GENERIC MEDICINES: KNOWLEDGE, PERCEPTIONS AND PRACTICE OF COMMUNITY PHARMACISTS, PHYSICIANS AND MEDICINE CONSUMERS IN RIYADH, SAUDI ARABIA

ALIAN AALY F ALRASHEEDY

UNIVERSITI SAINS MALAYSIA
2014

GENERIC MEDICINES: KNOWLEDGE, PERCEPTIONS AND PRACTICE OF COMMUNITY PHARMACISTS, PHYSICIANS AND MEDICINE CONSUMERS IN RIYADH, SAUDI ARABIA

By

ALIAN AALY F ALRASHEEDY

Thesis submitted in fulfilment of the requirements
for the Degree of
Doctor of Philosophy

September 2014

ACKNOWLEDGEMENTS

First of all, I thank Almighty Allah, the one and only, for all of his countless blessings and help to finish this work. Without his help and blessing, I am unable to do anything.

I would like to express my deepest gratitude to my main supervisor **Assoc. Professor Dr. Mohamed Azmi Ahmad Hassali** at Discipline of Social and Administrative Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia for his excellent supervision, constant support, scientific guidance, advice and encouragement. I would like to take this opportunity to thank him for teaching and training me in several research areas and methods including qualitative and quantitative methodology, systematic reviews and policy analysis studies. I am really grateful to him and proud to do my PhD under his supervision.

I would like to thank my co-supervisor **Professor Dr. Mohamed Izham Mohamed Ibrahim** at College of Pharmacy, Qatar University, Doha, Qatar for his constant support, advice and constructive comments throughout my PhD journey. I would like to thank my co-supervisor **Assoc. Professor Dr. Hisham Aljadhey** at Medication safety Research Chair, Department of Clinical Pharmacy, College of Pharmacy, King Saudi University, Riyadh, Saudi Arabia for his constant support and advice throughout my PhD journey.

I would like extend my sincere thanks to our discipline chairman **Assoc. Professor Dr. Asrul Akmal Shafie** and all the faculty members, staff and my colleagues from the Discipline of Social and Administrative Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia for their support and help.

Last but not the least, I express my gratitude to my parents, brothers and sisters for their prayers, love and support.

TABLE OF CONTENTS

LIST OF TABLES

Page

Page

LIST OF FIGURES

ABBREVIATIONS

ACA	Adaptive Conjoint Analysis
ACEIs	Angiotensin-Converting-Enzyme Inhibitors
AEDs	Anti-Epileptic Drugs
AIDS	Acquired Immunodeficiency Syndrome
ASE	Attitude, Social influence and Self-efficacy
ATC	Anatomical Therapeutic Chemical
AUC	Area Under Curve
AUD	Australian Dollar
BMI	Business Monitor International
BNF	British National Formulary
BPharm	Bachelor of Pharmacy
CDSI	Central Department of Statistics and Information
CI	Confidence Interval
CIF	Cost, Insurance and Freight
Cmax	Maximum Plasma Concentration
CME	Continuing Medical Education
CNS	Central Nervous System
Con	Consumer
COO	Country of Origin
COREQ	Consolidated criteria for reporting qualitative research
CP	Community Pharmacist
CPD	Continuing Professional Development

CSIC	Spanish National Research Council
DTCA	Direct-to-Consumer Advertising
EGA	European Generic Medicines Association
EMA	European Medicines Agency
EMRO	Eastern Mediterranean Regional Office
ENT	Ear, Nose and Throat
FGMP	Forum of General Medical Practitioners
Fimea	Finnish Medicines Agency
FIMP	Federazione Italiana Medici Pediatri
FPs	Family Paediatricians
GCC	Gulf Cooperation Council
GCS	Glasgow Coma Score
GERD	Gastro-oesophageal Reflux Disease
GIT	Gastrointestinal Tract
GMA	Greek Medical Association
GMP	Good Manufacturing Practice
GPs	General Practitioners
GS	Generic Substitution
H	Hour
HIV	Human Immunodeficiency Virus
ICGP	Irish College of General Practitioners
INN	International Nonproprietary Name
IQR	Interquartile Range

ISDB	International Society of Drug Bulletins
IVI	Item Validity Index
JAMA	Journal of the American Medical Association
KELA	(Kansaneläkelaitos) Social Insurance Institution of Finland
KFSH & RC	King Faisal Specialist Hospital & Research Centre
KNMP	Royal Dutch Pharmacists Association
KSA	Kingdom of Saudi Arabia
LFN	(Läkemedelsförmånsnämnden) Pharmaceutical Benefits Board
M	Mean
MA	Market Authorization
MBBS	Bachelor of Medicine, Bachelor of Surgery
MD	Doctor of Medicine
Md	Median
MEA	Middle East and Africa
MG	Milligram
MeSH	Medical Subject Heading
MHLW	Ministry of Health, Labour and Welfare of Japan
MODA	Ministry of Defence and Aviation
MOI	Ministry of Interior
MPA	Swedish Medical Products Agency
N	Number
NCDs	Non-Communicable Diseases
NHS	National Health Service

NPC	National Pharmacovigilance Centre
NPCB	National Pharmaceutical Control Bureau
NPS	National Prescribing Service Limited
NSAIDs	Non-Steroidal Anti-inflammatory Drugs
NT	Northern Territory
NTI	Narrow Therapeutic Index
OFT	Office of Fair Trading
OR	Odd Ratio
OTC	Over the Counter
P	Physician
Para.	Paragraph
PBS	Pharmaceutical Benefits Scheme
PDE-5	Phosphodiesterase type-5
PharmD	Doctor of Pharmacy
PHC	Primary Health Care
PFDI	Premium-Free Dispensing Incentive
PPIs	Proton Pump Inhibitors
PPQCs	Physicians-Pharmacists Quality Circles
QD	Qualitative Descriptive
RCTs	Randomized Controlled Trials
R&D	Research and Development
SA	South Australia
SANG	Saudi Arabian National Guard

SAR	Saudi Riyal
SCHS	Saudi Commission for Health Specialties
SD	Standard Deviation
SFDA	Saudi Food and Drug Authority
SMOH	Saudi Ministry of Health
SNF	Saudi National Formulary
SPSS	Statistical Package for Social Sciences
SSRIs	Selective Serotonin Reuptake Inhibitors
STDs	Sexually Transmitted Diseases
TGA	Therapeutic Goods Administration
Tmax	Time to Maximum Plasma Concentration
TV	Television
UAE	United Arab Emirates
UK	United Kingdom
USA	United States of America
US FDA	United States Food and Drug Administration
US$	United States Dollar
WHO	World Health Organization
WTP	Willingness to Pay

LIST OF APPENDICES

LIST OF PUBLICATIONS

A. Peer reviewed journal publications

1. **Alrasheedy AA**, Hassali MA, Aljadhey H, Ibrahim MIM, Al-Tamimi SK (2013). Is there a need for a formulary of clinically interchangeable medicines to guide generic substitution in Saudi Arabia? *Journal of Young Pharmacists*, 5(2): 73-75.

2. Hassali MA, **Alrasheedy AA,** McLachlan A, Nguyen TA, AL-Tamimi SK, Ibrahim MIM, Aljadhey H (2014). The experiences of implementing generic medicines policy in eight countries: a review and recommendations for a successful promotion of generic medicines use. *Saudi Pharmaceutical Journal.*
DOI: http://dx.doi.org/10.1016/j.jsps.2013.12.017

3. **Alrasheedy AA**, Hassali MA, Stewart K, Kong DCM, Aljadhey H, Ibrahim MIM, AL-Tamimi SK (2014). Patients' knowledge, perceptions and acceptance of generic medicines: a comprehensive review of the current literature. *Patient Intelligence,* 6(1): 1-29.

4. **Alrasheedy AA**, Hassali MA, Aljadhey H, AL-Tamimi SK (2014). The need to cover generic medications and generic substitution practice in the curricula of Pharmacy Colleges in Saudi Arabia. *American Journal of Pharmaceutical Education,* 78(5): Article 108.

B. Peer reviewed conference abstract

Alrasheedy AA, Hassali MA, Aljadhey H, Ibrahim MIM, AL-Tamimi SK (2013). A qualitative exploration of generic substitution practice of community pharmacists in Riyadh, Saudi Arabia. 1st National Conference on Quality Use of Medicine. Selangor, Malaysia.

UBAT-UBATAN GENERIK: PENGETAHUAN, PERSEPSI DAN PRAKTIS AHLI FARMASI KOMUNITI, AHLI PERUBATAN DAN PENGGUNA UBAT-UBATAN DI RIYADH, ARAB SAUDI

ABSTRAK

Ubat-ubatan generik secara lazimnya adalah sama seperti ubat-ubatan berjenama asli. Ia membekalkan hasil teraupetik yang sama, pada kos yang lebih rendah. Disebabkan itu, ubat-ubatan ini dipromosikan di pelbagai negara sebagai salah satu langkah untuk mengatasi kos perbelanjaan farmaseutikal yang kian meningkat. Di Arab Saudi, penggunaan ubat-ubatan generik pada masa ini adalah rendah. Oleh sebab itu, peranan serta pengaruh ahli farmasi komuniti dan pengguna perubatan dalam mengalakkan penggunaan ubat-ubatan generik adalah sangat penting. Oleh yang demikian, projek ini berfokus kepada kajian mengenai pengetahuan,persepsi dan praktis penggunaan ubat-ubatan generik. Dalam bahagian pertama tesis ini, tiga kajian kualitatif telah dijalankan dengan menggunakan sesi temubual separa berstruktur secara bersemuka bersama individu yang terlibat. Kajian kualitatif pertama dijalankan bersama 20 ahli farmasi komuniti. Kajian tersebut mendapati penukargantian generik proaktif bukanlah satu praktis yang menjadi kebiasaan di kalangan ahli farmasi komuniti. Tambahan lagi, terdapat faktor berbeza yang berkait dengan ahli farmasi komuniti, ahli perubatan dan pesakit yang menghalang mereka daripada praktis penukargantian generik. Kajian kedua dilakukan bersama 18 ahli perubatan. Kajian tersebut mendapati perskripsi khusus kepada produk dijadikan sebagai model praktis berbanding dengan perskripsi generik (INN) yang pada masa ini bukanlah satu praktis kebiasaan. Tambahan lagi, pelbagai faktor mempengaruhi ahli perubatan dalam memilih jenama ubat-ubatan tersebut, termasuklah faktor yang berkaitan dengan ahli perubatan tersebut, faktor yang

berkaitan dengan pengeluar/pengilang dan produk ubat-ubatan itu. Faktor yang berkaitan dengan pesakit, dan faktor yang berkaitan dengan pemasaran farmaseutikal. Kajian ketiga dijalankan bersama 15 pengguna perubatan. Kajian tersebut mendapati pengguna perubatan secara amnya lebih menggemari penggunaan ubat-ubatan berjenama asli berbanding dengan ubat-ubatan generik. Tambahan pula, terdapat banyak pengguna yang mempunyai persepsi negatif dan tanggapan salah mengenai ubat-ubatan generik. Perkara paling penting dalam hal ini, cadangan (dalam memberi perskripsi dan mendispens) oleh ahli perubatan dan ahli farmasi adalah faktor utama yang mempengaruhi penggunaan dan kadar penerimaan ubat-ubatan generik oleh pesakit. Dalam bahagian kedua tesis ini, dua kajian keratan rentas kuantitatif yang menggunakan borang soal selidik telah dijalankan. Salah satu kajian dijalankan bersama 251 ahli perubatan yang menjalankan praktis di poliklinik (kadar respons = 59.3%). Dalam kajian ini, 128 (51%) menyatakan yang mereka telah memberi perskripsi kedua-dua ubat-ubatan generik dan ubat-ubatan berjenama asli lebih kurang pada nisbah yang sama, 76 (30.3%) menyatakan mereka lebih banyak memberi perskripsi ubat-ubatan berjenama asli dan 46 (18.3%) menyatakan mereka lebih banyak memberi perskripsi ubat-ubatan generik.Satu kajian lain turut dijalankan bersama 381 ahli farmasi komuniti (kadar respons = 90.1%). Dalam kajian ini, hampir kesemua responden (379; 99.5%) menyatakan dalam kebanyakan situasi, mereka mengagih dan mendispens ubat-ubatan mengikut jenama dalam perskripsi yang diberikan tanpa menawarkan penukargantian generik. Mengenai praktis utama dalam mendispens ubat-ubatan OTC, 153 (40.2%) menyatakan mereka menawarkan ubat-ubatan generik kepada pengguna, 124 (32.5%) responden menawarkan ubat-ubatan berjenama, 101 (26.5%) responden menawarkan

kedua-dua jenama ini, kadangkala mereka menawarkan ubat-ubatan generik atau berjenama, dan hanya tiga responden (0.8%) menyatakan mereka menawarkan kedua-dua ubat-ubatan generik dan berjenama ini kepada pengguna untuk mereka membuat pilihan sendiri. Dapatan kajian utama dalam kajian kuantitatif ini menunjukkan bahawa terdapat sebilangan besar ahli perubatan dan ahli farmasi komuniti yang mempunyai tanggapan salah dan persepsi negatif terhadap ubat-ubatan generik. Kesimpulannya, salah satu cara dalam meningkatkan penggunaan ubat-ubatan generik adalah dengan mempromosikannya melalui pendekatan holistik dengan mengambil kira perspektif pihak berkepentingan, termasuklah ahli perubatan, ahli farmasi komuniti dan pengguna perubatan.

GENERIC MEDICINES: KNOWLEDGE, PERCEPTIONS AND PRACTICE OF COMMUNITY PHARMACISTS, PHYSICIANS AND MEDICINE CONSUMERS IN RIYADH, SAUDI ARABIA

ABSTRACT

Generic medicines are essentially the same as their counterpart brand medicines. They provide the same therapeutic outcomes, but at a much cheaper price. Therefore, they are promoted in many countries to confront the problem of escalating pharmaceutical expenditures. In Saudi Arabia, the use of generic medicines is currently low. Therefore, to promote generic medicines, the roles of physicians, community pharmacists and medicine consumers are essential. Hence, this research project aimed to study their knowledge, perceptions and practice regarding the use of generic medicines. In the first part of the thesis, three qualitative studies were conducted, using face-to-face individual semi-structured interviews. The first qualitative study was conducted with 20 community pharmacists. The study findings showed that proactive generic substitution is currently not a common practice in community pharmacies. Moreover, different factors related to community pharmacists, physicians and patients hindered the generic substitution practice. The second qualitative study was conducted with 18 physicians. The study findings showed that generic (international nonproprietary name) prescribing is currently not a common practice but rather product-specific prescribing is the practice model. Moreover, different factors influenced the physicians' choice of the brands of medicines, including factors related to the physician, factors related to the drug product and its manufacturer/drug company, factors related to the patient, and factors related to pharmaceutical marketing. The third qualitative study was conducted with 15 medicine consumers. The study findings showed that medicine consumers generally preferred the

use of brand medicines over generic medicines. Moreover, many consumers have negative perceptions and misconceptions about generic medicine. More importantly, recommendations (i.e. prescribing and dispensing) by physicians and pharmacists were the main factors influencing the use and acceptance of generic medicines by patients. In the second part of the thesis, two quantitative cross-sectional questionnaire-based studies were conducted. One study was conducted with 251 physicians practising in polyclinics (response rate = 59.3%). In this study, 128 (51%) stated that they prescribe both generic medicines and original brand medicines at approximately the same ratio, 76 (30.3%) stated that they prescribe more original brand medicines and 46 (18.3%) stated that they prescribe more generic medicines. Similarly, another study was conducted with 381 community pharmacists (response rate = 90.1%). In this study, almost all participants (379; 99.5%) stated that they dispense brand medicine in the prescription as written by prescribers without offering generic substitution in most situations. Regarding the main dispensing practice for OTC medicines, 153 (40.2%) stated that they offer generic medicines to consumers, 124 (32.5%) participants offer brand medicines, 101 (26.5%) participants offer both – sometimes they offer generic medicines and sometimes brand medicines – and only three participants (0.8%) stated that they offer both original brand and generic medicines and left the choice to the consumer. The quantitative studies showed that a considerable proportion of physicians and community pharmacists have misconceptions and negative perceptions of generic medicines. In conclusion, to increase utilization of generic medicines, it needs to be promoted in a holistic approach by considering the perspectives of all stakeholders, including physicians, community pharmacists and medicine consumers.

CHAPTER ONE: GENERAL INTRODUCTION

1.1 Background

Generic medicine can be defined in different ways (Birkett, 2003; Davit et al., 2013; Dunne et al., 2013). However, the term is commonly understood as defined by the World Health Organization (WHO) as 'a pharmaceutical product, usually intended to be interchangeable with an innovator product that is manufactured without a licence from the innovator company and marketed after the expiry date of the patent or other exclusive rights' (WHO, 2012, para. 1). Generic medicines are required to have the same active substance, strength, route of administration, identity, quality, purity, efficacy and the same intended use as their counterpart brand medicines (US Food and Drug Administration (FDA), 2012a; European Generic Medicines Association (EGA), 2013a; Saudi Food and Drug Authority (SFDA), 2013a) but they can be different in some aspects, such as the inactive ingredient, colour, shape and product packaging (EGA, 2007; US FDA, 2012a). Before registration, similar to all medicines including original brand medicines, generic medicines must pass through a rigorous registration process and stringent requirements to ensure their quality, safety and efficacy, and that they meet all the required standards (SFDA, 2009; US FDA, 2012a; EGA, 2013a; SFDA, 2013a) Furthermore, the concept of bioequivalence is an essential requirement for approval of generic medicines in many countries (Galgatte et al., 2013), including Saudi Arabia (Executive Board of the Health Ministers' Council for GCC States, 2013a). Bioequivalence is performed to demonstrate the clinical equivalence of the generic medicine with its counterpart original brand and to allow a bridging with the clinical studies performed on the original medicine. Hence repeating preclinical and clinical testing done on the original brand is not required (European Medicines Agency (EMA), 2010; Dunne et al., 2013).

Generic medicines are much cheaper than their equivalent brand medicine (Matin, 1999; Simoens & Coster, 2006; Shafie & Hassali, 2008; EGA, 2013b) and are available as a standard therapy for many acute and chronic diseases (Sheppard 2011; EGA, 2013b). Thus, use of generic medicines is essential to the affordability of and access to medicines (Cameron et al., 2009; Hassali et al., 2014). Moreover, generic medicines play a major role in lowering the prices of off-patent innovator medicines and other generic equivalents (Pharmaceutical Benefits Board (LFN), 2007; Aalto-Setälä, 2008; US FDA, 2010; Hassali et al., 2014). Thus, by using generic medicines, the health-care system can save a huge amount of money that can be utilized to pay for the more expensive patented and new innovative products that are needed to treat some diseases where generic medicines are not available (EGA, 2007). Hence, the wide use of generic medicines is instrumental to the creation and maintenance of sustainable health-care systems (Simoens, 2010). Thus, generic medicines are considered an essential part of the health-care system (Al-Tamimi et al., 2013).

Health-care expenditure, including pharmaceutical expenditure, is steadily increasing in many countries around the globe. In fact, pharmaceutical expenditure is one of the rapid growing components of health-care expenditures (Henriksson et al., 1999; Schneeweiss et al., 2002; Ess et al., 2003; Zuvekas & Cohen, 2007; Saudi Ministry of Health (SMOH), 2008; Wettermark et al., 2008; Coma et al., 2009; Godman et al., 2009; Godman et al., 2010a; Godman et al., 2010b; Sermet et al., 2010; Leng et al., 2011; Hoffman et al., 2012; Hoffman et al., 2013). Therefore, in recent years, to confront the escalation of health-care expenditure in general, and pharmaceutical expenditure in particular, many governments and third-party payers have encouraged the use of generic

medicines as an integral part of the health-care system by instigating and implementing various policies, initiatives and strategies (Simoens & DeCoster, 2006; Sermet et al., 2010; Godman et al., 2010a; Godman et al., 2012a; Godman et al., 2012b; Ministry of Health, Labour and Welfare of Japan (MHLW), 2012).

Amidst them all, the role of health-care professionals (physicians and pharmacists) and medicine consumers/patients is an important issue and an essential factor for the wide use of generic medicines in the health-care system. In fact, correct understanding, knowledge and positive perceptions among health-care professionals and patients are prerequisite to the use of generic medicines (Dylst et al., 2013; Hassali et al. 2014). Therefore, the aim of this thesis is to study the perspectives of health-care professionals (physicians and community pharmacists) and medicine consumers/patients of generic medicines and current issues surrounding their use in the Saudi health-care system.

1.2 Rationale and significance of the study

In Saudi Arabia, the total health expenditure is steadily increasing; it has increased tremendously by approximately 165% over one decade (2000–2011). It increased from approximately SAR 30.100 billion in 2000 to SAR 79.795 billion in 2011 (1 Saudi Riyal (SAR) = 3.75 US dollar) (WHO, 2011). Similarly, pharmaceutical expenditure has greatly increased in recent years. Within a span of only four years, it increased by approximately 69% from SAR 12.06 billion in 2009 to reach SAR 20.37 billion in 2012. Thus, pharmaceutical expenditure represented approximately 23.15% of the total health expenditure in 2012 (Business Monitor International (BMI), 2013a). In fact, the pharmaceutical expenditure is one the most fast-growing components of health-care

expenditure in Saudi Arabia (SMOH, 2008). Meanwhile, generic medicines represented only 8.12% of the total medicine market and only 9.1% of the prescription medicines market in 2012. Moreover, it is forecasted to reach only approximately 11.5% in 2020 (BMI, 2013a). In fact, the Saudi drug market is heavily dominated by original and patented medicine brands. These represented approximately 80.8% of the total medicine market and 90.9% of the prescription medicines market in 2012 (BMI, 2013a). Therefore, to confront the escalating health-care cost in general and pharmaceutical expenditure in particular, it is essential to promote the use of generic medicines in the Saudi health-care system. As shown in Figure 1.1, for the promotion of generic medicines, policies, strategies and initiatives are broadly classified into two categories (Godman et al., 2010b). One category is the supply-side measures (i.e. those policies related to the prices and pricing system of generic medicines e.g. reference pricing system) and the other category is called the utilization or demand-side measures. The latter targets health-care professionals and patients/consumers and aims to ensure that they are supporting the use of generic medicines, to address any barriers or obstacles that may hinder the quality use of generic medicines and to introduce policies that facilitate the wide use of generic medicines by targeting key players, namely physicians, pharmacists and medicine consumers (i.e. it addresses knowledge, perceptions, practice, barriers to or facilitators of prescribing, dispensing or using generic medicines among physicians, pharmacists and patients, respectively) (Godman et al., 2010b). In fact, the essential difference between mature generic markets and developing generic markets is the presence/absence of demand-side policies (Simoens, 2013).

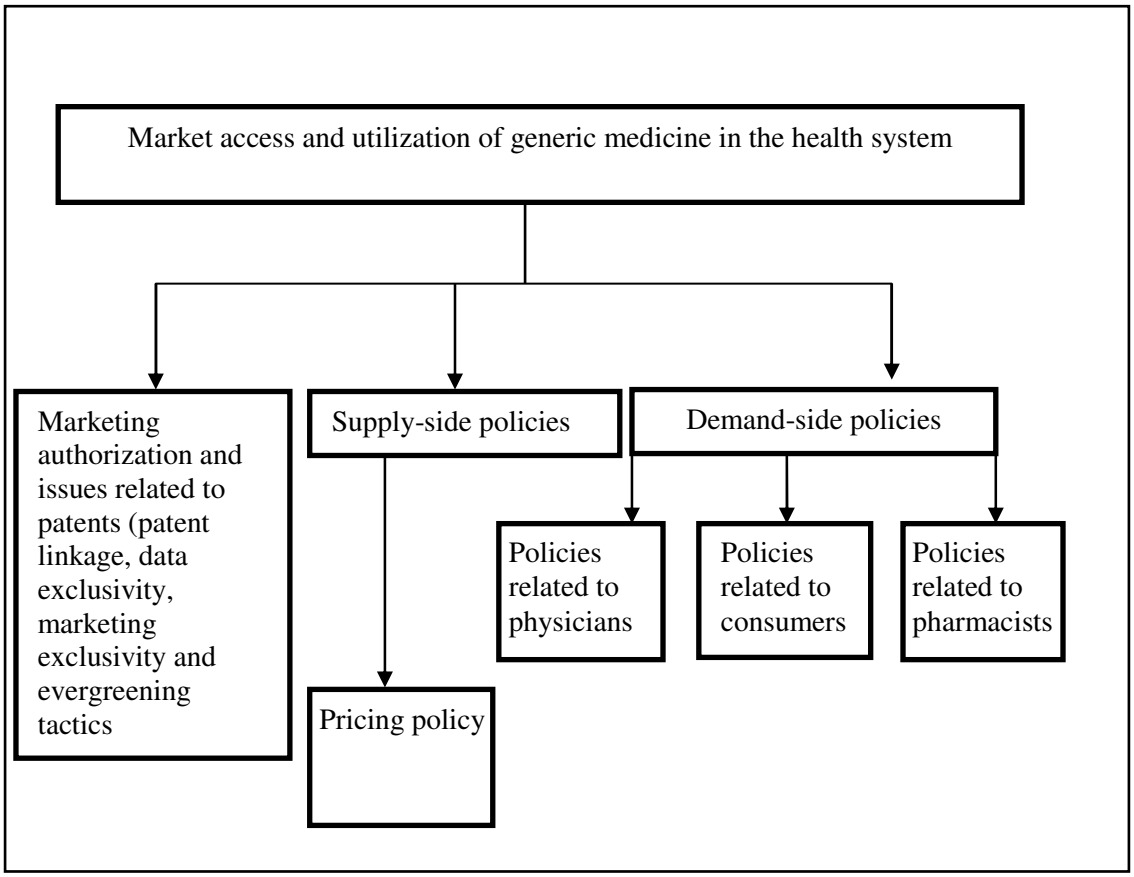

Figure 1.1 Policies and factors influencing access and utilization of generic medicines in the health system (adapted and modified from: Godman et al., 2010b; Simoens, 2013)

Currently, in Saudi Arabia, based on an extensive literature search in several electronic research databases and search engines, there is a paucity of data regarding the perspectives of physicians, community pharmacists and patients of generic medicines. Moreover, the extrapolation of findings of other studies conducted in other countries is not appropriate due to the large differences between health-care systems (Hassali et al., 2005a; Hassali et al., 2014). In fact, although it could be useful to learn from the experiences and challenges faced while promoting the use of generic medicines in other countries whenever applicable and relevant to the Saudi health-care system, it is not

possible to extrapolate the findings from these different health-care systems to the local situation in Saudi Arabia due to the substantial differences in the health policies, health systems, medicine regulations and the views and practices of health-care professionals from one country to another (Hassali et al., 2005a; Hassali et al., 2014). Therefore, it is highly important to study the perspectives of physicians, community pharmacists and patients on the use of generic medicines in Saudi Arabia.

According to the WHO (2001, p. 4), a national medicine policy is 'a commitment to a goal and a guide for action' with the objective of promoting equity and sustainability of both public and private pharmaceutical sectors. In addition, it should ensure not only the availability and accessibility to high-quality, safe and effective medicines, but also promote the cost-effective use of medicines to health-care professionals and consumers (WHO, 2001). Therefore, the promotion of generic medicines is recommended to be included as part of a national medicine policy (Cameron et al., 2012) as it helps to achieve a comprehensive and sustainable health-care system in developed countries (Godman et al., 2010a) and improve the affordability, and thus accessibility of medicines in developing countries (Cameron et al., 2009). In fact, generic medicine utilization has led to substantial cost savings for health-care systems (Andersson et al., 2007; Coombes, 2009; The Social Insurance Institution of Finland (KELA) 2009; Sheppard, 2011; Generic Pharmaceutical Association, 2012; EGA, 2013c). For example, in the US, generic medicines saved the health-care system approximately one trillion dollars over ten years from 2002 to 2011 (Generic Pharmaceutical Association, 2012). Therefore, the use of generic medicines needs to be promoted in Saudi Arabia to confront the escalating pharmaceutical expenditure. In view of the current low

utilization of generic medicines in the country, there is large scope to further increase the use of generic medicines. Thus, this research project would provide health authorities and other involved parties and stakeholders with valuable data related to the perspectives of physicians, community pharmacists and patients, and related to current issues surrounding the use of generic medicines. This research project would provide useful data that could be used to inform the design or implementation of strategies, initiatives, or programmes to promote generic medicines, such as educational interventions or educational campaigns targeting physicians, pharmacists and patients/medicine consumers.

1.3 Ethical approval of the research project

The research project was granted ethical approval by the Human Research Ethics Committee at the College of Pharmacy, Qassim University (approval number: 501-K-11) (Appendix A). Also, a letter was given by the research centre, the College of Pharmacy, Qassim University to show that the researcher is a PhD student and conducting a research project to study generic medicines in Saudi Arabia (Appendix B).

CHAPTER TWO: LITERATURE REVIEW

2.1 Health-care system in Saudi Arabia

2.1.1 Saudi health-care system: a brief overview

The Kingdom of Saudi Arabia is located in the south-west corner of Asia and covers an area of approximately 2 million km^2; the total population reached approximately 29.2 million in 2010 (Central Department of Statistics and Information (CDSI), 2012). Saudi Arabia is organized administratively into 13 administrative regions, namely Riyadh, Makkah, Madinah, Qassim, Eastern Province, Asir, Tabuk, Hail, Northern Border Province, Jazan, Najran, Baha and Al-Jouf region (Ministry of Foreign Affairs, 2006). Riyadh is the capital of Saudi Arabia and located in the heart of the country. In 2013, its population was estimated to be 5.7 million. It is estimated that 61% of population in Riyadh are Saudi while the rest (39%) are residents from different parts of the world such as, India, China, Bangladesh, Pakistan, Indonesia, Philippines, Yemen, Egypt, Sudan, Lebanon, Syria, Europe, US, Canada, South Africa and Russia. Thus, Riyadh is considered to be one of the most cosmopolitan cities in the Arab world (High Commission of Development of Arriyadh, 2013).

The country has witnessed a huge improvement in socio-economic development during the past three decades. Tremendous efforts have been made to advance all sectors, including health, education, housing and the environment (WHO, 2007). Currently, the country has a good infrastructure, including an extensive network of modern roads, highways, airports, seaports, power, desalination plants and huge industrial complexes (WHO, 2007). This, in turn, has transformed the country into one of the most urbanized countries in the Middle East (Khaliq, 2012).

Similarly, the Saudi health-care system has gone through huge improvements in the last 50 years on all levels and aspects of the health-care services in terms of quality and quantity (WHO, 2007; Almalki et al., 2011; Khaliq, 2012). Thus, a large network of modern health-care facilities, including hundreds of hospitals and thousands of primary care centres, are currently established in the country to provide health-care to all citizens and residents in the country (Almalki et al., 2011; Khaliq, 2012). In terms of quality of care, for example, the King Faisal Specialist Hospital & Research Centre (KFSH & RC) was ranked in 2013 by the Spanish National Research Council (CSIC) (2013) as the top hospital in the Middle East. However, the health-care system is currently facing many real challenges. In addition to the major challenge of escalating costs in providing health-care services, there are many other factors that challenge the sustainability and efficiency of the system. These factors include: a shortage of local health-care professionals, as the majority of health-care professionals are expatriates; a rapid population growth; the ageing of the population; the high burden of chronic diseases (e.g. asthma 13%, hypertension 11%, diabetes 28%); a growing demand for health-care services; a poor referral system between primary centres and hospitals; long waiting times; the unavailability of some medicines at some periods, underutilization of e-health and information systems; the maldistribution of health-care services across geographical areas (SMOH, 2009a; Almalki et al., 2011). In the public sector, for example, the waiting time for non- emergency surgery might be several months to a year (Walston et al., 2008). Moreover, the general perception of the quality of care in Ministry of Health (MOH) facilities is much lower than of that in the private sector and other government sectors (Walston et al., 2008). Therefore, currently, sustainability and maintaining the efficiency of the health-care system is a major challenge (Khaliq,

2012). However, to address these challenges and improve the current health-care system, the new Saudi health strategy was introduced in 2009 to be implemented by the MOH in cooperation with other organizations and agencies. In this strategy, many issues were addressed, such as health promotion and prevention of diseases, including non-communicable diseases (NCDs), which are a high burden and require costly treatment and high utilization of the system. Thus, the expansion of primary health-care centres was recommended. Due to the tremendous increase in health-care expenditure, alternative means of funding health-care services were recommended. Thus, the cost-effective use of medicines was encouraged to lower the escalating trend in health expenditure in general and pharmaceutical expenditure in particular. Moreover, the involvement of the private sector in the provision of health services needed to be increased to cover at least 50% of the total health expenditure. Also, for government hospitals, in addition to annual allocations from government, other modes of financing (e.g. the privatization of some health-care services) needed to be found (SMOH, 2009a).

2.1.2. Health system organization and provision of health-care

Health-care in Saudi Arabia is provided by a three-level system (primary, secondary and tertiary health-care). The concept of primary health-care (PHC) started in the early 1980s via the establishment of PHC centres; secondary and tertiary health-care are provided via general and specialist hospitals. The integrated health-care services system, via referral with the feedback system, is the adopted approach in the provision of health-care. In this approach, patients who need secondary or more specialized care are referred to the appropriate health-care facility (Regional Health Systems Observatory – The Eastern Mediterranean Regional Office (EMRO), 2006; SMOH, 2008).

Health-care is provided via a dual system (i.e. public and private sector). The public sector is currently the main provider of health-care and is funded mainly by the government budget. The Ministry of Health (MOH) and other government sectors are provided with financial appropriations on a yearly basis from the general government budget. Health-care services provided by the private sector are financed by cooperative health insurance schemes and out-of-pocket payments (Regional Health Systems Observatory – EMRO, 2006; SMOH, 2008). In the public sector, the Ministry of Health (MOH), established in 1951, is the major health-care provider as it provides approximately 60% of all health services (Regional Health Systems Observatory – EMRO, 2006; SMOH, 2008). In 2011, the MOH operated 251 hospitals and 2109 PHC centres. In terms of manpower, there were 33,999 physicians (23% were Saudi), 3020 dentists (43.1% were Saudi), 77,946 nurses (51.9% were Saudi nurses), 1897 pharmacists (82.4% were Saudi), and 43,422 allied health personnel (87.25% were Saudi) (SMOH, 2011).

Other government agencies also participate in the provision of health-care. However, unlike the MOH, health-care is provided mainly to these organizations or ministries' employees and their families/dependents. These government sectors include the health-care facilities of the Ministry of Defence and Aviation (MODA) , the Ministry of Interior (MOI), the Saudi Arabian National Guard (SANG), ARAMCO health services, health services in the Royal Commission for Jubail & Yanbua, Ministry of Education health units and university teaching hospitals (SMOH, 2008; Almalki et al., 2011).

The private sector has grown over the years and is now considered an important component of the Saudi health-care system (Walston et al., 2008; Khaliq, 2012). In 2011, there were 130 private hospitals and 2185 private polyclinics (SMOH, 2011). In terms of manpower in the private sector, there were 22,479 physicians, 5919 dentists, 28,373 nurses and 10,174 allied health-care professionals. It should be noted that most private sector premises are located mainly in urban cities, particularly in two regions: Riyadh and Jeddah. In fact, 23.8% of private hospitals (n=31) are located in Riyadh and 22.3% are located in Jeddah. Similarly, for private polyclinics, 33.5% (n=732) and 20.8% (n=454) are located in Riyadh and Jeddah, respectively. Thus, almost half of the health-care sector is available in just two regions of the total 13 regions of Saudi Arabia (SMOH, 2011). However, the growth of this sector is rapid and the government is encouraging its expansion to cover all regions (SMOH, 2009).

The community pharmacy sector represents a major component of the primary health-care system in Saudi Arabia in general and the private sector in particular. In 2011, the total number of community pharmacies was 6373, which were run by 11,583 pharmacists. In Riyadh, for example, there were 1804 community pharmacies according to 2011 statistics (SMOH, 2011).

2.1.3 Health-care expenditure and financing

Total health expenditure is steadily increasing; it has increased tremendously from approximately SAR 30.100 billion in 2000 to SAR 79.795 billion in 2011 (1 Saudi Riyal (SAR) = 3.75 US Dollar). General government health expenditure represented approximately 68.9% of the total health expenditure (SAR 55.003 billion) in 2011 (WHO, 2011). Moreover, financial appropriations from government budget to the MOH

increased from approximately SAR 22.808 billion in 2007 to reach SAR 39.860 billion in 2011 (SMOH, 2011). Regarding health funding, in the public sector, health-care is mainly funded by the government budget. The Ministry of Health (MOH) and other government sectors are provided with financial appropriations yearly from the general government budget.

The total private health expenditure increased tremendously from SAR 8.534 billion in 2000 to reach SAR 24.792 billion. Hence, it represented 31.1% of total health expenditure in 2011. The health-care and expenses in the private sector are financed by out-of-pocket payments and private health insurance (e.g. cooperative health insurance). In fact, currently, the expenses of health in the private sector are mainly financed by out-of-pocket payments, as these represented 58.1% (SAR 14.394 billion) in 2011 (WHO, 2011). Figure 2.1 shows the trend of total health expenditure in Saudi Arabia from 2000–2011.

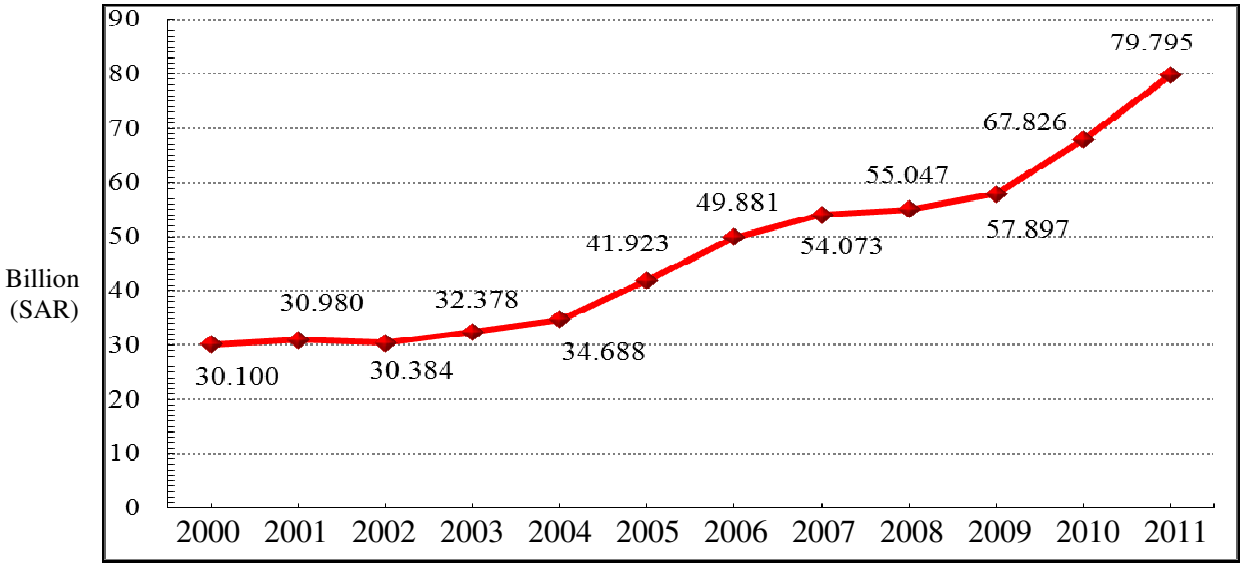

Figure 2.1 The trend of total health expenditure in Saudi Arabia from 2000–2011 (data source: WHO, 2011)

2.1.4 Saudi pharmaceutical market

Similar to the total health expenditure, pharmaceutical expenditure increased tremendously from SAR 12.06 billion in 2009 to reach SAR 20.37 billion in 2012. Thus, pharmaceutical expenditure represented approximately 23.15% of the total health expenditure in 2012 (BMI, 2013a). The trend of pharmaceutical expenditure in Saudi Arabia for the period of 2009–2012 is presented in Figure 2.2.

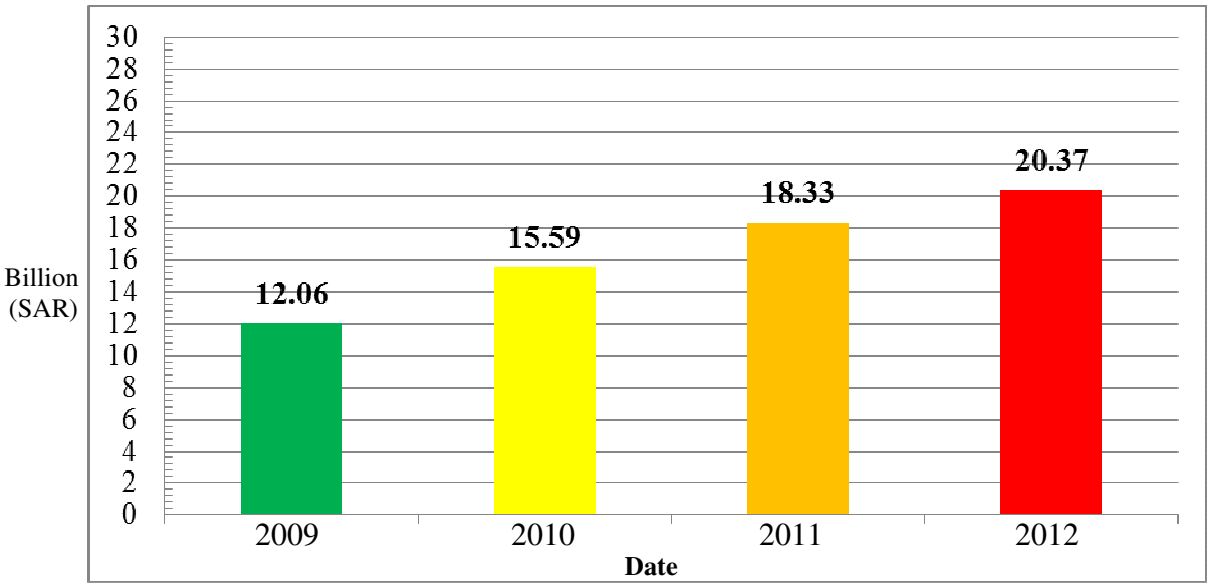

Figure 2.2 The trend of pharmaceutical expenditure in Saudi Arabia for the period 2009–2012 (data source: BMI, 2013a)

Moreover, as shown in Figure 2.3, the Saudi pharmaceutical market represented more than 50% of the total pharmaceutical sales of the Gulf Cooperative Council (GCC) countries (the GCC region includes Saudi Arabia, United Arab Emirates (UAE), Oman, Kuwait, Qatar and Bahrain). Also, the Saudi pharmaceutical market is currently the largest market in the Middle East and Africa (MEA) region (BMI, 2013a; BMI, 2013b; BMI, 2013c; BMI, 2013d; BMI, 2013e; BMI, 2013f).

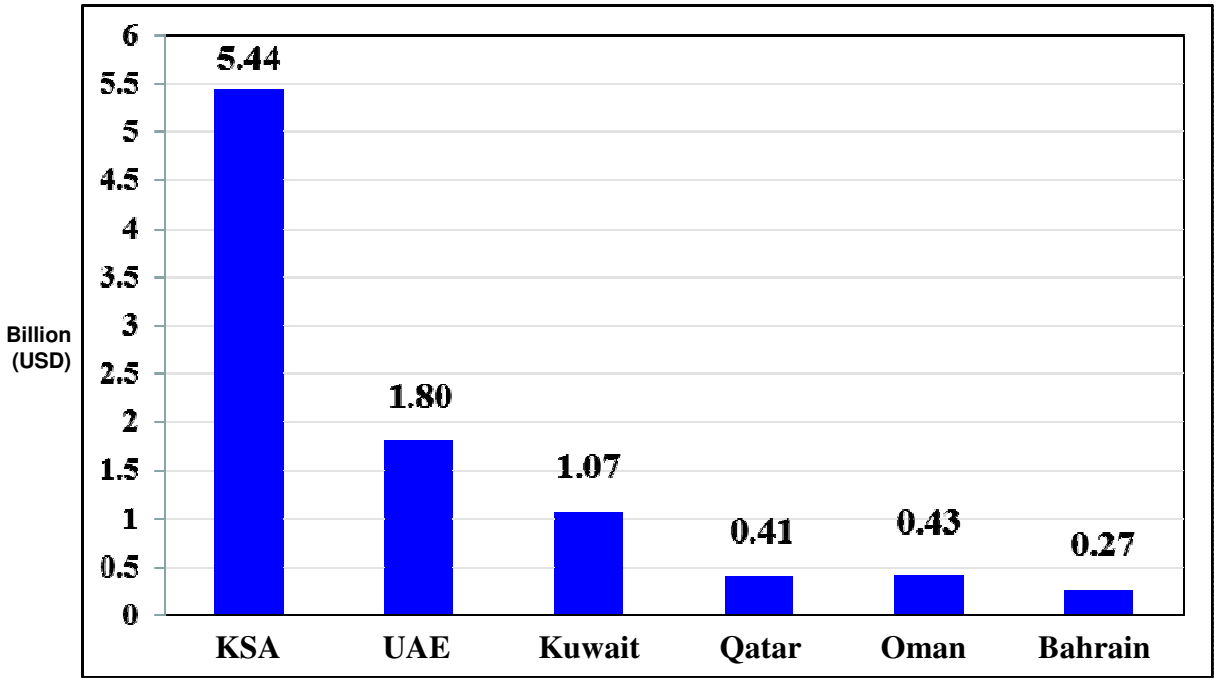

Figure 2.3 Pharmaceutical expenditure in GCC countries in 2012 (data source: BMI, 2013a; BMI, 2013b; BMI, 2013c; BMI, 2013d; BMI, 2013e; BMI, 2013f)

Regarding original brand medicines and generic medicines, the Saudi market is heavily dominated by original and patented medicine brands. These represented approximately 80.8% of the total medicine market and 90.9% of the prescription medicines market in 2012. On the other hand, generic medicines represented only 8.12% of the total medicine market and only 9.1% of the prescription medicines market in 2012. Moreover, this is forecasted to reach approximately 11.5% in 2020 (BMI, 2013a). The over-the-counter market represented approximately 11.06% of the market in 2012 (BMI, 2013a).

In Saudi Arabia, local pharmaceutical companies produce only approximately 16% of the domestic pharmaceuticals. Moreover, a large number of these medicines produced by local companies are not generic products but patented medicines produced by

licensing from multinational companies (BMI, 2013a). The presence of multinational drug companies is extensive in the Saudi market. The USA and European countries are the major suppliers of medicines to the market. Also, several drug companies from the Middle East such as Egypt, Jordon, UAE and Oman have a presence in the Saudi drug market (BMI, 2013a).

2.1.5 Regulation and registration of generic medicines in Saudi Arabia

The Saudi Food and Drug Authority (SFDA), established in 2003, is the national regulatory body responsible for the regulation, registration and approval of medicines in Saudi Arabia. Hence, one of its main objectives is to ensure and observe the effectiveness, safety and quality of medicines (SFDA, 2013b). In addition, it is responsible for developing and implementing policies and procedures related to medicines. Moreover, as well as the regulatory role, it is tasked with consumer awareness on all matters related to medicines (SFDA, 2013b). Historically, the Ministry of Health (MOH) was the regulatory body responsible for the regulation, approval and registration of medicines in the country. In 2003, the SFDA was established as an independent body that directly reports to the President of the Council of Ministers. It stated its regulatory role in two phases. In the first phase, which lasted five years, the SFDA developed and reviewed all policies, guidelines, regulations and standard specifications related to food, medicines and medical devices. In the second phase, in 2008, the SFDA started its regulatory and supervisory tasks and started receiving submissions for the approval and registration of medicines (SFDA, 2013b).

The SFDA applies strict requirements and a rigorous registration system to ensure the efficacy, safety and quality of generic medicines (SFDA, 2009; SFDA, 2013a). In fact, the registration system in Saudi Arabia applies the most stringent policies in the Middle East (Tantash, 2012). In Saudi Arabia, manufacturers and drug companies must seek approval from the SFDA before marketing any medicine. Moreover, manufacturers and drug companies must first register with the SFDA to be able to register their products in the country (SFDA, 2011a). Regarding generic medicines' approval and registration, as shown in Figure 2.4, according to the Regulatory Framework for Drug Approvals Version 4 (SFDA, 2009), the generic medicines will be assessed over a six-process procedure before being granted market authorization (MA) as follows:

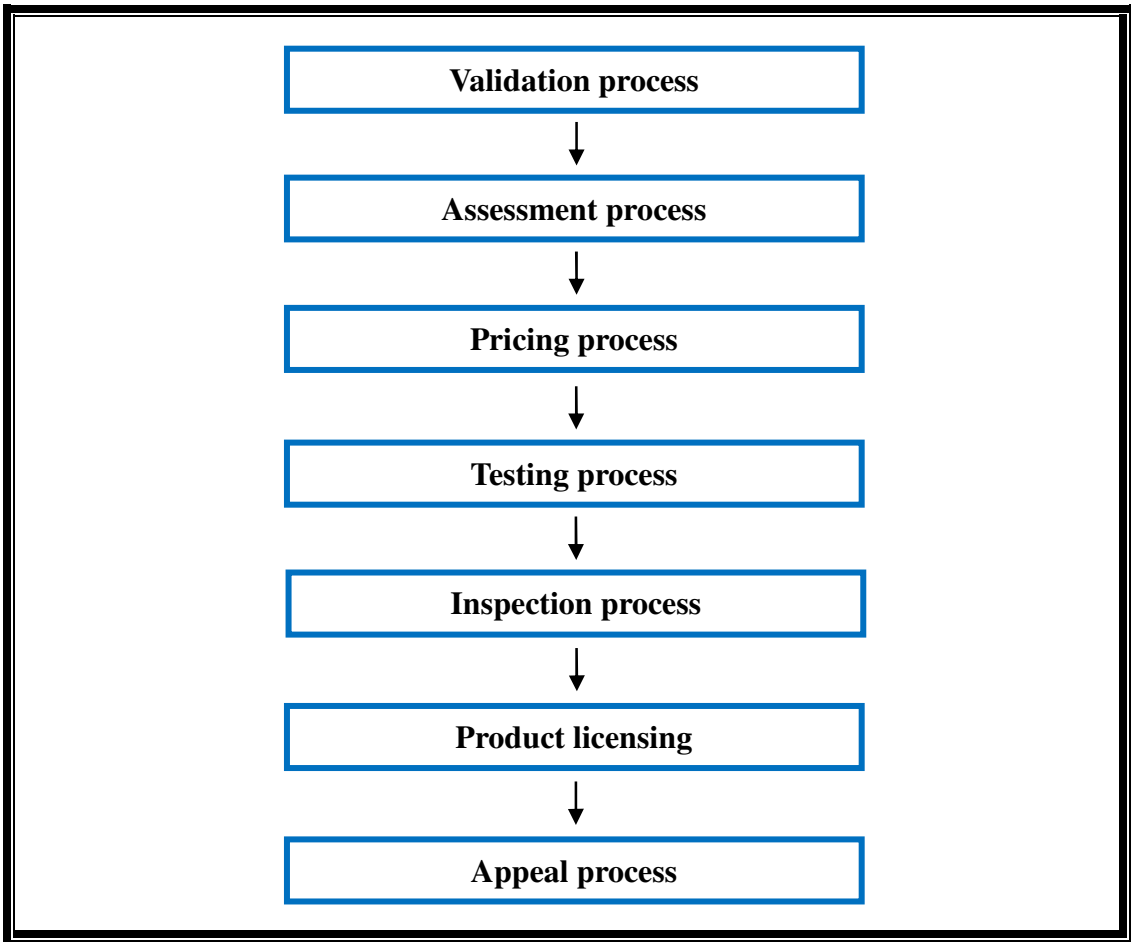

Figure 2.4 The generic medicines approval process for granting market authorization (data source: SFDA, 2009)

- Validation process: in this process, the SFDA will validate and evaluate the drug file in terms of the completeness and accuracy of all the information according to the SFDA generic medicine market authorization requirements and procedure. At this stage, the manufacturer must provide samples of the product for testing in a further step.
- Assessment process: in this process, the product file will be assessed by two groups, namely the quality and efficacy teams in the SFDA. The product file can proceed to the next step only after recommendation for approval and successfully passing the quality and efficacy assessment, otherwise it will be rejected.
- Pricing process: the price of the product will be determined by the pricing unit according to the SFDA pricing rules.
- Testing process: the drug samples received from the drug company will be sent to the laboratory for testing.
- Inspection process: in this process, the SFDA will check the product manufacturing line to ensure compliance with current good manufacturing practice (GMP). It must hold a valid certificate from the Saudi MOH or SFDA, otherwise, an inspection team will be sent to check the line before granting the approval.
- Product licensing: this is the final stage in which the product will be granted marketing authorization (MA) based on reviewing all the reports (quality and efficacy assessment reports, pricing report, testing report, GMP inspection report and company registration) by the SFDA registration committee.
- Appeal process: the company has the right to appeal within 30 days of the final decision by the SFDA.

After approval and before marketing, the first batch must be tested by the SFDA before distribution to make sure it meets the required specifications. After testing, the company will be notified with the result as they can distribute their product only after notification. However, if the company is not notified within 35 days, it may distribute the product under their own liability (SFDA, 2009). In addition, the National Pharmacovigilance Centre (NPC), under the umbrella of the SFDA, is responsible for post-marketing drug surveillance (SFDA, 2009).

2.1.6 Pricing policy of generic medicines

The medicine prices in Saudi Arabia are strictly controlled. Moreover, article no. 14 of the Pharmacy, Pharmaceutical Institutions and Pharmaceuticals Law (2005) stipulated that any drug product must be priced before marketing and the price should be written on the product package in a clear way. Currently, the Saudi Food and Drug Authority (SFDA) is the national regulatory body responsible for registering, approving and pricing medicines. In fact, pricing is one of the essential steps during the registration process (SFDA, 2009). The pricing of generic medicines is based on two guidelines, namely the common pricing criteria and the pricing rules of generic medicines (Hajed, 2008). The common pricing criteria include considering the following factors when pricing any medicine (Hajed, 2008):

- Ex-factory price in the country of origin (COO)
- Wholesale price in the COO
- Public (retail) prices in the COO and other countries where product is marketed
- Cost, insurance and freight (CIF) price to Saudi Arabia in the COO currency

- CIF prices to countries in which the product is marketed (currently there are 30 reference countries, namely Algeria, Argentina, Australia, Bahrain, Belgium, Canada, Cyprus, Denmark, Egypt, France, Germany, Greece, Holland, Hungary, Ireland, Italy, Japan, Jordan, Kuwait, Lebanon, New Zealand, Oman, Portugal, South Korea, Spain, Sweden, Switzerland, Turkey, UAE and UK)
- The price in official pricing references (if available)
- Therapeutic significance of the product

Based on the common pricing criteria, the lowest price should be selected and in all cases the pricing rules for generic medicines should be considered. The SFDA pricing rules for generic medicines stated that the price of the first generic medicine to be marketed should be at least 30% lower than the price of the original brand medicine. After that, the price of the second generic medicine to be marketed should be at least 10% lower than the first generic medicine registered on the market. Then, when registering any generic medicine (3rd or 4th etc), it should be 10% lower than the price of the last generic medicine registered on the market.

Thus, based on the common pricing criteria and pricing rule of generic medicines, the lowest price should be selected and fixed as the price of the generic medicine. This pricing system has led to significant differences in price between original brand medicines and generic medicines. Moreover, there is a significant difference in price among generic medicines for the same original brand medicine as shown by the study conducted by Alnutafy (2009). Table 2.1 and Table 2.2 illustrate the prices of simvastatin and ciprofloxacin as examples.

Table 2.1 The cost of simvastatin 40 mg (30s)*

Trade name	Price (SAR)	Price difference of brand to generic (SAR)	Price difference of generic to brand (%)
Zocor	215.45	–	–
Simvaten	89.40	126.05	140.99
Simvast	80.45	135.05	167.87
Vasta	72.40	143.05	197.58
Simva	65.15	150.3	230.70
Simvagen	59.80	155.65	260.28

*Data source: Saudi National Formulary (SNF) (2010)

Table 2.2 The cost of ciprofloxacin 500 mg (10s)*

Trade name	Price (SAR)	Price difference of brand to generic (SAR)	Price difference of generic to brand (%)
Ciprobay	101.35	–	–
Cipromax	62.05	39.30	63.34
Ciproxen	50.25	51.10	101.69
Omacip	33.05	68.30	206.56
Ciproflacin	21.05	80.30	381.47
Ciprolet	9.70	91.65	944.85

*Data source: Saudi National Formulary (SNF) (2010)

2.1.7 Access to health-care and medicines

In the public health-care sector, health-care services and medicines are provided free of charge to all citizens and also to expatriates working in the government sector (Walston et al., 2008; Almaliky et al., 2011; Bawazir et al., 2013). However, due to several reasons (e.g. quality of care, long waiting times), it is common for those who are entitled to free health-care to seek treatment and medical care at private hospitals and polyclinics. In 2011, it was estimated that 61.6% (n=26,327,464) of those who received care in the private sector were Saudi patients despite the fact that they were entitled to free care in the public sector (SMOH, 2011).

As expatriates working in the private sector are not entitled to free health-care in the public sector, in order to provide them with basic health-care cover, the Cooperative Health Insurance Act was passed in 1999. The aim of this insurance is to provide health cover for expatriates and their families or dependents who are working in the private sector in the kingdom. In this insurance scheme, it is compulsory for all employers to purchase health insurance for their employees and their families in the kingdom (Cooperative Health Insurance Act, 1999). The insurance covers all medical examinations and consultations, medical treatments, medicines, vaccines, child and maternity care, laboratory investigations, X-rays and hospital admissions and hospitalizations, including those related to pregnancy and delivery and surgical operations. However, some conditions are excluded from the cover. General health examinations, treatment for sexually transmitted diseases (STDs), HIV and AIDS medicines, treatment for hair loss, contraceptives, treatment for infertility, impotence, acne and any treatment related to obesity are not covered as stated in the executive regulation of this insurance (Cooperative Health Insurance Policy, 2009).

Regarding access to medicines, according to the Health Professions Act 2005, medicines can be kept and sold only in pharmacies. Moreover, by law, the pharmacist is the only health-care professional who is authorized to dispense medicines. It is also prohibited for other health-care professionals to dispense or keep medicines in their clinics or offices except for emergency medicines (Health Professions Act 2005). Therefore, in the public sector, each hospital has a pharmacy services department. A pharmacy department usually has an inpatient pharmacy, outpatient pharmacy and emergency pharmacy. For primary health-care (PHC) centres, there is one pharmacy in