose = 30	450	92.59		
			30< dose <450	22	4.54		
			dose = 450	12	2.47		
		Total		486	100.02		
		Male (M)	4< dose <30	12	0.57	39.85	63.03
			dose = 30	2027	93.45		
			30< dose <60	22	1.01		
			dose = 60	57	2.63		
			60< dose <450	9	0.41		
	dose = 450		40	1.84			
	dose = 900	2	0.09				
	Total		2169	100.00			
Unspecified (U)	dose = 30	12	100.00	30.00	0.00		
Total		12	100.00				
Ritalin LA 40mg Cap®	Female (F)	dose = 40	182	98.38	44.45	45.30	
		40< dose <600	2	1.08			
		dose = 600	1	0.54			
	Total		185	100.00			
	Male (M)	1.33< dose <40	9	1.64	48.70	67.67	
		dose = 40	517	94.69			
		40< dose <600	12	2.20			
		dose = 600	8	1.47			
	Total		546	100.00			
	Unspecified (U)	dose = 30.67	1	33.33	36.89	5.39	
dose = 40		2	66.67				
Total		3	100.00				

Table A.37 : Prescribed daily dose according to trade name and gender for 2005 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Ritalin SR 20mg Tab®	Female (F)	8 < dose < 20	3	0.78	36.47	62.22
			dose = 20	328	84.75		
			20 < dose < 40	3	0.78		
			dose = 40	31	8.01		
			40 < dose < 300	2	0.52		
			dose = 300	20	5.17		
		Total		387	100.01		
		Male (M)	10 < dose < 20	14	1.08	31.24	71.78
			dose = 20	1180	90.35		
			20 < dose < 40	12	0.92		
	dose = 40		43	3.29			
	40 < dose < 300		29	2.22			
	dose = 300		16	1.23			
	300 < dose < 1200		11	0.85			
	dose = 1200	1	0.08				
Total		1306	100.02				
Unspecified (U)	dose = 20	1	100.00	20.00			
Total		1	100.00				
Strattera 10mg Cap®	Female (F)	dose = 9.33	1	2.44	14.81	20.48	
		dose = 10	33	80.49			
		10 < dose < 140	6	14.64			
		dose = 140	1	2.44			
	Total		41	100.01			

Table A.37 : Prescribed daily dose according to trade name and gender for 2005 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)	
2005	Strattera 10mg Cap®	Male (M)	2.33< dose <10	7	5.47	12.23	13.12	
			dose = 10	107	83.59			
			10< dose <20	5	3.90			
			dose = 20	5	3.91			
			20< dose <140	3	2.34			
			dose = 140	1	0.78			
		Total		128	99.99			
	Strattera 18mg Cap®	Female (F)	4.2< dose <18	3	5.66	19.73	8.06	
			dose = 18	43	81.13			
			18< dose <63	6	11.33			
			dose = 63	1	1.89			
			Total		53	100.01		
		Male (M)	4.2< dose <18	5	2.59	21.47	22.12	
			dose = 18	178	91.75			
			18< dose <252	10	5.17			
			dose = 252	1	0.52			
			Total		194	100.03		
		Unspecified (U)	dose = 18	2	100.00	18.00	0.00	
		Total		2	100.00			
	Strattera 25mg Cap®	Female (F)	dose = 25	58	89.23	36.20	58.70	
25< dose <375			6	9.23				
dose = 375			1	1.54				
		Total		65	100.00			

Table A.37 : Prescribed daily dose according to trade name and gender for 2005 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Strattera 25mg Cap®	Male (M)	12.5< dose <25	13	4.34	31.76	36.46
			dose = 25	253	84.62		
			25< dose <50	12	3.99		
			dose = 50	10	3.34		
			50< dose <375	10	3.33		
			dose = 375	1	0.33		
	Total		299	99.95			
	Strattera 40mg Cap®	Female (F)	dose = 40	100	97.09	41.11	6.47
			dose = 74.67	1	0.97		
			dose = 80	2	1.94		
	Total		103	100.00			
	Strattera 40mg Cap®	Male (M)	20< dose <40	11	3.72	49.05	55.24
			dose = 40	258	87.16		
			40< dose <80	6	2.04		
dose = 80			14	4.73			
80< dose <560			4	1.36			
dose = 560			3	1.01			
Total		296	100.02				
	Unspecified (U)	dose = 40	2	100.00	40.00	0.00	
Total			2	100.00			

Table A.37 : Prescribed daily dose according to trade name and gender for 2005 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2005	Strattera 60mg Cap®	Female (F)	dose = 56	8	14.29	59.73	2.76
			dose = 60	47	83.93		
			dose = 77.14	1	1.79		
		Total		56	100.01		
		Male (M)	dose = 56	3	2.14	66.01	65.96
			dose = 60	132	94.29		
			60< dose <840	4	2.85		
			dose = 840	1	0.71		
		Total		140	99.99		

Table A.38 : Prescribed daily dose according to trade name and gender for 2006

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Adaphen 10mg Tab®	Female (F)	5< dose <10	23	6.76	24.78	32.24
			dose = 10	129	37.94		
			10< dose <20	13	3.82		
			dose = 20	101	29.71		
			20< dose <30	2	0.58		
			dose = 30	23	6.76		
			30< dose <60	16	4.7		
			dose = 60	18	5.29		
			dose = 100	1	0.29		
			dose = 150	13	3.82		
	dose = 300	1	0.29				
	Total			340	99.96		
	2006	Adaphen 10mg Tab®	Male (M)	2.67< dose <10	11	1.5	22.42
dose = 10				322	43.69		
10< dose <20				42	5.7		
dose = 20				208	28.22		
20< dose <30				21	2.85		
dose = 30				32	4.34		
30< dose <60				34	4.61		
dose = 60				52	7.06		
dose = 100				1	0.14		
dose = 150				13	1.76		
dose = 300	1	0.14					
Total			737	100.01			

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Table A.38 : Prescribed daily dose according to trade name and gender for 2006 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Adaphen 10mg Tab®	Unspecified (U)	dose = 10	1	100	10.00	0.00
	Total			1	100		
	Adaphen 5mg Tab®	Female (F)	dose = 2.5	1	50	3.75	1.77
			dose = 5	1	50		
	Total			2	100		
	Adaphen 5mg Tab®	Male (M)	dose = 5	3	100	5.00	0.00
	Total			3	100		
	Adaphen XL 20mg Tab®	Female (F)	dose = 20	28	70	26.00	9.28
			dose = 40	12	30		
	Total			40	100		
	Adaphen XL 20mg Tab®	Male (M)	dose = 20	78	91.76	25.65	31.41
			20 < dose < 300	6	7.06		
			dose = 300	1	1.18		
	Total			85	100		
	Concerta 18mg Oros®	Female (F)	dose = 10.8	1	0.15	20.46	20.26
			dose = 18	624	95.56		
			dose = 20	1	0.15		
	dose = 36		12	1.84			
	dose = 45		1	0.15			
	dose = 54		10	1.53			
	dose = 270	4	0.61				
Total			653	99.99			

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Table A.38 : Prescribed daily dose according to trade name and gender for 2006 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Concerta 18mg Oros®	Male (M)	5.4< dose <18	7	0.4	19.58	14.42
			dose = 18	1674	95.88		
			18< dose <36	9	0.51		
			dose = 36	21	1.2		
			dose = 38,57	1	0.06		
			dose = 54	28	1.6		
			dose = 90	1	0.06		
	dose = 270	5	0.29				
	Total			1746	100		
	Concerta 36mg Oros®	Female (F)	18< dose <36	2	0.2	41.66	51.77
			dose = 36	1015	97.88		
			36< dose <540	9	0.87		
			dose = 540	11	1.06		
	Total			1037	100.01		
	Concerta 36mg Oros®	Male (M)	6< dose <36	7	0.23	36.79	16.37
dose = 36			3014	98.75			
36< dose <72			2	0.07			
dose = 72			25	0.82			
dose = 180			1	0.03			
dose = 540			3	0.1			
Total			3052	100			
Concerta 36mg Oros®	Unspecified (U)	dose = 36	15	100	36.00	0.00	
Total			15	100			
Concerta 54mg Oros®	Female (F)	dose = 50.4	2	0.84	53.97	0.33	
		dose = 54	236	99.16			
Total			238	100			

Table A.38 : Prescribed daily dose according to trade name and gender for 2006 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Concerta 54mg Oros®	Male (M)	27< dose <54	7	0.8	55.79	36.34
			dose = 54	861	98.63		
			dose = 108	3	0.34		
			dose = 810	2	0.23		
	Total			873	100		
	Methylphenidate HCl-Douglas®	Female (F)	dose = 5	4	0.94	19.68	17.50
			dose = 10	190	44.71		
			10< dose <20	26	6.12		
			dose = 20	124	29.18		
			20< dose <30	12	2.83		
			dose = 30	36	8.47		
			30< dose <60	8	1.89		
			dose = 60	21	4.94		
	dose = 150	4	0.94				
Total			425	100.02			

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Table A.38 : Prescribed daily dose according to trade name and gender for 2006 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Methylphenidate HCl-Douglas®	Male (M)	2.67 < dose < 10	38	3.08	18.00	10.85
			dose = 10	522	42.34		
			10 < dose < 15	4	0.32		
			dose = 15	115	9.33		
			dose = 15.71	1	0.08		
			dose = 20	285	23.11		
			20 < dose < 25	5	0.41		
			dose = 25	58	4.7		
			25 < dose < 30	5	0.41		
			dose = 30	94	7.62		
			30 < dose < 40	19	1.54		
			dose = 40	50	4.06		
			40 < dose < 60	12	0.97		
			dose = 60	24	1.95		
			dose = 75	1	0.08		
Total			1233	100			
	Methylphenidate HCl-Douglas®	Unspecified (U)	dose = 10	6	100	10.00	0.00
Total				6	100		

Table A.38 : Prescribed daily dose according to trade name and gender for 2006 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Ritalin 10mg Tab®	Female (F)	dose = 1.33	1	0.05	19.28	42.74
			dose = 5	62	3.2		
			5< dose <10	15	0.77		
			dose = 10	1050	54.15		
			10< dose <15	14	0.73		
			dose = 15	133	6.86		
			15< dose <20	6	0.3		
			dose = 20	396	20.42		
			20< dose <25	5	0.26		
			dose = 25	42	2.17		
			dose = 26.67	1	0.05		
			dose = 30	68	3.51		
			30< dose <40	8	0.41		
			dose = 40	28	1.44		
			40< dose <60	36	1.85		
			dose = 60	55	2.84		
			60< dose <1200	18	0.92		
dose = 1200	1	0.05					
Total				1939	99.98		

Table A.38 : Prescribed daily dose according to trade name and gender for 2006 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Ritalin 10mg Tab®	Male (M)	3.33< dose <5	9	0.18	17.20	25.25
			dose = 5	171	3.5		
			5< dose <10	24	0.5		
			dose = 10	2626	53.76		
			10< dose <15	39	0.8		
			dose = 15	411	8.41		
			15< dose <20	22	0.45		
			dose = 20	921	18.85		
			20< dose <30	82	1.68		
			dose = 30	259	5.3		
			30< dose <60	169	3.46		
			dose = 60	111	2.27		
			60< dose <450	37	0.76		
			dose = 450	3	0.06		
			dose = 1200	1	0.02		
Total			4885	100			
	Ritalin 10mg Tab®	Unspecified (U)	dose = 10	4	100	10.00	0.00
Total				4	100		

Table A.38 : Prescribed daily dose according to trade name and gender for 2006 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Ritalin LA 20mg Cap®	Female (F)	5.33< dose <20	7	0.38	23.17	24.69
			dose = 20	1721	93.89		
			20< dose <40	7	0.38		
			dose = 40	49	2.67		
			dose = 60	35	1.91		
			60< dose <300	5	0.27		
			dose = 300	8	0.44		
			dose = 600	1	0.05		
	Total			1833	99.99		
	Ritalin LA 20mg Cap®	Male (M)	0.67< dose <20	8	0.14	23.84	25.68
			dose = 20	5373	93.39		
			20< dose <40	36	0.63		
			dose = 40	125	2.17		
			dose = 42.86	1	0.02		
			dose = 60	160	2.78		
60< dose <300			5	0.09			
dose = 300			45	0.78			
Total			5753	100			
Ritalin LA 20mg Cap®	Unspecified (U)	dose = 20	6	100	20.00	0.00	
Total			6	100			

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Table A.38 : Prescribed daily dose according to trade name and gender for 2006 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Ritalin LA 30mg Cap®	Female (F)	4< dose <30	2	0.38	41.26	52.19
			dose = 30	479	89.87		
			dose = 45	2	0.38		
			dose = 60	29	5.44		
			60< dose <450	17	3.19		
			dose = 450	4	0.75		
	Total			533	100.01		
	Ritalin LA 30mg Cap®	Male (M)	20< dose <30	4	0.2	33.45	28.87
			dose = 30	1857	93.41		
			30< dose <60	16	0.81		
			dose = 60	102	5.13		
			dose = 450	9	0.45		
	Total			1988	100		
	Ritalin LA 30mg Cap®	Unspecified (U)	dose = 30	2	100	30.00	0.00
	Total			2	100		
	Ritalin LA 40mg Cap®	Female (F)	dose = 40	126	97.67	60.00	145.43
			dose = 300	1	0.78		
dose = 1200			2	1.55			
Total			129	100			
Ritalin LA 40mg Cap®	Male (M)	5.33< dose <40	2	0.32	40.95	22.83	
		dose = 40	612	99.19			
		40< dose <600	2	0.33			
		dose = 600	1	0.16			
Total			617	100			

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Table A.38 : Prescribed daily dose according to trade name and gender for 2006 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Ritalin SR 20mg Tab®	Female (F)	dose = 10	6	2.61	27.18	37.17
			dose = 20	191	83.04		
			20< dose <40	5	2.17		
			dose = 40	20	8.7		
			40< dose <300	4	1.74		
			dose = 300	4	1.74		
	Total			230	100		
	Ritalin SR 20mg Tab®	Male (M)	6.67< dose <20	4	0.48	24.12	26.01
			dose = 20	751	89.94		
			dose = 30	7	0.84		
			dose = 40	33	3.95		
			dose = 60	31	3.71		
			60< dose <600	8	0.96		
			dose = 600	1	0.12		
	Total			835	100		
	Strattera 10mg Cap®	Female (F)	2.33< dose <10	10	10	12.46	5.48
			dose = 10	64	64		
			10< dose <20	6	6		
dose = 20			17	17			
20< dose <37.33			2	2			
dose = 37.33			1	1			
Total			100	100			

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Table A.38 : Prescribed daily dose according to trade name and gender for 2006 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Strattera 10mg Cap®	Male (M)	1.67 < dose < 10	6	2.91	13.63	15.20
			dose = 10	170	82.52		
			10 < dose < 20	6	2.92		
			dose = 20	11	5.34		
			20 < dose < 140	11	5.34		
			dose = 140	2	0.97		
	Total			206	100		
	Strattera 18mg Cap®	Female (F)	dose = 16.8	7	5.3	18.96	5.16
			dose = 18	118	89.39		
			18 < dose < 63	6	4.56		
			dose = 63	1	0.76		
	Total			132	100.01		
	Strattera 18mg Cap®	Male (M)	4.2 < dose < 18	14	3.77	19.82	6.73
			dose = 18	321	86.52		
			18 < dose < 36	2	0.54		
			dose = 36	26	7.01		
			36 < dose < 72	7	1.89		
			dose = 72	1	0.27		
	Total			371	100		
	Strattera 25mg Cap®	Female (F)	2.5 < dose < 23.33	5	2.16	27.56	23.82
dose = 23.33			27	11.64			
dose = 25			186	80.17			
25 < dose < 350			13	5.6			
dose = 350			1	0.43			
Total			232	100			

Table A.38 : Prescribed daily dose according to trade name and gender for 2006 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Strattera 25mg Cap®	Male (M)	4.167 < dose < 25	28	3.58	29.83	28.45
			dose = 25	679	86.83		
			25 < dose < 50	14	1.79		
			dose = 50	40	5.12		
			50 < dose < 350	16	2.05		
			dose = 350	5	0.64		
	Total			782	100.01		
	Strattera 25mg Cap®	Unspecified (U)	dose = 25	1	100	25.00	0.00
	Total			1	100		
	Strattera 40mg Cap®	Female (F)	2.67 < dose < 40	27	5.96	49.36	57.29
			dose = 40	379	83.66		
			40 < dose < 80	9	1.99		
			dose = 80	27	5.96		
			80 < dose < 560	6	1.33		
			dose = 560	3	0.66		
			dose = 600	2	0.44		
	Total			453	100		
Strattera 40mg Cap®	Male (M)	4.29 < dose < 40	50	3.92	44.15	23.70	
		dose = 40	1106	86.68			
		40 < dose < 80	23	1.8			
		dose = 80	82	6.43			
		80 < dose < 560	13	1.02			
		dose = 560	2	0.16			
Total			1276	100.01			
Strattera 40mg Cap®	Unspecified (U)	dose = 40	14	100	40.00	0.00	
Total			14	100			

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Table A.38 : Prescribed daily dose according to trade name and gender for 2006 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2006	Strattera 60mg Cap®	Female (F)	54 < dose < 60	16	7.66	84.50	130.73
			dose = 60	177	84.69		
			60 < dose < 120	2	0.96		
			dose = 120	8	3.83		
			dose = 840	6	2.87		
	Total			209	100.01		
	Strattera 60mg Cap®	Male (M)	46.67 < dose < 60	23	4.2	60.81	7.45
			dose = 60	514	93.8		
			60 < dose < 120	5	0.92		
			dose = 120	6	1.09		
	Total			548	100.01		
Strattera 60mg Cap®	Unspecified (U)	dose = 60	12	100	60.00	0.00	
Total			12	100			

Table A.39 : Prescribed daily dose according to trade name and gender for 2007

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Adaphen 10mg Tab®	Female (F)	dose = 5	5	1.53	25.43	17.69
			dose = 10	106	32.52		
			10< dose <20	7	2.15		
			dose = 20	97	29.75		
			20< dose <30	4	1.23		
			dose = 30	32	9.82		
			30< dose <60	22	6.75		
			dose = 60	53	16.26		
	Total			326	100.01		
	Adaphen 10mg Tab®	Male (M)	3.33< dose <10	11	1.62	24.90	19.20
			dose = 10	262	38.47		
			10< dose <20	37	5.43		
			dose = 20	158	23.2		
			20< dose <30	7	1.03		
			dose = 30	50	7.34		
dose = 40			28	4.11			
40< dose <60			15	2.21			
dose = 60			100	14.68			
dose = 80			12	1.76			
dose = 90	1	0.15					
Total			681	100			
	Adaphen 5mg Tab®	Female (F)	dose = 50	1	100	50.00	0.00
Total				1	100		

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Table A.39 : Prescribed daily dose according to trade name and gender for 2007 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Adaphen 5mg Tab®	Male (M)	dose = 5	1	33.33	25.00	22.91
			dose = 20	1	33.33		
			dose = 50	1	33.33		
	Total			3	99.99		
	Adaphen XL 20mg Tab®	Female (F)	dose = 20	11	78.57	28.57	17.03
			dose = 60	3	21.43		
	Total			14	100		
	Adaphen XL 20mg Tab®	Male (M)	dose = 20	52	91.23	22.11	7.25
			dose = 40	4	7.02		
			dose = 60	1	1.75		
	Total			57	100		
	Concerta 18mg Oros®	Female (F)	dose = 10.8	1	0.13	19.72	6.75
			dose = 18	738	92.48		
			18< dose <36	6	0.75		
dose = 36			30	3.76			
36< dose <54			2	0.25			
Total			798	100			
Concerta 18mg Oros®	Male (M)	12< dose <18	2	0.08	18.91	4.98	
		dose = 18	2290	95.66			
		18< dose <36	23	0.96			
		dose = 36	39	1.63			
		36< dose <54	6	0.25			
Total			2394	100			
Concerta 18mg Oros®	Unspecified (U)	dose = 18	1	100	18.00		
Total			1	100			

Table A.39 : Prescribed daily dose according to trade name and gender for 2007 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)	
2007	Concerta 36mg Oros®	Female (F)	12< dose <36	4	0.27	36.68	5.02	
			dose = 36	1427	97.41			
			36< dose <72	6	0.41			
			dose = 72	28	1.91			
	Total				1465	100		
	Concerta 36mg Oros®	Male (M)	12< dose <36	5	0.12	37.30	6.76	
			dose = 36	4048	95.99			
			36< dose <72	16	0.38			
			dose = 72	147	3.49			
			dose = 108	1	0.02			
	Total				4217	100		
	Concerta 54mg Oros®	Female (F)	dose = 54	465	98.94	54.36	4.31	
			dose = 57.86	2	0.43			
			dose = 108	3	0.64			
Total				470	100.01			
Concerta 54mg Oros®	Male (M)	27< dose <54	2	0.14	54.09	2.56		
		dose = 54	1444	99.65				
		dose = 108	3	0.21				
Total				1449	100			
Concerta 54mg Oros®	Unspecified (U)	dose = 54	4	100	54.00	0.00		
Total				4	100			

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Table A.39 : Prescribed daily dose according to trade name and gender for 2007 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Methylphenidate HCl-Douglas®	Female (F)	dose = 5	6	1.7	16.83	10.12
			dose = 10	166	47.03		
			10< dose <20	36	10.19		
			dose = 20	96	27.2		
			20< dose <50	35	9.91		
			dose = 50	8	2.27		
			dose = 60	6	1.7		
	Total			353	100		
	Methylphenidate HCl-Douglas®	Male (M)	5< dose <10	21	2.31	18.24	11.46
			dose = 10	369	40.55		
			10< dose <15	8	0.88		
			dose = 15	119	13.08		
			dose = 16.67	1	0.11		
			dose = 20	226	24.84		
dose = 25			21	2.31			
dose = 30			57	6.26			
30< dose <40			2	0.22			
dose = 40			52	5.71			
40< dose = 60			5	0.55			
dose = 60	29	3.19					
Total			910	100.01			

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Table A.39 : Prescribed daily dose according to trade name and gender for 2007 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Ritalin 10mg Tab®	Female (F)	2.33 < dose < 10	72	4.03	16.49	12.33
			dose = 10	983	54.98		
			10 < dose < 15	9	0.51		
			dose = 15	130	7.27		
			15 < dose < 20	2	0.11		
			dose = 20	351	19.63		
			20 < dose < 30	18	1.01		
			dose = 30	100	5.59		
			30 < dose < 60	56	3.13		
			dose = 60	60	3.36		
			60 < dose < 110	6	0.33		
			dose = 110	1	0.06		
Total				1788	100.01		

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Table A.39 : Prescribed daily dose according to trade name and gender for 2007 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Ritalin 10mg Tab®	Male (M)	3.33< dose <5	6	0.13	15.96	10.99
			dose = 5	177	3.96		
			5< dose <10	10	0.23		
			dose = 10	2431	54.37		
			10< dose <15	50	1.12		
			dose = 15	337	7.54		
			15< dose <20	15	0.33		
			dose = 20	889	19.88		
			20< dose <30	44	0.99		
			dose = 30	230	5.14		
			30< dose <40	9	0.2		
			dose = 40	94	2.1		
			dose = 45	2	0.04		
			dose = 50	41	0.92		
	50< dose <60	12	0.27				
	dose = 60	124	2.77				
	Total				4471	99.99	
	Ritalin 10mg Tab®	Unspecified (U)	dose = 10	2	100	10.00	0.00
Total				2	100		
	Ritalin LA 20mg Cap®	Female (F)	1.33< dose <20	8	0.44	22.02	8.02
			dose = 20	1682	92.06		
			20< dose <40	13	0.71		
			dose = 40	61	3.34		
			40< dose <60	2	0.11		
dose = 60	61	3.34					
Total				1827	100		

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Table A.39 : Prescribed daily dose according to trade name and gender for 2007 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)	
2007	Ritalin LA 20mg Cap®	Male (M)	2.67 < dose < 20	9	0.16	21.74	7.42	
			dose = 20	5178	93.35			
			20 < dose < 40	38	0.69			
			dose = 40	168	3.03			
			40 < dose < 60	4	0.08			
			dose = 60	149	2.69			
		dose = 120	1	0.02				
		Total			5547	100.02		
	Ritalin LA 30mg Cap®	Female (F)	15 < dose < 30	5	0.96	32.05	17.67	
			dose = 30	495	94.83			
			dose = 60	20	3.83			
			dose = 300	2	0.38			
		Total			522	100		
	Ritalin LA 30mg Cap®	Male (M)	2 < dose < 30	28	1.31	31.59	8.61	
			dose = 30	1986	92.76			
30 < dose < 60			18	0.84				
dose = 60			101	4.72				
dose = 120			8	0.37				
	Total			2141	100			
Ritalin LA 40mg Cap®	Female (F)	dose = 40	145	96.67	41.09	6.47		
		dose = 42.86	1	0.67				
		dose = 80	4	2.67				
	Total			150	100.01			
Ritalin LA 40mg Cap®	Male (M)	13.33 < dose < 40	3	0.52	40.46	4.86		
		dose = 40	571	98.11				
		dose = 80	8	1.37				
	Total			582	100			

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Table A.39 : Prescribed daily dose according to trade name and gender for 2007 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Ritalin SR 20mg Tab®	Female (F)	7.33 < dose < 20	2	1.98	23.13	10.74
			dose = 20	89	88.12		
			20 < dose < 60	4	3.96		
			dose = 60	6	5.94		
	Total			101	100		
	Ritalin SR 20mg Tab®	Male (M)	dose = 10	2	0.72	22.51	8.47
			dose = 20	246	89.13		
			dose = 26.09	2	0.72		
			dose = 40	17	6.16		
			dose = 60	9	3.26		
	Total			276	99.99		
	Strattera 10mg Cap®	Female (F)	dose = 10	57	78.08	12.37	5.09
			dose = 18.67	5	6.85		
			dose = 20	10	13.7		
dose = 40			1	1.37			
Total			73	100			
Strattera 10mg Cap®	Male (M)	5 < dose < 10	7	3.89	13.09	10.96	
		dose = 10	153	85			
		10 < dose < 40	6	3.33			
		dose = 40	12	6.67			
		dose = 70	1	0.56			
		dose = 100	1	0.56			
Total			180	100.01			

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Table A.39 : Prescribed daily dose according to trade name and gender for 2007 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Strattera 18mg Cap®	Female (F)	6< dose <18	4	3.54	21.47	12.11
			dose = 18	92	81.42		
			dose = 29.65	1	0.88		
			dose = 36	14	12.39		
			dose = 54	1	0.88		
			dose = 126	1	0.88		
	Total			113	99.99		
	Strattera 18mg Cap®	Male (M)	4.5< dose <18	10	3.1	19.88	9.90
			dose = 18	287	88.85		
			18< dose <36	7	2.17		
			dose = 36	12	3.72		
			36< dose <126	5	1.55		
	dose = 126	2	0.62				
	Total			323	100.01		
	Strattera 25mg Cap®	Female (F)	dose = 23.33	12	4.43	26.97	10.22
dose = 25			243	89.67			
25< dose <70			6	2.21			
dose = 70			8	2.95			
dose = 87.5			1	0.37			
dose = 116.67			1	0.37			
Total			271	100			

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Table A.39 : Prescribed daily dose according to trade name and gender for 2007 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Strattera 25mg Cap®	Male (M)	dose = 23.33	39	6.43	27.00	7.93
			dose = 25	509	83.86		
			25 < dose < 50	18	2.97		
			dose = 50	36	5.93		
			dose = 70	4	0.66		
			dose = 116.67	1	0.16		
	Total			607	100.01		
	Strattera 40mg Cap®	Female (F)	13.33 < dose < 40	28	5.94	42.99	11.37
			dose = 40	405	85.99		
			40 < dose < 80	11	2.34		
			dose = 80	24	5.1		
			80 < dose < 120	2	0.43		
			dose = 120	1	0.21		
	Total			471	100.01		
	Strattera 40mg Cap®	Male (M)	18.67 < dose < 40	65	4.9	44.35	13.41
dose = 40			1101	83.03			
40 < dose < 80			31	2.34			
dose = 80			111	8.37			
80 < dose < 112			8	0.61			
dose = 112			9	0.68			
dose = 120			1	0.08			
Total			1326	100.01			
	Strattera 40mg Cap®	Unspecified (U)	dose = 40	7	100	40.00	0.00
Total				7	100		

Table A.39 : Prescribed daily dose according to trade name and gender for 2007 (continued)

Study period	Trade name	Gender	Daily Dosage (mg)	Number of prescriptions	Percent (%)	Average dose (mg)	Standard deviation (mg)
2007	Strattera 60mg Cap®	Female (F)	30< dose <60	23	8.91	61.97	11.90
			dose = 60	219	84.88		
			60< dose <120	6	2.32		
			dose = 120	10	3.88		
	Total			258	99.99		
	Strattera 60mg Cap®	Male (M)	dose = 56	24	3.59	61.71	10.28
			dose = 60	623	93.12		
			60< dose <120	5	0.75		
			dose = 120	17	2.54		
	Total			669	100		
Strattera 60mg Cap®	Unspecified (U)	dose = 60	2	100	60.00	0.00	
Total			2	100			

Table A.40 : Number of patients according to gender and age groups for the study period 2005 to 2007

Study period	Total number of patients	Gender				Age groups							
		Male		Female		≤ 5 years		5<and≤12 years		12<and≤18 years		> 18 years	
		n	%	n	%	n	%	n	%	n	%	n	%
2005	7,990	5,755	72.03	2,217	27.75	73	0.91	4,284	53.62	2,103	26.32	1,530	19.15
2006	8,575	6,184	72.12	2,380	27.76	79	0.92	4,474	52.17	2,283	26.62	1,739	20.28
2007	7,828	5,549	70.89	2,274	29.05	87	1.11	3,854	49.23	2,143	27.38	1,744	22.28

APPENDIX B

Appendix B

Table B.1: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2005

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient			Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2005	Methylphenidate		Imipramine			6	170.59	45.56	1,023.51
	Methylphenidate		Imipramine			1	243.29	0.00	243.29
	Methylphenidate		Imipramine			18	416.43	101.08	7,495.76
	Methylphenidate	Methylphenidate	Imipramine			1	759.32	0.00	759.32
	Methylphenidate	Methylphenidate	Imipramine			1	157.42	0.00	157.42
	Methylphenidate		Imipramine			26	443.46	72.79	11,530.03
	Methylphenidate		Imipramine			1	618.99	0.00	618.99
	Methylphenidate		Imipramine			1	746.30	0.00	746.30
	Methylphenidate		Imipramine			3	524.16	19.19	1,572.47
	Methylphenidate		Imipramine			26	143.95	60.64	3,742.82
	Methylphenidate		Imipramine			88	314.74	173.86	27,696.82
	Methylphenidate		Imipramine			7	591.54	142.61	4,140.77
	Methylphenidate		Imipramine			4	407.50	41.54	1,629.99
	Methylphenidate	Methylphenidate	Imipramine			7	571.89	119.30	4,003.21
	Methylphenidate	Methylphenidate	Imipramine			1	485.04	0.00	485.04
	Methylphenidate	Methylphenidate	Imipramine	Buspirone		1	748.07	0.00	748.07
	Methylphenidate	Methylphenidate	Imipramine	Clonidine		1	679.65	0.00	679.65
	Methylphenidate		Imipramine	Fluoxetine		56	339.43	39.89	19,008.29
	Methylphenidate		Imipramine	Imipramine		6	466.61	49.23	2,799.66
	Methylphenidate		Imipramine	Imipramine		14	478.00	86.12	6,691.95
Methylphenidate		Imipramine	Lamotrigine	Risperidone	1	947.15	0.00	947.15	

Table B.1 Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2005 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient			Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2005	Methylphenidate		Imipramine	Lamotrigine		26	604.94	26.25	15,728.42
	Methylphenidate		Imipramine	Lamotrigine		5	313.06	0.00	1,565.30
	Methylphenidate		Imipramine	Lamotrigine		4	532.69	15.56	2,130.76
	Methylphenidate		Imipramine	Lamotrigine	Risperidone	1	946.14	0.00	946.14
	Methylphenidate		Imipramine	Risperidone		2	601.35	0.00	1,202.70
	Methylphenidate		Imipramine	Risperidone	Risperidone	2	949.83	5.22	1,899.66
	Methylphenidate		Imipramine	Risperidone		2	529.47	0.00	1,058.94
	Atomoxetine		Imipramine	Risperidone		1	1047.67	0.00	1,047.67
	Atomoxetine	Atomoxetine	Imipramine	Risperidone		1	648.15	0.00	648.15
	Atomoxetine	Atomoxetine	Imipramine			1	1228.03	0.00	1,228.03
	Atomoxetine		Imipramine			4	486.56	203.91	1,946.22
	Atomoxetine		Imipramine			1	622.52	0.00	622.52
	Methylphenidate		Carbamazepine	Imipramine		1	385.38	0.00	385.38
	Methylphenidate		Carbamazepine	Imipramine		1	1042.35	0.00	1,042.35
	Methylphenidate		Escitalopram	Imipramine		1	799.41	0.00	799.41
	Methylphenidate		Escitalopram	Imipramine		1	1189.35	0.00	1,189.35
	Methylphenidate		Imipramine			3	399.71	54.70	1,199.13
	Methylphenidate	Methylphenidate	Imipramine	Imipramine		1	485.04	0.00	485.04
	Methylphenidate		Methysergide	Imipramine		2	1062.18	0.00	2,124.36
	Methylphenidate		Risperidone	Imipramine		8	611.86	43.23	4,894.86
Methylphenidate		Sucrose / phosphoric acid	Imipramine		1	265.74	0.00	265.74	
Methylphenidate		Valproate (sodium)	Imipramine		5	785.16	0.00	3,925.80	
Methylphenidate		Valproic acid	Imipramine		3	615.08	35.05	1,845.25	
Methylphenidate		Valproic acid	Imipramine		2	463.16	26.64	926.32	

Appendix B

Table B.1: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2005 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient			Number of prescriptions	Average cost per prescription (Rand)	Standard deviation (Rand)	Total cost (Rand)
2005	Methylphenidate		Valproic acid	Imipramine	Imipramine	1	559.15	0.00	559.15
	Methylphenidate		Imipramine	Imipramine	Lamotrigine Risperidone	1	946.14	0.00	946.14
	Methylphenidate		Clonidine	Imipramine		2	625.99	10.16	1,251.97
	Methylphenidate		Methysergide	Imipramine		2	994.38	0.00	1,988.76
	Methylphenidate		Risperidone	Risperidone	Imipramine	1	535.54	0.00	535.54
	Methylphenidate		Valproic acid	Valproic acid	Imipramine	2	512.31	3.98	1,024.61
	Methylphenidate		Valproic acid	Valproic acid	Imipramine	1	553.39	0.00	553.39
	Methylphenidate	Atomoxetine	Valproic acid	Valproic acid	Imipramine	1	821.61	0.00	821.61
	Atomoxetine	Atomoxetine	Valproic acid	Valproic acid	Imipramine	1	828.13	0.00	828.13
	Methylphenidate		Amitriptyline			1	204.77	0.00	204.77
	Methylphenidate		Amitriptyline			3	345.40	141.21	1,036.20
	Methylphenidate		Amitriptyline			19	438.83	68.45	8,337.81
	Methylphenidate	Methylphenidate	Amitriptyline			5	656.00	107.82	3,280.00
	Methylphenidate		Amitriptyline			2	508.77	6.55	1,017.53
	Methylphenidate	Methylphenidate	Amitriptyline			1	638.31	0.00	638.31
	Methylphenidate		Amitriptyline			5	142.54	40.33	712.71
	Methylphenidate		Amitriptyline			83	341.34	110.21	28,331.20
	Methylphenidate	Methylphenidate	Amitriptyline			5	561.74	160.77	2,808.68
	Methylphenidate	Methylphenidate	Amitriptyline			1	868.95	0.00	868.95
	Methylphenidate	Methylphenidate	Amitriptyline	Carbamazepine		1	875.64	0.00	875.64
	Methylphenidate		Amitriptyline			19	317.72	18.23	6,036.60
	Methylphenidate		Amitriptyline			5	448.27	16.41	2,241.34
	Methylphenidate		Amitriptyline			6	314.22	3.36	1,885.32
Methylphenidate		Amitriptyline	Amitriptyline		1	293.45	0.00	293.45	
Methylphenidate		Amitriptyline	Carbamazepine		2	604.92	0.00	1,209.84	

Table B.1: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2005 (continued)

Period	Methylphenidate and/or Atomoxetine containing products	Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)	
2005	Methylphenidate		Buspirone	Amitriptyline		6	564.83	27.11	3,388.95	
	Methylphenidate		Buspirone	Amitriptyline		12	440.63	116.97	5,287.58	
	Methylphenidate		Citalopram	Amitriptyline		2	399.48	0.00	798.96	
	Methylphenidate		Escitalopram	Amitriptyline		1	460.44	0.00	460.44	
	Methylphenidate		Escitalopram	Amitriptyline		1	566.86	0.00	566.86	
	Methylphenidate		Fluoxetine	Amitriptyline		1	337.82	0.00	337.82	
	Methylphenidate		Lamotrigine	Amitriptyline		1	492.74	0.00	492.74	
	Methylphenidate		Risperidone	Amitriptyline		1	574.85	0.00	574.85	
	Methylphenidate		Risperidone	Amitriptyline		1	723.08	0.00	723.08	
	Methylphenidate		Valproate (sodium)	Amitriptyline		1	607.54	0.00	607.54	
	Methylphenidate		Valproate (sodium)	Clothiapine	Amitriptyline	1	372.27	0.00	372.27	
	Methylphenidate		Lamotrigine	Fluoxetine	Amitriptyline	1	596.18	0.00	596.18	
	Methylphenidate		Valproate (sodium)	Valproate (sodium)	Amitriptyline	1	518.28	0.00	518.28	
	Methylphenidate		Valproate (sodium)	Fluoxetine	Diazepam	Amitriptyline	1	570.36	0.00	570.36
	Methylphenidate		*			1	758.48	0.00	758.48	
	Methylphenidate		Carbamazepine			6	202.24	95.13	1,213.42	
	Methylphenidate		Carbamazepine			2	590.43	0.00	1,180.86	
	Methylphenidate		Carbamazepine			3	554.32	45.48	1,662.96	
Methylphenidate		Carbamazepine			1	303.45	0.00	303.45		
Methylphenidate		Carbamazepine			4	249.06	112.21	996.23		

Table B.1: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2005 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient			Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2005	Methylphenidate		Carbamazepine			12	425.13	43.50	5,101.51
	Methylphenidate		Carbamazepine			3	555.24	37.92	1,665.71
	Methylphenidate		Carbamazepine			1	594.72	0.00	594.72
	Atomoxetine	Atomoxetine	Carbamazepine			1	773.49	0.00	773.49
	Atomoxetine		Carbamazepine			1	392.96	0.00	392.96
	Atomoxetine		Carbamazepine			3	706.15	40.36	2,118.44
	Atomoxetine		Carbamazepine			2	705.09	0.00	1,410.18
	Methylphenidate		Carbamazepine	Carbamazepine		1	499.89	0.00	499.89
	Methylphenidate		Carbamazepine	Carbamazepine		1	210.23	0.00	210.23
	Methylphenidate		Carbamazepine	Imipramine		1	385.38	0.00	385.38
	Methylphenidate		Carbamazepine	Imipramine		1	1042.35	0.00	1,042.35
	Methylphenidate		Carbamazepine			3	481.45	0.00	1,444.35
	Methylphenidate		Carbamazepine	Sulpiride		1	203.81	0.00	203.81
	Methylphenidate	Methylphenidate	Amitriptyline	Carbamazepine		1	875.64	0.00	875.64
	Methylphenidate		Amitriptyline	Carbamazepine		2	604.92	0.00	1,209.84
	Methylphenidate		Carbamazepine	Carbamazepine		1	499.89	0.00	499.89
	Methylphenidate		Carbamazepine	Carbamazepine		1	210.23	0.00	210.23
	Methylphenidate		Citalopram	Carbamazepine		1	268.11	0.00	268.11
	Methylphenidate		Clonazepam	Carbamazepine		1	492.17	0.00	492.17
	Methylphenidate		Lorazepam	Carbamazepine		1	552.16	0.00	552.16
Methylphenidate		Phenytoin	Carbamazepine		1	365.30	0.00	365.30	
Methylphenidate		Risperidone	Carbamazepine		3	391.13	23.08	1,173.39	

Table B.1: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2005 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient			Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2005	Methylphenidate		Risperidone	Carbamazepine		5	556.57	62.61	2,782.87
	Atomoxetine	Atomoxetine	Risperidone	Carbamazepine		1	1086.80	0.00	1,086.80
	Atomoxetine	Atomoxetine	Risperidone	Carbamazepine		1	1123.72	0.00	1,123.72
	Atomoxetine	Atomoxetine	Risperidone	Carbamazepine		1	952.70	0.00	952.70
	Atomoxetine		Risperidone	Carbamazepine		1	787.40	0.00	787.40
	Atomoxetine		Risperidone	Carbamazepine		2	934.78	208.42	1,869.55
	Atomoxetine		Risperidone	Carbamazepine		1	1086.73	0.00	1,086.73
	Methylphenidate		Zopiclone	Reboxetine	Carbamazepine	1	960.22	0.00	960.22
	Methylphenidate		Clomipramine			1	282.66	0.00	282.66
	Methylphenidate		Clomipramine			1	450.76	0.00	450.76
	Methylphenidate		Clomipramine			3	503.87	36.06	1,511.61
	Methylphenidate		Clomipramine			4	331.07	46.49	1,324.28
	Methylphenidate		Clomipramine			1	472.68	0.00	472.68
	Methylphenidate		Clomipramine			5	428.47	15.33	2,142.36
	Methylphenidate		Clomipramine			3	724.30	211.56	2,172.91
	Methylphenidate		Clomipramine			1	629.07	0.00	629.07
	Methylphenidate		Clomipramine			1	443.15	0.00	443.15
	Methylphenidate		Clomipramine	Clomipramine		2	468.77	0.00	937.54
	Methylphenidate		Clomipramine	Clomipramine		2	350.86	0.00	701.72
	Methylphenidate		Phenytoin	Carbamazepine		1	365.30	0.00	365.30
	Methylphenidate		Phenytoin			1	536.57	0.00	536.57
Methylphenidate		Paroxetine	Phenytoin	Valproate (sodium)	1	898.03	0.00	898.03	
Methylphenidate		Sulpiride	Trimipramine		1	682.22	0.00	682.22	

* Midazolam, Chlorpromazepine, Chlorpromazepine, Diazepam, Diazepam and Amitriptyline.

Table B.2: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2006

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2006	Methylphenidate		Amitriptyline				85	311.04	92.76	26,438.00
	Methylphenidate		Amitriptyline				44	442.50	69.47	19,470.21
	Methylphenidate		Amitriptyline				15	317.12	9.50	4,756.82
	Methylphenidate		Amitriptyline				9	403.02	13.54	3,627.22
	Methylphenidate	Methylphenidate	Amitriptyline				5	600.83	162.22	3,004.17
	Methylphenidate		Amitriptyline				4	496.21	21.95	1,984.84
	Methylphenidate		Amitriptyline				4	138.29	42.23	553.15
	Methylphenidate	Methylphenidate	Amitriptyline				3	465.43	1.78	1,396.30
	Methylphenidate		Amitriptyline				2	231.64	190.14	463.28
	Methylphenidate		Amitriptyline				2	275.76	0.00	551.52
	Methylphenidate		Amitriptyline	Amitriptyline			1	330.12	0.00	330.12
	Methylphenidate		Amitriptyline				1	239.01	0.00	239.01
	Atomoxetine		Amitriptyline				1	596.85	0.00	596.85
	Atomoxetine	Atomoxetine	Amitriptyline				1	801.63	0.00	801.63
	Atomoxetine		Amitriptyline				1	636.33	0.00	636.33
	Methylphenidate		Amitriptyline	Amitriptyline			1	330.12	0.00	330.12
	Methylphenidate		Amitriptyline				1	193.72	0.00	193.72
	Methylphenidate		Amitriptyline				1	446.41	0.00	446.41
	Methylphenidate		Amitriptyline				1	557.93	0.00	557.93
	Methylphenidate		Buspirone	Amitriptyline			5	398.43	31.75	1,992.14
Methylphenidate		Buspirone	Amitriptyline			4	547.63	12.40	2,190.53	

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Table B.2: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2006 (continued)

Period	Methylphenidate and/or Atomoxetine containing products	Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)	
2006	Atomoxetine		Carbamazepine	Amitriptyline			1	897.98	0.00	897.98
	Methylphenidate		Amitriptyline				1	557.07	0.00	557.07
	Methylphenidate		Citalopram	Amitriptyline			4	412.46	62.64	1,649.82
	Methylphenidate		Citalopram	Amitriptyline			1	590.88	0.00	590.88
	Methylphenidate		Citalopram	Amitriptyline			1	591.66	0.00	591.66
	Methylphenidate		Amitriptyline				1	147.51	0.00	147.51
	Methylphenidate		Amitriptyline				1	345.21	0.00	345.21
	Methylphenidate		Amitriptyline				1	447.48	0.00	447.48
	Methylphenidate		Duloxetine hydrochloride	Amitriptyline			3	610.62	0.00	1,831.86
	Methylphenidate		Amitriptyline				1	385.84	0.00	385.84
	Methylphenidate		Amitriptyline				2	492.70	19.95	985.39
	Methylphenidate		Amitriptyline				1	357.04	0.00	357.04
	Methylphenidate		Amitriptyline				1	845.99	0.00	845.99
	Methylphenidate		Amitriptyline				1	767.77	0.00	767.77
	Methylphenidate		Amitriptyline				1	156.04	0.00	156.04
	Methylphenidate		Risperidone	Amitriptyline			2	419.46	0.00	838.92
	Methylphenidate		Risperidone	Amitriptyline			2	723.07	0.00	1,446.14
	Methylphenidate		Valproate (sodium)	Amitriptyline			7	466.47	30.43	3,265.31
	Methylphenidate		Valproate (sodium)	Amitriptyline			2	526.40	0.00	1,052.80
	Methylphenidate		Valproate (sodium)	Amitriptyline			2	636.93	0.00	1,273.86

Table B.2: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2006 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient					Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2006	Methylphenidate		Valproate (sodium)	Amitriptyline				1	304.93	0.00	304.93
	Methylphenidate		Duloxetine hydrochloride	Duloxetine hydrochloride	Amitriptyline			1	529.23	0.00	529.23
	Methylphenidate		Lamotrigine	Flunarizine	Amitriptyline			1	841.44	0.00	841.44
	Methylphenidate		Amitriptyline					2	641.75	19.54	1,283.49
	Methylphenidate		Amitriptyline					1	575.76	0.00	575.76
	Methylphenidate		Valproate (sodium)	Valproate (sodium)	Amitriptyline			1	662.37	0.00	662.37
	Methylphenidate		Lamotrigine		Flunarizine	Amitriptyline		1	1268.98	0.00	1,268.98
	Methylphenidate		Amitriptyline	Flunarizine				1	1348.47	0.00	1,348.47
	Methylphenidate		Escitalopram	Tolteradine	Amitriptyline			1	1279.13	0.00	1,279.13
	Methylphenidate		Alprazolam	Escitalopram	Amitriptyline		^a	1	2146.63	0.00	2,146.63
	Methylphenidate		Imipramine					59	349.41	62.90	20,615.36
	Methylphenidate		Imipramine					53	219.83	100.06	11,650.99
	Methylphenidate		Imipramine					24	470.42	47.92	11,289.96
	Methylphenidate		Imipramine					21	154.43	59.21	3,242.96
	Methylphenidate		Imipramine					19	456.10	177.30	8,665.83
	Methylphenidate		Imipramine					13	149.44	74.54	1,942.72
	Methylphenidate	Methylphenidate	Imipramine					9	885.72	19.44	7,971.48
	Methylphenidate		Imipramine					9	595.47	24.66	5,359.23
	Methylphenidate		Imipramine					7	456.73	33.46	3,197.09
	Methylphenidate		Imipramine					4	401.70	268.23	1,606.80
Methylphenidate	Methylphenidate	Imipramine					4	276.75	174.97	1,106.99	
Atomoxetine		Imipramine					4	646.44	18.62	2,585.76	

Table B.2: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2006 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)	
2006	Methylphenidate		Imipramine				3	326.53	11.67	979.58	
	Methylphenidate	Atomoxetine	Imipramine				2	1008.77	26.33	2,017.54	
	Methylphenidate		Imipramine				1	228.19	0.00	228.19	
	Methylphenidate	Methylphenidate	Imipramine				1	1004.14	0.00	1,004.14	
	Methylphenidate	Methylphenidate	Imipramine				1	390.61	0.00	390.61	
	Methylphenidate	Methylphenidate	Imipramine				1	759.96	0.00	759.96	
	Atomoxetine		Imipramine				1	618.51	0.00	618.51	
	Atomoxetine		Imipramine				1	657.27	0.00	657.27	
	Atomoxetine		Imipramine				1	597.41	0.00	597.41	
	Methylphenidate	Methylphenidate	Imipramine				1	393.17	0.00	393.17	
	Methylphenidate		Imipramine				1	158.97	0.00	158.97	
	Methylphenidate		Imipramine				4	538.72	4.30	2,154.88	
	Methylphenidate		Imipramine				3	392.47	9.53	1,177.41	
	Methylphenidate		Imipramine				1	342.48	0.00	342.48	
	Methylphenidate		Imipramine				1	583.30	0.00	583.30	
	Methylphenidate		Imipramine				1	888.26	0.00	888.26	
	Methylphenidate		Imipramine	Imipramine				3	466.53	0.00	1,399.59
	Methylphenidate	Methylphenidate	Imipramine	Imipramine				2	456.56	0.00	913.12
	Methylphenidate		Imipramine	Imipramine				1	389.37	0.00	389.37
	Methylphenidate		Imipramine	Imipramine				1	228.05	0.00	228.05
Methylphenidate		Imipramine	Imipramine				1	480.59	0.00	480.59	
Methylphenidate		Imipramine	Imipramine				1	100.11	0.00	100.11	
Methylphenidate		Imipramine					1	392.80	0.00	392.80	

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Table B.2: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2006 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2006	Methylphenidate		Imipramine				2	394.58	0.00	789.16
	Methylphenidate		Imipramine				1	47.99	0.00	47.99
	Methylphenidate		Imipramine				1	578.50	0.00	578.50
	Methylphenidate		Imipramine				2	395.07	10.53	790.13
	Methylphenidate		Imipramine	Risperidone			6	444.24	36.31	2,665.41
	Methylphenidate		Imipramine	Risperidone			4	529.47	0.00	2,117.88
	Methylphenidate		Imipramine	Risperidone			2	311.84	0.00	623.68
	Methylphenidate		Imipramine	Risperidone			1	551.38	0.00	551.38
	Methylphenidate		Imipramine				1	803.61	0.00	803.61
	Methylphenidate		Imipramine				1	691.42	0.00	691.42
	Methylphenidate		Imipramine				2	0.00	0.00	-
	Methylphenidate		Imipramine	Risperidone			1	1112.90	0.00	1,112.90
	Methylphenidate	Methylphenidate	Imipramine	Carbamazepine			1	943.90	0.00	943.90
	Methylphenidate		Imipramine			f	1	844.90	0.00	844.90
	Methylphenidate		Imipramine				1	518.38	0.00	518.38
	Methylphenidate		Imipramine				1	306.52	0.00	306.52
	Methylphenidate		Carbamazepine	Imipramine			2	294.31	0.00	588.62
	Methylphenidate		Carbamazepine	Imipramine			1	132.46	0.00	132.46
	Methylphenidate		Carbamazepine	Imipramine			1	693.44	0.00	693.44
	Methylphenidate		Carbamazepine	Imipramine	Imipramine		1	913.58	0.00	913.58
Methylphenidate		Citalopram	Imipramine	Imipramine		1	192.64	0.00	192.64	
Methylphenidate		Clonidine	Imipramine			1	446.52	0.00	446.52	

Table B.2: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2006 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2006	Methylphenidate		Imipramine				1	698.32	0.00	698.32
	Methylphenidate		Imipramine				1	466.12	0.00	466.12
	Methylphenidate		Escitalopram	Imipramine			1	799.41	0.00	799.41
	Methylphenidate		Imipramine	Imipramine			3	466.53	0.00	1,399.59
	Methylphenidate	Methylphenidate	Imipramine	Imipramine			2	456.56	0.00	913.12
	Methylphenidate		Imipramine	Imipramine			1	389.37	0.00	389.37
	Methylphenidate		Imipramine	Imipramine			1	228.05	0.00	228.05
	Methylphenidate		Imipramine	Imipramine			1	480.59	0.00	480.59
	Methylphenidate		Imipramine	Imipramine			1	100.11	0.00	100.11
	Methylphenidate		Imipramine				1	1024.67	0.00	1,024.67
	Methylphenidate		Lamotrigine	Imipramine			1	626.33	0.00	626.33
	Methylphenidate		Lamotrigine	Imipramine			1	734.18	0.00	734.18
	Methylphenidate		Imipramine				2	571.07	0.00	1,142.14
	Methylphenidate		Imipramine				1	346.52	0.00	346.52
	Methylphenidate		Imipramine				1	346.37	0.00	346.37
	Methylphenidate		Risperidone	Imipramine			2	681.90	0.00	1,363.80
	Methylphenidate		Risperidone	Imipramine			1	0.00	0.00	-
	Methylphenidate		Sulpiride	Imipramine	Lamotrigine		3	502.65	24.02	1,507.95
	Methylphenidate		Imipramine				1	389.72	0.00	389.72
	Methylphenidate		Valproate (sodium)	Imipramine			6	785.16	0.00	4,710.96
Methylphenidate		Valproate (sodium)	Imipramine			3	842.16	0.00	2,526.48	
Methylphenidate		Valproate (sodium)	Imipramine			1	696.15	0.00	696.15	
Methylphenidate		Valproic acid	Imipramine			2	647.51	19.60	1,295.02	

Table B.2: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2006 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2006	Methylphenidate		Imipramine				1	734.92	0.00	734.92
	Methylphenidate		Imipramine				1	197.54	0.00	197.54
	Methylphenidate		Risperidone	Carbamazepine	Imipramine		1	1060.36	0.00	1,060.36
	Methylphenidate	Methylphenidate	Risperidone	Carbamazepine	Imipramine		1	1252.80	0.00	1,252.80
	Methylphenidate		Imipramine				1	265.83	0.00	265.83
	Methylphenidate		Imipramine				1	1125.50	0.00	1,125.50
	Methylphenidate		Imipramine	Risperidone			1	0.00	0.00	-
	Methylphenidate		Imipramine				1	330.86	0.00	330.86
	Methylphenidate		Carbamazepine	Imipramine	Imipramine		1	913.58	0.00	913.58
	Methylphenidate		Citalopram	Imipramine	Imipramine		1	192.64	0.00	192.64
	Methylphenidate		Lamotrigine	Imipramine			2	570.37	14.62	1,140.74
	Methylphenidate		Valproic acid	Imipramine			1	632.06	0.00	632.06
	Methylphenidate	Atomoxetine	Valproic acid	Valproic acid	Imipramine		1	989.52	0.00	989.52
	Methylphenidate		Valproic acid	Valproic acid	Imipramine		1	276.80	0.00	276.80
	Methylphenidate		Imipramine				1	370.76	0.00	370.76
	Methylphenidate		Imipramine				2	1299.23	0.00	2,598.46
	Methylphenidate		Imipramine				3	1187.37	139.19	3,562.11
	Methylphenidate		Imipramine				3	1486.60	65.15	4,459.79
	Atomoxetine		Carbamazepine				21	752.14	177.24	15,794.98
	Methylphenidate		Carbamazepine				13	410.95	163.67	5,342.29
Methylphenidate		Carbamazepine				3	668.61	76.24	2,005.84	

Appendix B

Table B.2: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2006 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient			Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2006	Methylphenidate		Carbamazepine			3	281.95	111.40	845.84
	Methylphenidate		Carbamazepine			3	543.91	65.96	1,631.72
	Atomoxetine		Carbamazepine			3	587.75	242.24	1,763.26
	Atomoxetine		Carbamazepine			3	785.73	146.51	2,357.20
	Methylphenidate		Carbamazepine			2	241.64	0.31	483.28
	Methylphenidate		Carbamazepine			2	556.95	64.54	1,113.89
	Methylphenidate		Carbamazepine			2	273.77	41.98	547.53
	Methylphenidate	Methylphenidate	Carbamazepine			1	736.76	0.00	736.76
	Methylphenidate		Carbamazepine			1	626.68	0.00	626.68
	Methylphenidate	Methylphenidate	Carbamazepine			1	613.55	0.00	613.55
	Atomoxetine	Atomoxetine	Carbamazepine			1	781.86	0.00	781.86
	Atomoxetine		Carbamazepine	Amitriptyline		1	897.98	0.00	897.98
	Methylphenidate		Carbamazepine	Carbamazepine		2	641.71	0.00	1,283.42
	Atomoxetine		Carbamazepine	Carbamazepine		1	705.09	0.00	705.09
	Methylphenidate		Carbamazepine	Imipramine		2	294.31	0.00	588.62
	Methylphenidate		Carbamazepine	Imipramine		1	132.46	0.00	132.46
	Methylphenidate		Carbamazepine	Imipramine		1	693.44	0.00	693.44
	Methylphenidate		Carbamazepine			3	452.23	1.72	1,356.68
	Methylphenidate		Carbamazepine	Sertraline		1	857.35	0.00	857.35
	Atomoxetine		Carbamazepine			1	955.56	0.00	955.56
Methylphenidate		Carbamazepine	Imipramine	Imipramine	1	913.58	0.00	913.58	
Atomoxetine		Carbamazepine	Topiramate	Topiramate	1	1502.19	0.00	1,502.19	
Methylphenidate		Citalopram	Carbamazepine		1	308.81	0.00	308.81	
Atomoxetine		Citalopram	Carbamazepine	Topiramate	Topiramate	1	1566.92	0.00	1,566.92

Table B.2: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2006 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2006	Atomoxetine		Clomipramine	Carbamazepine			6	130.04	318.52	780.22
	Methylphenidate		Escitalopram	Carbamazepine			1	587.28	0.00	587.28
	Atomoxetine		Carbamazepine				1	348.92	0.00	348.92
	Atomoxetine		Carbamazepine				1	889.25	0.00	889.25
	Atomoxetine		Carbamazepine				1	970.51	0.00	970.51
	Methylphenidate		Carbamazepine				1	634.97	0.00	634.97
	Atomoxetine		Risperidone	Carbamazepine			15	925.43	70.44	13,881.40
	Atomoxetine		Risperidone	Carbamazepine			4	921.12	161.41	3,684.46
	Atomoxetine		Risperidone	Carbamazepine			3	1038.83	41.48	3,116.49
	Methylphenidate		Risperidone	Carbamazepine			2	601.40	3.27	1,202.80
	Methylphenidate		Risperidone	Carbamazepine			1	540.63	0.00	540.63
	Methylphenidate		Risperidone	Carbamazepine			1	737.29	0.00	737.29
	Methylphenidate		Risperidone	Carbamazepine			1	771.48	0.00	771.48
	Methylphenidate		Risperidone	Carbamazepine			1	376.01	0.00	376.01
	Atomoxetine	Atomoxetine	Risperidone	Carbamazepine			1	666.67	0.00	666.67
	Atomoxetine		Risperidone	Carbamazepine			1	882.74	0.00	882.74
	Atomoxetine	Atomoxetine	Risperidone	Carbamazepine			1	991.46	0.00	991.46
	Atomoxetine	Atomoxetine	Risperidone	Carbamazepine			1	986.50	0.00	986.50
	Atomoxetine	Atomoxetine	Risperidone	Carbamazepine			1	1429.47	0.00	1,429.47
	Atomoxetine		Risperidone	Carbamazepine			1	1086.41	0.00	1,086.41
Methylphenidate		Risperidone	Carbamazepine	Imipramine		1	1060.36	0.00	1,060.36	
Methylphenidate	Methylphenidate	Risperidone	Carbamazepine	Imipramine		1	1252.80	0.00	1,252.80	
Methylphenidate		Sertraline	Carbamazepine			1	0.00	0.00	-	

Table B.2: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2006 (continued)

Period	Methylphenidate and/or Atomoxetine containing products	Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2006	Methylphenidate		Carbamazepine			1	820.28	0.00	820.28
	Methylphenidate		Citalopram	Domperidone	Carbamazepine	1	822.20	0.00	822.20
	Atomoxetine		Risperidone	Risperidone	Carbamazepine	1	915.99	0.00	915.99
	Methylphenidate		Risperidone	Carbamazepine		1	1149.07	0.00	1,149.07
	Methylphenidate	Methylphenidate	Imipramine	Sertraline	Carbamazepine	1	943.90	0.00	943.90
	Methylphenidate		Clomipramine			3	395.87	33.51	1,187.60
	Methylphenidate		Clomipramine			2	567.28	31.17	1,134.56
	Atomoxetine		Clomipramine			2	610.00	6.89	1,220.00
	Methylphenidate		Clomipramine			1	462.04	0.00	462.04
	Methylphenidate		Clomipramine			1	693.52	0.00	693.52
	Atomoxetine		Clomipramine			1	676.76	0.00	676.76
	Atomoxetine		Clomipramine	Carbamazepine		6	130.04	318.52	780.22
	Methylphenidate		Clomipramine	Clomipramine		1	468.77	0.00	468.77
	Methylphenidate	^a	Clomipramine	Clomipramine		1	465.64	0.00	465.64
	Methylphenidate		Clomipramine	Modafinil	Zolpidem	1	1244.01	0.00	1,244.01
	Methylphenidate		Clomipramine	Clomipramine		1	468.77	0.00	468.77
	Methylphenidate	^a	Clomipramine	Clomipramine		1	465.64	0.00	465.64
	Methylphenidate		Clomipramine			1	1071.23	0.00	1,071.23
	Methylphenidate		Trimipramine			2	332.74	122.27	665.48
	Methylphenidate		Trimipramine			1	400.19	0.00	400.19
Methylphenidate		Loprazolam	Trimipramine		1	489.64	0.00	489.64	
Methylphenidate		Midazolam	Trimipramine		1	373.65	0.00	373.65	

Table B.2: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2006 (continued)

a Flupenthixol; Bromazepam; Zolpidem

Table B.3: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2007

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2007	Methylphenidate	Methylphenidate	Amitriptyline				1	353.33	0.00	353.33
	Methylphenidate		Amitriptyline				7	421.85	12.60	2952.97
	Methylphenidate	Methylphenidate	Amitriptyline				1	631.88	0.00	631.88
	Methylphenidate		Amitriptyline				46	459.21	65.31	21123.76
	Methylphenidate	Methylphenidate	Amitriptyline				8	537.13	34.54	4297.07
	Methylphenidate	Methylphenidate	Amitriptyline				1	793.35	0.00	793.35
	Methylphenidate		Amitriptyline				11	493.88	137.92	5432.66
	Methylphenidate		Amitriptyline				4	178.18	54.85	712.73
	Methylphenidate		Amitriptyline				87	303.41	101.15	26396.89
	Methylphenidate	Methylphenidate	Amitriptyline				8	465.01	32.41	3720.09
	Methylphenidate	Methylphenidate	Amitriptyline				1	547.93	0.00	547.93
	Methylphenidate		Amitriptyline				16	334.06	22.98	5344.98
	Methylphenidate		Amitriptyline				1	595.05	0.00	595.05
	Atomoxetine	Atomoxetine	Amitriptyline				1	1166.32	0.00	1166.32
	Atomoxetine		Amitriptyline				4	633.43	0.00	2533.72
	Atomoxetine		Amitriptyline				4	613.96	22.48	2455.84
	Methylphenidate		Alprazolam	Amitriptyline			1	511.37	0.00	511.37
	Methylphenidate	Methylphenidate	Amitriptyline				1	520.32	0.00	520.32
Methylphenidate		Buspirone	Amitriptyline			1	638.20	0.00	638.20	

Table B.3: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2007 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2007	Methylphenidate	Methylphenidate	Buspirone	Amitriptyline			1	654.66	0.00	654.66
	Methylphenidate		Buspirone	Amitriptyline			1	606.14	0.00	606.14
	Methylphenidate		Buspirone	Amitriptyline			3	423.09	33.30	1269.27
	Methylphenidate		Carbamazepine	Amitriptyline			1	1036.09	0.00	1036.09
	Methylphenidate		Citalopram	Amitriptyline			2	338.24	0.00	676.48
	Methylphenidate		Citalopram	Amitriptyline			1	538.28	0.00	538.28
	Methylphenidate		Citalopram	Amitriptyline			1	651.43	0.00	651.43
	Methylphenidate		Citalopram	Amitriptyline			1	481.67	0.00	481.67
	Methylphenidate		Citalopram	Amitriptyline			1	517.93	0.00	517.93
	Methylphenidate		Citalopram	Amitriptyline			4	451.57	139.83	1806.26
	Methylphenidate		Amitriptyline				2	475.02	0.00	950.04
	Atomoxetine		Fluoxetine	Amitriptyline			2	668.03	0.00	1336.06
	Methylphenidate		Amitriptyline				1	397.23	0.00	397.23
	Methylphenidate		Amitriptyline				1	377.22	0.00	377.22
	Methylphenidate		Amitriptyline				1	85.20	0.00	85.20
	Methylphenidate		Paroxetine	Amitriptyline			3	502.50	25.58	1507.51
	Methylphenidate		Paroxetine	Amitriptyline			5	601.90	21.31	3009.51
	Methylphenidate		Amitriptyline				1	414.58	0.00	414.58
	Methylphenidate		Risperidone	Amitriptyline			8	675.16	7.86	5401.30
	Methylphenidate	Methylphenidate	Risperidone	Amitriptyline			1	705.24	0.00	705.24
Methylphenidate		Amitriptyline				1	618.55	0.00	618.55	
Methylphenidate		Topiramate	Amitriptyline			1	430.54	0.00	430.54	

Table B.3: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2007 (continued)

Period	Methylphenidate and/or Atomoxetine containing products	Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2007	Methylphenidate	Valproate (sodium)	Amitriptyline			1	544.59	0.00	544.59
	Methylphenidate	Valproate (sodium)	Amitriptyline			7	443.15	306.60	3102.05
	Methylphenidate	Valproate (sodium)	Amitriptyline			1	304.24	0.00	304.24
	Methylphenidate	Valproate (sodium)	Amitriptyline			1	305.36	0.00	305.36
	Methylphenidate	Valproate (sodium)	Amitriptyline			3	454.88	1.99	1364.65
	Methylphenidate	Amitriptyline				1	476.75	0.00	476.75
	Methylphenidate	Paroxetine	Amitriptyline			1	849.12	0.00	849.12
	Methylphenidate	Citalopram	Amitriptyline			1	726.13	0.00	726.13
	Methylphenidate	Amitriptyline				1	335.92	0.00	335.92
	Methylphenidate	Paroxetine	Amitriptyline			1	658.19	0.00	658.19
	Methylphenidate	Amitriptyline				1	525.67	0.00	525.67
	Methylphenidate	Paroxetine	Pramipexole	Amitriptyline		1	799.19	0.00	799.19
	Methylphenidate	Topiramate	Amitriptyline			1	198.20	0.00	198.20
	Methylphenidate	Amitriptyline				1	763.62	0.00	763.62
	Methylphenidate	Zolpidem	Amitriptyline			1	794.38	0.00	794.38
	Methylphenidate	Escitalopram	Amitriptyline			1	1537.30	0.00	1537.30
	Methylphenidate	Amitriptyline				1	493.51	0.00	493.51
	Methylphenidate	Amitriptyline				1	677.93	0.00	677.93
Methylphenidate	Imipramine				8	74.18	60.64	593.41	
Methylphenidate	Imipramine				16	399.05	204.55	6384.87	

Table B.3: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2007 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2007	Methylphenidate	Methylphenidate	Imipramine				1	608.22	0.00	608.22
	Methylphenidate		Imipramine				36	469.41	72.92	16898.67
	Methylphenidate	Atomoxetine	Imipramine				2	1140.97	2.97	2281.94
	Methylphenidate		Imipramine				11	529.33	16.64	5822.66
	Methylphenidate		Imipramine				4	179.56	34.60	718.24
	Methylphenidate		Imipramine				67	222.54	84.46	14910.46
	Methylphenidate	Methylphenidate	Imipramine				8	440.41	76.58	3523.29
	Methylphenidate	Methylphenidate	Imipramine				1	651.39	0.00	651.39
	Methylphenidate		Imipramine				46	344.37	76.37	15840.96
	Methylphenidate	Methylphenidate	Imipramine				1	911.41	0.00	911.41
	Methylphenidate		Imipramine				7	348.71	243.88	2441.00
	Methylphenidate	Atomoxetine	Imipramine				1	380.97	0.00	380.97
	Methylphenidate		Imipramine				15	628.06	50.27	9420.92
	Atomoxetine		Imipramine				1	51.17	0.00	51.17
	Atomoxetine	Atomoxetine	Imipramine				1	845.58	0.00	845.58
	Atomoxetine	Atomoxetine	Imipramine				1	1068.45	0.00	1068.45
	Atomoxetine		Imipramine				4	493.66	233.97	1974.65
	Atomoxetine		Imipramine				4	635.87	33.88	2543.49
	Atomoxetine	Atomoxetine	Imipramine				1	789.12	0.00	789.12
	Atomoxetine	Atomoxetine	Imipramine				1	750.36	0.00	750.36
	Atomoxetine		Imipramine				6	712.05	22.12	4272.28
	Methylphenidate		Imipramine				1	477.51	0.00	477.51
Atomoxetine		Imipramine				1	719.79	0.00	719.79	
Methylphenidate		Imipramine	Buspirone			2	519.60	0.00	1039.20	

Table B.3: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2007 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2007	Methylphenidate		Imipramine				2	496.43	18.37	992.86
	Methylphenidate		Imipramine				1	447.58	0.00	447.58
	Methylphenidate		Imipramine	Imipramine			3	446.14	8.17	1338.43
	Methylphenidate		Imipramine	Imipramine			1	498.15	0.00	498.15
	Methylphenidate		Imipramine	Imipramine			1	196.41	0.00	196.41
	Methylphenidate		Imipramine	Imipramine			1	408.17	0.00	408.17
	Methylphenidate		Imipramine				1	497.16	0.00	497.16
	Methylphenidate		Imipramine	Lamotrigine			1	542.98	0.00	542.98
	Methylphenidate		Imipramine				3	358.43	9.75	1075.29
	Atomoxetine	Atomoxetine	Imipramine				1	0.00	0.00	0.00
	Atomoxetine		Imipramine				1	0.00	0.00	0.00
	Methylphenidate		Imipramine				1	0.00	0.00	0.00
	Methylphenidate		Imipramine				1	371.39	0.00	371.39
	Methylphenidate		Imipramine	Risperidone			6	637.67	136.23	3826.04
	Methylphenidate		Imipramine				1	831.56	0.00	831.56
	Methylphenidate		Imipramine				1	286.95	0.00	286.95
	Methylphenidate		Imipramine				1	636.62	0.00	636.62
	Methylphenidate	Methylphenidate	Imipramine	Sertraline	Carbamazepine		1	1030.70	0.00	1030.70
	Methylphenidate		Imipramine				1	235.80	0.00	235.80
	Methylphenidate		Bupirone	Imipramine			1	591.73	0.00	591.73
Methylphenidate		Desloratadine	Imipramine			2	688.45	0.00	1376.90	
Methylphenidate		Desloratadine	Imipramine			1	529.84	0.00	529.84	

Table B.3: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2007 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2007	Methylphenidate		Imipramine				1	1160.11	0.00	1160.11
	Methylphenidate		Imipramine				1	559.85	0.00	559.85
	Methylphenidate		Escitalopram	Imipramine	Lamotrigine	Lamotrigine	1	973.23	0.00	973.23
	Methylphenidate		Imipramine				1	507.79	0.00	507.79
	Methylphenidate		Imipramine	Imipramine			3	446.14	8.17	1338.43
	Methylphenidate		Imipramine	Imipramine			1	498.15	0.00	498.15
	Methylphenidate		Imipramine	Imipramine			1	196.41	0.00	196.41
	Methylphenidate		Imipramine	Imipramine			1	408.17	0.00	408.17
	Methylphenidate		Imipramine				1	511.49	0.00	511.49
	Methylphenidate		Lamotrigine	Imipramine			1	432.25	0.00	432.25
	Methylphenidate		Lamotrigine	Imipramine			1	821.95	0.00	821.95
	Methylphenidate		Lamotrigine	Imipramine			4	664.87	71.84	2659.47
	Methylphenidate	Methylphenidate	Imipramine				1	520.29	0.00	520.29
	Methylphenidate		Imipramine				1	688.03	0.00	688.03
	Methylphenidate		Risperidone	Imipramine			6	117.16	286.97	702.94
	Methylphenidate		Risperidone	Imipramine			1	610.36	0.00	610.36
	Methylphenidate		Risperidone	Imipramine			1	687.99	0.00	687.99
	Methylphenidate		Imipramine				2	578.12	0.00	1156.24
	Methylphenidate		Imipramine				1	230.65	0.00	230.65
	Methylphenidate		Valproate (sodium)	Imipramine			2	0.00	0.00	0.00
Methylphenidate		Valproate (sodium)	Imipramine			1	462.09	0.00	462.09	
Methylphenidate		Valproate (sodium)	Imipramine			1	719.48	0.00	719.48	
Methylphenidate		Valproate (sodium)	Imipramine	Imipramine		5	471.01	27.30	2355.05	

Table B.3: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2007 (continued)

Period	Methylphenidate and/or Atomoxetine containing products	Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2007	Methylphenidate	Valproic acid	Imipramine			1	585.43	0.00	585.43
	Methylphenidate	Valproic acid	Imipramine			2	396.44	312.83	792.87
	Methylphenidate	Valproic acid	Imipramine			1	770.95	0.00	770.95
	Methylphenidate	Valproic acid	Imipramine			1	136.46	0.00	136.46
	Methylphenidate	Risperidone	Carbamazepine	Imipramine		2	725.75	234.22	1451.50
	Methylphenidate	Salbutamol	Imipramine			1	785.24	0.00	785.24
	Methylphenidate	Salbutamol	Imipramine	Buspirone		2	828.95	0.00	1657.90
	Methylphenidate	Imipramine				1	1129.88	0.00	1129.88
	Methylphenidate	Valproate (sodium)	Imipramine	Imipramine		5	471.01	27.30	2355.05
	Methylphenidate	Propranolol	Imipramine			1	233.71	0.00	233.71
	Methylphenidate	Valproate (sodium)	Imipramine			1	910.54	0.00	910.54
	Methylphenidate	Valproic acid	Imipramine			1	919.66	0.00	919.66
	Methylphenidate	Valproic acid	Imipramine			1	664.33	0.00	664.33
	Methylphenidate	Valproic acid	Valproic acid	Imipramine		2	298.77	422.52	597.53
	Methylphenidate	Valproic acid	Valproic acid	Imipramine		7	436.54	192.56	3055.77
	Methylphenidate	Valproic acid	Valproic acid	Imipramine		2	550.27	2.81	1100.54
	Methylphenidate	Valproic acid	Valproic acid	Imipramine		1	0.00	0.00	0.00
	Methylphenidate	Imipramine				1	174.14	0.00	174.14
	Methylphenidate	Imipramine				1	1102.04	0.00	1102.04
	Methylphenidate	Imipramine				1	1421.28	0.00	1421.28
Methylphenidate		Carbamazepine			1	264.14	0.00	264.14	
Methylphenidate	Atomoxetine	Carbamazepine			2	671.29	233.53	1342.58	

Table B.3: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2007 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2007	Methylphenidate		Carbamazepine				8	573.59	73.67	4588.72
	Methylphenidate		Carbamazepine				2	325.04	17.34	650.08
	Methylphenidate		Carbamazepine				4	295.91	72.82	1183.63
	Methylphenidate		Carbamazepine				3	482.46	0.00	1447.38
	Methylphenidate		Carbamazepine				3	597.77	34.03	1793.30
	Atomoxetine	Atomoxetine	Carbamazepine				1	375.28	0.00	375.28
	Atomoxetine		Carbamazepine				14	651.46	279.36	9120.41
	Atomoxetine		Carbamazepine				1	870.32	0.00	870.32
	Atomoxetine		Carbamazepine				1	1101.50	0.00	1101.50
	Atomoxetine		Carbamazepine				2	1101.50	0.00	2203.00
	Methylphenidate		Carbamazepine	Amitriptyline			1	1036.09	0.00	1036.09
	Methylphenidate	Methylphenidate	Carbamazepine	Carbamazepine			1	967.43	0.00	967.43
	Atomoxetine		Carbamazepine				2	888.60	0.00	1777.20
	Methylphenidate		Carbamazepine	Sertraline			3	557.33	335.17	1671.99
	Atomoxetine		Carbamazepine	Topiramate	Topiramate		5	1566.88	94.34	7834.40
	Methylphenidate	Methylphenidate	Carbamazepine	Carbamazepine			1	967.43	0.00	967.43
	Methylphenidate		Citalopram	Carbamazepine			1	675.10	0.00	675.10
	Atomoxetine		Citalopram	Carbamazepine	Topiramate		1	2085.23	0.00	2085.23
	Atomoxetine		Citalopram	Carbamazepine	Topiramate	Topiramate	2	1754.82	0.00	3509.64
	Methylphenidate		Carbamazepine				3	652.06	0.00	1956.18
Methylphenidate		Carbamazepine				1	796.28	0.00	796.28	
Methylphenidate		Risperidone	Carbamazepine			1	0.00	0.00	0.00	
Methylphenidate		Risperidone	Carbamazepine			4	600.88	389.95	2403.53	

Table B.3: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2007 (continue)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2007	Methylphenidate		Risperidone	Carbamazepine			4	617.15	9.64	2468.58
	Atomoxetine		Risperidone	Carbamazepine			7	1001.77	16.05	7012.38
	Atomoxetine		Risperidone	Carbamazepine			2	911.62	0.00	1823.24
	Methylphenidate		Risperidone	Carbamazepine	Imipramine		2	725.75	234.22	1451.50
	Methylphenidate	Methylphenidate	Sertraline	Carbamazepine			1	824.41	0.00	824.41
	Methylphenidate		Venlafaxine	Carbamazepine			1	960.23	0.00	960.23
	Methylphenidate		Clonazepam	Carbamazepine			1	487.73	0.00	487.73
	Atomoxetine		Risperidone	Carbamazepine			1	1021.78	0.00	1021.78
	Methylphenidate		Valproate (sodium)	Risperidone	Carbamazepine		2	748.08	0.00	1496.16
	Methylphenidate	Atomoxetine	Carbamazepine				1	0.00	0.00	0.00
	Methylphenidate		Pantoprazole	Carbamazepine		n	1	1727.72	0.00	1727.72
	Methylphenidate	Methylphenidate	Imipramine	Sertraline	Carbamazepine		1	1030.70	0.00	1030.70
	Methylphenidate		Clomipramine				2	758.28	388.07	1516.56
	Methylphenidate		Clomipramine				1	636.98	0.00	636.98
	Methylphenidate		Clomipramine				6	799.32	299.89	4795.90
	Methylphenidate		Clomipramine				1	895.62	0.00	895.62
	Methylphenidate		Clomipramine				1	1062.18	0.00	1062.18
Methylphenidate		Clomipramine	Buspirone			3	1320.98	6.46	3962.94	

Table B.3: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2007 (continued)

Period	Methylphenidate and/or Atomoxetine containing products		Central nervous system (CNS) active ingredient				Number of prescriptions	Average cost per prescription (R)	Standard deviation (R)	Total cost (R)
2007	Methylphenidate		Clomipramine	Clomipramine			1	491.61	0.00	491.61
	Methylphenidate		Clomipramine	Buspirone	Lamotrigine		1	1514.39	0.00	1514.39
	Methylphenidate		Clomipramine	Lamotrigine	Lamotrigine		1	894.76	0.00	894.76
	Methylphenidate		Clomipramine	Zolpidem	Enalapril		1	1245.64	0.00	1245.64
	Methylphenidate		Clomipramine	Lamotrigine	Lamotrigine	Buspirone	1	707.14	0.00	707.14
	Methylphenidate	Methylphenidate	Cyclizine	Clomipramine			1	0.00	0.00	0.00
	Methylphenidate		Omeprazole	Clomipramine			2	1108.20	0.00	2216.40
	Methylphenidate		Simvastatin	Clomipramine			2	1112.40	0.00	2224.80
	Methylphenidate		Phenytoin				1	832.47	0.00	832.47
									0	
	Methylphenidate		Trimipramine				3	390.99	24.01	1172.97
	Methylphenidate		Trimipramine				1	2297.33	0.00	2297.33
Methylphenidate		Risperidone	Thiamine	Trimipramine	Bupropion	1	1562.70	0.00	1562.70	

Table B.3: Number of prescriptions containing methylphenidate and/or atomoxetine products with other Central Nervous System (CNS) products for 2007 (continued)

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