Comparison of Prices of

Originator and Generic Medicines

A thesis submitted in partial fulfilment of the

requirements of the degree of

Master of Pharmacy

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2020

Acknowledgments

I would like to express my sincere thanks to my supervisor and head of the Department of Pharmacy, University of Malta, Professor Lilian M Azzopardi for her immense support to my studies and to this research. Her guidance, patience, and expertise contributed a lot to make this dissertation relevant and reliable.

I am also grateful to my co-supervisor Dr Francesca Wirth for sharing her knowledge and expertise. Her dedication to her work serves as an inspiration to me to work harder on my studies and this research.

I would also like to thank Professor Anthony Serracino-Inglott, the Chairperson of the Malta Medicines Authority, for the opportunity to be included in the International Fellowship Programme of the Authority which enabled me to pursue further studies in Malta.

I also thank my family and friends for their unconditional love and support.

Above all I am grateful to God Almighty, for giving me much experiences in life that made me realize how wonderful this life to live in. In Him I offer all what I have and whatever earthly endeavour I will pursue in the future.

Abstract

Generic medicines have gained popularity throughout the past years as these enable cost savings and create competition and contribute to driving down prices and promoting access to medicines.

The aim of the study was to compare the prices of originator medicines with their generic counterparts available on the Maltese market.

The study employed a quantitative descriptive approach with a focus on solid oral dosage forms available on the Maltese market as of January 2020. A tally of the originator medicines with their generic counterparts available in a community pharmacy was generated. Each drug was classified according to the Anatomical Therapeutic Chemical (ATC) Classification System. The prices of the medicines were listed and compared. Percentage price differences in each ATC class and the overall average percentage price difference were determined. The ratio of available generic counterparts for each originator medicine was computed.

In total, 76 originator medicines and their generic counterparts (n=148) were compiled. The list includes drugs from 9 ATC classes. Drugs for blood disorders showed the highest average percentage price difference from the originator (-51.93%) followed by drugs for cardiovascular disorders (-46.37%). Drugs for respiratory conditions had the lowest average price difference (-5.50%). The overall average price difference between originator and generic medicines among all ATC classes is -29.12%. Analysis showed that there is a 1:2 ratio of originator to generic medicines in the market.

The results infer that the use of generic medicines decreases the patient's cost of therapy. Generic alternatives are available for most of the commonly used medications.

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List of Abbreviations

ATC	Anatomic Therapeutic Chemical Classification System
EU	European Union
OTC	Over the counter medicines
SME	Small and medium enterprises
SPC	Summary of product characteristics
WHO	World Health Organization

Chapter 1

Introduction

1.1 Background

The increasing costs of medicines is a current global challenge, especially in low- and middle-income countries, since this is seen as a deterrent for patients to gain access to vital treatment modalities (Cameron et al., 2011; Gast and Mathes, 2019). Improvements in the affordability of essential medicines are most important in countries where there are still high out-of-pocket payments, which may result in patients not gaining access to treatment. The United Nations laid out seventeen sustainable development goals to be met by 2030. The third goal puts high priority in ensuring that every person has access to treatment through a universal health coverage and is able to have access to safe and effective medicines and vaccines.[1] Generic medicines could play a vital role in addressing the problem of medicines' access since they allow cost savings by creating competition with the originator medicines, while rendering the same therapeutic effect (Simoens, 2012).

1.2 Originator medicines and innovation

Originator medicines are products which are authorised for marketing based on documentation of efficacy, safety and quality according to requirements at the time of authorisation.[2] These products are usually sold at very high prices in many markets to cover costs related to research and development activities of pharmaceutical companies (Tessema et al., 2020). During market exclusivity periods due to approved

[1] United Nations General Assembly. Transforming our world: the 2030 Agenda for Sustainable Development (A/RES/70). Geneva; 2015. Available from: https://sustainabledevelopment.un.org/post2015/transformingourworld

[2] World Health Organization. Measuring medicine prices, availability, affordability and price components 2nd Edition. In Geneva; 2008 [cited 2020 Jul 28]. Available from: https://www.who.int/medicines/areas/access/OMS_Medicine_prices.pdf?ua=1

patents, developers of originator medicines may be able to dictate the price of the medicines with minima regulation (Gupta et al., 2019). This period is advocated for to provide to feedback revenue to the originator pharmaceutical company to cover for Research and Development expenses and in this way secure funding for research for new innovations.

An ongoing argument is whether excessive regulation in the prices of originator medicines should be implemented, since this may decrease innovation in pharmaceuticals. Presently, there exist different forms of incentives for originator medicines which include patent and data protection, and market exclusivity, among others. The problem however lies with the possibility for the pharmaceutical industry to take advantage of their market power by charging more than what is justifiable, mainly because there are no alternatives on the market (Moreno and Epstein, 2019).

It is known that innovation in medicines is important to pursue progress in the treatment and prevention of diseases. However, since the start of the 2000s, there has been an intensified discussion on the potential "innovation crisis" in the pharmaceutical sector.[3] Since 2010, a stable declining trend in development productivity of major pharmaceutical manufacturers has been observed.[4] Most of the research on new drugs

[3] Panteli D, Edwards S. Ensuring access to medicines: How to stimulate innovation to meet patients' needs? Copenhagen: 2018. Available from: https://www.who.int/medicines/areas/access/OMS_Medicine_prices.pdf?ua=1

[4] A new future for R&D: Measuring the return from pharmaceutical innovation [Internet]. 2017. Available from: https://www2.deloitte.com/content/dam/Deloitte/uk/Documents/life-sciences-health-care/deloitte-uk-measuring-roi-pharma.pdf

originates from small or medium-sized enterprises (SMEs) or academic institutions, public bodies, and public-private partnerships. This means that large pharmaceutical companies are mostly in charge of commercialisation of new products, however SMEs, academic institutions, and public institutions play a vital role in driving innovation of new drugs (Lincker et al., 2014).

1.3 Generic medicines and public health

A generic medicine is a drug product that is developed and intended to be the same as a previously authorised medicine. Its authorisation is based on efficacy and safety data from studies conducted on the authorised medicine. A company can market a generic medicine once the ten-year exclusivity period for the originator medicine has expired.[5] Utilising generic medicines which are bioequivalent to originator drugs has been shown to decrease health care costs (Babar et al., 2014). Generic medicines can only be produced upon the expiry of patents of originator medicines, making them less expensive (Vondeling et al., 2018).

Regulatory authorities in each country are expected to conduct or approve bioequivalency studies which ensure that generic medicines shall deliver the same quantity of the drug. However, biowaivers are also permitted by regulatory authorities in which *in vivo* bioequivalence and/or bioavailability studies may be waived and instead use *in vitro* tests like the dissolution test as a basis for decision making [6]. To harmonize

[5] European Medicines Agency. Generic medicine [Internet]. [cited 2020 Jul 28]. Available from: https://www.ema.europa.eu/en/glossary/generic-medicine

[6] Karam R, Kurdi M. Biowaivers : criteria and requirements [Internet]. 2015. Available from: www.moph.gov.lb

the different information on biowaivers, the International Pharmaceutical Federation or FIP initiated the Biowaiver monograph project in 2004. The monograph serves as guidance for different regulatory authorities by stating conditions when a biowaiver could be granted. [7]

The use of generic medicines may result in cost savings of about 85% compared to originator medicines. The lower costs incurred in purchasing generic medicines increases the likelihood that patients take medications prescribed by their physicians, and may result in improving patients' overall health outcomes (Razmaria, 2016).

1.3.1 Global impact of generic drugs on pricing

The value of conducting studies on generic medicines production and utilisation has been increasing in the past years as governments and healthcare payers have been alarmed by rising healthcare expenditures. Countries from the Organization for Economic Co-operation and Development (OECD) note that expenditures arising from pharmaceutical commodities account for about 1.5% of a country's gross domestic product.[8] The United States of America has facilitated the approval of generic drugs by regulatory authorities as early as 1984 through the Hatch-Waxman Act, requiring only a demonstration of bioequivalence before approval (Boehm et al., 2013).

[7] Biowaiver Monographs 2004-2012 [Internet]. Netherlands; Available from: https://www.fip.org/file/1377

[8] OECD. Health at a Glance 2013: OECD Indicators [Internet]. Paris; 2013. Available from: http://dx.doi.org/10.1787/health_glance-2013-en

The impact of using generic medicines has been variable in different countries. A systematic review, showed that although there is an evident similarity in terms of clinical effects of generics with the originators, there was no guarantee of cost savings in applying generic substitution (Gothe et al., 2015). In a study conducted in Croatia focusing on drugs acting on the renin-angiotensin system, the introduction of generic medicines on the market in a span of thirteen years led to an average decrease of 48.91% for all medicines, both originator and generics. Despite decreases in prices of medicines, consumption shares of generics persist at 68%, hence there is a need to introduce policies to promote the use of generics among the general public (Kucan et al., 2015).

In a study conducted in South Africa, candesartan and rosuvastatin utilisation and expenditure was studied over a four-year period. The study revealed that the introduction of generics on the market did not have any impact on utilisation but reduced the expenditures of people on both medicines through price reduction. In that span of time, total savings of 54.8% for candesartan and 31.9% for rosuvastatin were observed (de Jager and Suleman, 2019).

1.4 Perception of Generic Medicines

A study in France revealed that prescribing using the INN is generally accepted by health care professionals, but there are concerns for potential adverse effects brought about by generic medicines. In that study, health professionals perceived it as important that a patient receives the same generic medicine each time for their maintenance treatment, regardless of the brand (Lagarce et al., 2005). In Slovenia, concern about the

cost of prescribed drugs and the improved willingness to prescribe generic medicines has been reported. The majority of general practitioners perceived generic medicines to have the same effectiveness as branded ones (Kersnik and Peklar, 2006).

In a study conducted in India, patients and health workers perceive branded medicines to have better quality compared to generic medicines despite quality tests revealing comparable quality. In focus group discussions conducted, it was revealed that the negative perceptions on generic medicines by pharmaceutical companies influence the behaviour of prescribers and thus affects trust in the healthcare provided in the public services. The study concluded that the system should invest in promoting information on the quality of generic medicines and develop strategies to build trust in public health services (Aivalli et al., 2017).

A systematic review, which included 52 articles from an initial screening of 2,737 articles since 1980, shows that there is a high proportion of physicians, pharmacists and lay persons who have negative perceptions on generic medicines. Lay persons were more likely to see generics as less effective than the branded medicines (37.6%), followed by physicians (28.7%) and pharmacists (23.6%). Of the three groups of respondents, pharmacists (33.4%) were most likely to perceive generics to be of inferior quality compared to branded medications. Physicians were most concerned about the safety of generic medications. These attitudes of different groups present a hindrance in promoting the expanded use of generic medicines (Colgan et al., 2015).

1.5 Boosting generic medicine production in the European Union

The Council of the European Union (EU) in 2019 has adopted a regulation which introduced an exception to the protection granted to an originator medicine through a supplementary protection certificate (SPC) for purposes of exportation or stockpiling. The EU is currently supporting measures to improve the competitiveness of EU producers of generic medicines and biosimilar products. It is envisaged that the new regulations will create high-value jobs and boost the availability of generic medicines in the EU.[9] As production of generic medicines increase in the EU region, the challenge for Member countries is to improve public perception on generic medicines to maximise utilisation of these new products.

1.6 Generic medicines and public policy

Several countries have applied various strategies to improve utilisation of generic medicines. These strategies have different success rates, but all are intended to allow more people to receive the benefits from using generics. The promotion of the use of generic medicines is recommended to be included in a country's national medicine policy to attain sustainable healthcare (Godman et al., 2010). A program on generic medicines improves affordability and further access to medicines in developing nations (Cameron et al., 2009).

[9] European Parliament and Council. Amending Regulation (EC) No 469/2009 concerning the supplementary protection certificate for medicinal products [Internet]. 2018. Available from: https://data.consilium.europa.eu/doc/document/PE-52-2019-INIT/en/pdf

1.6.1 Drivers in the generic medicines market

To better understand the prescribing and dispensing behaviours in countries, analysis of the drivers in the generics market is required. In a 2009 report, generic medicines accounted to 80% of market share of medicines sold in Denmark and this is mainly driven by pharmacists. Another country where pharmacists are considered as the driver in the market is Sweden. The United Kingdom has a mixed medicines market driven by both physicians and pharmacists. The market in Germany and the Netherlands are driven by payers or health insurance funds. Other countries included in the study such as France, Belgium and Austria, are driven by physicians. Though the relationship was not examined, what is interesting is the trend of generic medicines market share in each country considering the driver. Those countries which were mainly driven by pharmacists and payers have a higher market share of generic medicines, while those driven by physicians have a lower market share.[10]

1.6.2 Generic medicines promotion through prescribing regulations

A method used to improve the utilisation of generic medicines is through imposition of prescribing quotas. One country which implemented this strategy is Belgium. Imposing a prescription quota means that generics or biosimilars should account for a certain share of the total volume of medicines prescribed by a prescriber (Ferrario et al., 2020). Belgium implemented a system where physicians were required to prescribe 27% of medicines which are considered “cheap medicines”, which included generics. The policy was successful since from 2006 to 2009 most groups of physicians met the minimum

[10] European Parliament and Council. Amending Regulation (EC) No 469/2009 concerning the supplementary protection certificate for medicinal products [Internet]. 2018. Available from: https://data.consilium.europa.eu/doc/document/PE-52-2019-INIT/en/pdf

annual percentages. The percentage of prescribed generic medicines increased from 22.9% to 44.2% in four years (Dylst et al., 2014). In Europe, the countries which provide incentives for physicians to prescribe generic medicines include France, Germany, the UK, and Sweden. These countries have employed concrete economic measures to promote prescribing of generic medicines. A study suggests that competition in the pharmaceutical market is enhanced when physicians are encouraged to prescribe, and customers are encouraged to use generic medicines, thus driving prices down (Emilien, 1997).

1.7 Generic medicines in Malta

In an article written by Dr Paul Cassar of the University of Malta in 1987, patented medicines started to be imported in Malta in 1823 by Louis Calleja, owner of English Dispensary in Valletta, who imported patented medicines from the United Kingdom. In 1844, Mr. Calleja produced his own patented medicine, 'Calleja's Life Pills' which were used for liver diseases and constipation. It was also reported that foreign patent medicines became regular items in stock of Maltese pharmacies by mid-19th century (Cassar, 1987).

At the present time, prescribers in Malta are not mandated by law to prescribe medicines by generic name or the International Non-proprietary Name (INN). In 2006, there was a proposal to amend the present Medicines Act, whereby prescribers would be legally required to prescribe in the generic name. This would entail improved exposure of generic medicines and would open greater competition as patients would have the choice to purchase different brands with the same generic name. This proposal

was turned down due to contentions that physicians or any prescriber should have the discretion which brands to prescribe and should not be overruled by legislation. In addition, persons who objected to the proposal pointed out that dispensers would sell products which are more profitable should the legislation be revised. [11]

In a study conducted in 2012 to assess the perception of Maltese people on generic medicines, 51% of respondents did not know the meaning of the term generic medicinal product. When given an example, 58% of those respondents were able to recognise using such products in the past. The study also showed that 3% of participants would opt not to take any medication until the originator is back in stock rather than use a generic alternative. There was also a positive association with the knowledge of generic medicines and the possibility of continued taking of generic alternatives (Azzopardi and Zarb Adami, 2012).

A similar study was conducted in 2020 to determine the perception of the general public in Malta on generic medications. Results revealed that 61% of respondents were aware of the correct definition of a generic medicine and 55% have used generics before. Among the participants, 20% have not used generic medicines as they think that these products have inferior quality or less effective than originators (Sammut Bartolo et al., 2020).

[11] Farrugia M. Proposal to ban prescription of brand medicines turned down [Internet]. Times of Malta. 2006 [cited 2020 Jul 28]. Available from: https://timesofmalta.com/articles/view/proposal-to-ban-prescription-of-brand-medicines-turned-down.41494

1.7.1 Pricing of medicines in Malta

Upon the accession of Malta to the European Union in May 2004, it was expected that there would be an eventual increase in the prices of medicines, but no mechanism was in place to prevent excessive increase in prices. Reference pricing was introduced to potentially solve the problem. Malta has two reference pricing systems in place. One is a voluntary mechanism for the private market, which was introduced in 2008, and an obligatory reference pricing for the public sector (medicines in the government formulary) which was introduced in 2010. The two mechanisms utilise external reference pricing through a cross-country referencing, where prices of medicines produced by the same company are compared across several countries. However, on some degree, internal reference pricing is still implemented for new medicines introduced on the government formulary by comparing the prices to others within the same therapeutic group already on the formulary (Formosa, 2012).

1.8 Aim of the study

The aim of the study was to compare the prices of originator medicines with their generic counterparts available in the Maltese market. Likewise, the study aimed to determine whether there is enough availability of generic counterparts for originator medicines in the market. The difference in prices of the products shall elucidate whether the entry of generic medicines in the market created significant impact leading to reduction in market prices. The results of the study will be important for economic and health regulatory authorities to gain information as to the relevance of generic medicines availability and production in improving access to drug treatment and improve overall health outcomes.

Chapter 2

Method

2.1 Study design

The study employed a quantitative descriptive approach. A quantitative descriptive research design typically elicits data on the current situation and reveals the operational adequacy of a service or phenomenon (Fawcett and Garity, 2009).

2.2 Data collection

The study focused on solid oral dosage form pharmaceuticals available on the Maltese market as of January 2020. The conduct of the study started by generating a list of originator medicines and generic counterparts available in a private community pharmacy. Products on the pharmacy point of sale system but which were out of stock during the data collection period were not included in the data set.

2.3 Data analysis

The class of each medicinal product included in the list was determined according to the Anatomic Therapeutic Chemical (ATC) classification system. For each product, price in Euro and number of doses per pack were compiled. The levels employed in the ATC classification system are shown in Table 2.1. The price per unit dose for all products was calculated. The price per unit dose of the originator and the generic medicines were compared and the percentage price difference per ATC class was determined. An overall average percentage price difference between originators and generics was computed. The ratio of generic counterpart(s) per originator medicine was determined from the data gathered. A process flow of the methods used are shown in Figure 2.1.

Table 2.1 Levels of ATC classes

Level	Level Abbreviation	ATC Code	Level Identification	Example
1	ATC1	C	Anatomic group	Cardiovascular system
2	ATC2	C08	Therapeutic subgroup	Calcium channel blockers
3	ATC3	C08C	Pharmacological subgroup	Selective calcium channel blockers with mainly vascular effects
4	ATC4	C08CA	Chemical subgroup	Dihydropyridine derivatives
5	ATC5	C08CA01	Chemical substance	Amlodipine

Adapted from: Andrade LF, Sermet C, Pichetti S. Entry time effects and follow-on drug competition. Eur J Heal Econ [Internet]. 2016 Jan 1 [cited 2020 Aug 14];17(1):45–60. Available from: https://link.springer.com/article/10.1007/s10198-014-0654-9

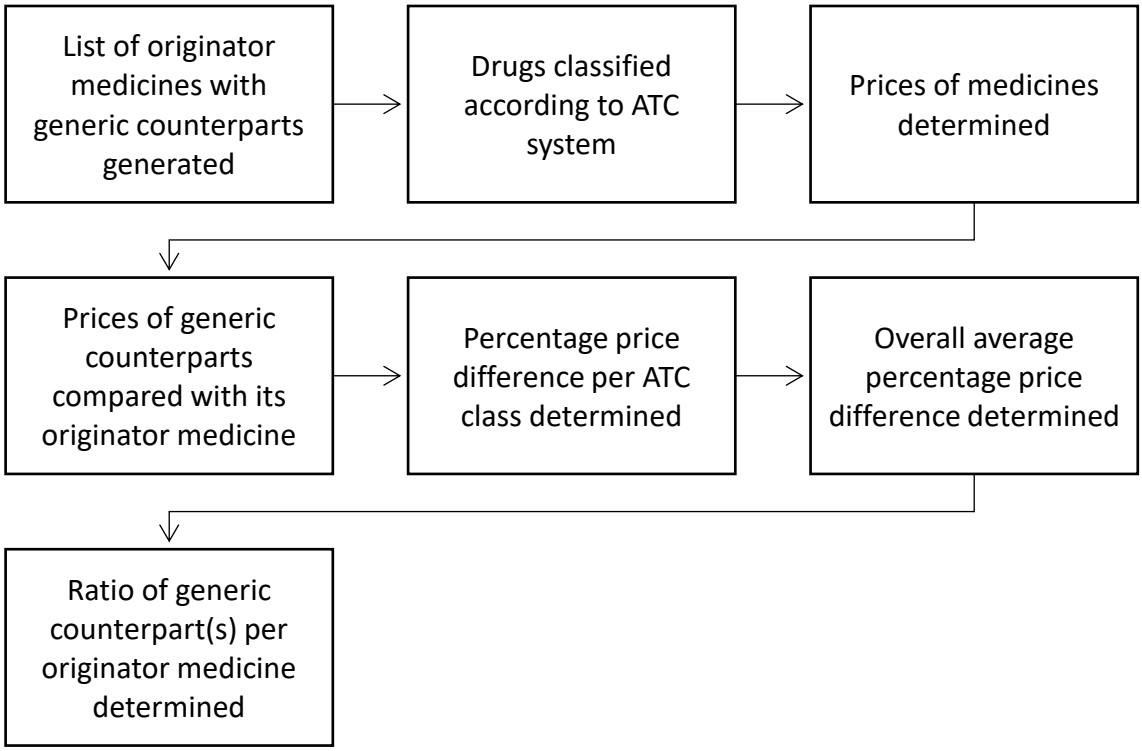

Figure 2.1 Process flow employed in the study

2.4 Ethical consideration

A protocol of the study was submitted to the University of Malta Faculty of Medicine and Surgery Research and Ethics Committee (FREC). The acknowledgment email from the FREC is shown in Appendix 2

Chapter 3

Results

There were 76 originator medicines and their generic counterparts (N=148) included in the study, following the set criteria. The generated list encompasses drugs from 9 different ATC anatomic classes (level 1).

3.1 Generic medicines availability in the market

Figure 3.1 shows the distribution of medicines included in the study based on marketing classification, resulting in a 1:2 ratio of originator (66%) to generic medicines (34%)

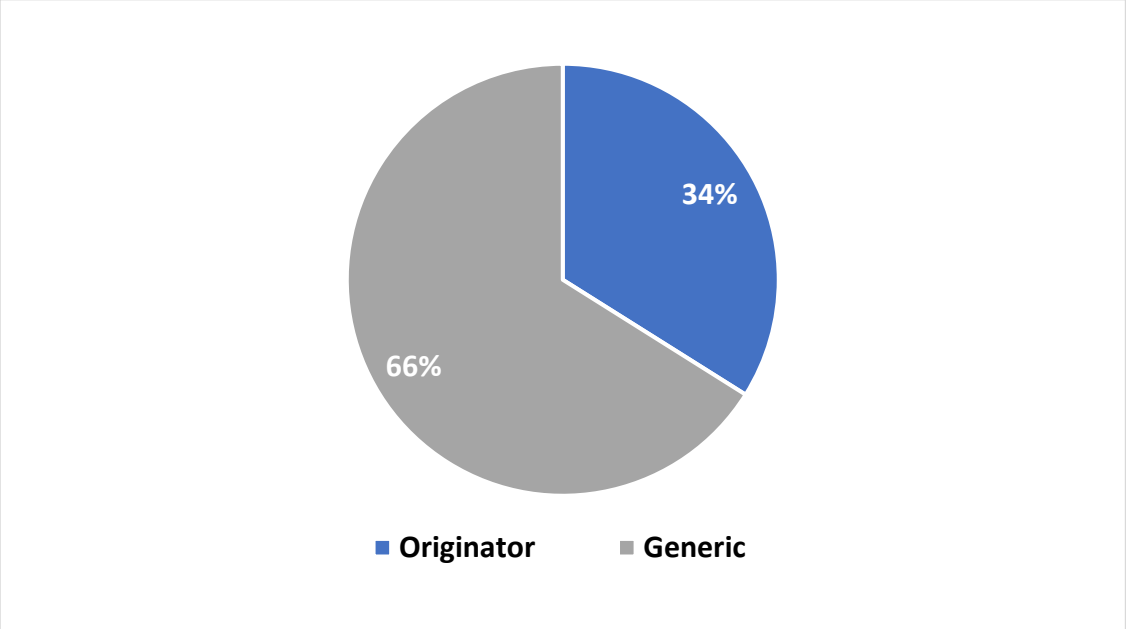

Figure 3.1 Percentage distribution of originator and generic medicines available on the Maltese market (N=224)

Figure 3.2 illustrates the number of available generic counterparts for every originator medicine, sorted by ATC class. The anatomic class which had the highest number of generic counterparts are originators in drugs for blood disorders with an average of four generics for every originator medicine. All the other classes have an average of two generic counterparts for every originator medicine, which validates the ratio of 1:2,

which means that for every originator, there are two generic medicine counterparts on the Maltese market.

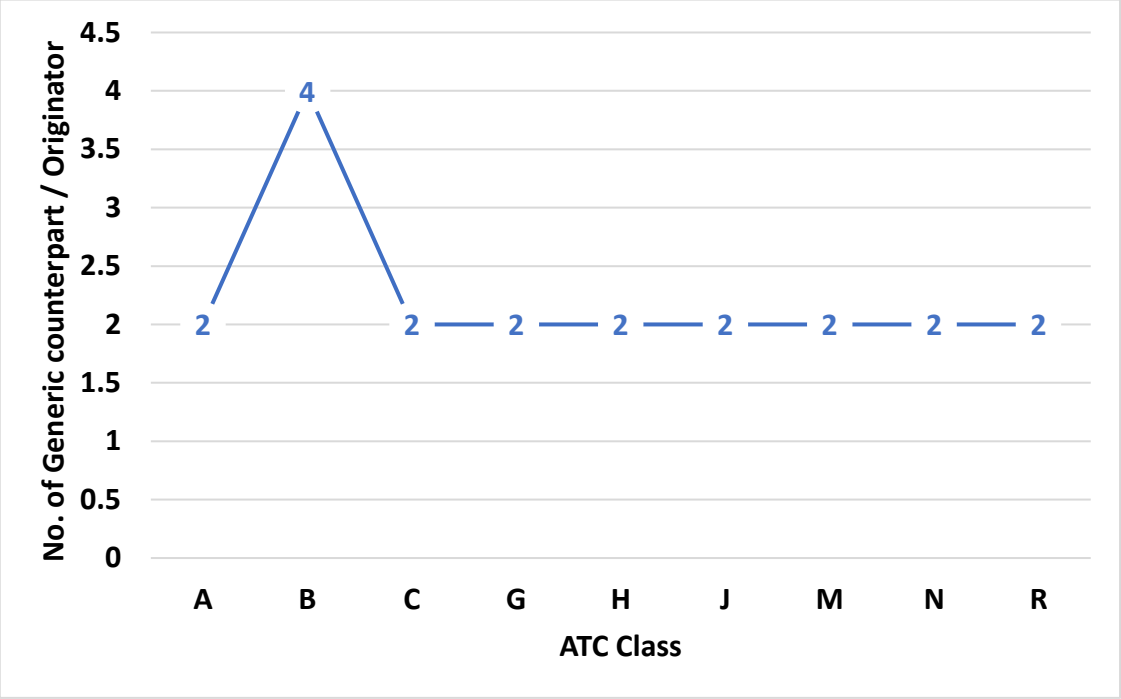

Figure 3.2 Number of generic counterpart(s) per originator medicine by ATC class

A: Alimentary tract and metabolism, B: Blood and blood forming organs, C: Cardiovascular system, G: Genito urinary system and sex hormones, H: Systemic hormonal preparations, J: Anti-infective for systemic use, M: Musculoskeletal system, N: Nervous system, R: Respiratory system

Figure 3.3 illustrates the distribution of originator and generic medicines for each ATC class. Among the ATC classes, the one which has highest number of generic medicines is the class for anti-infectives for systemic use (n=34), followed by the class of drugs for cardiovascular disorders (n=32). Both mentioned classes have the same number of originator medicines (n=15).

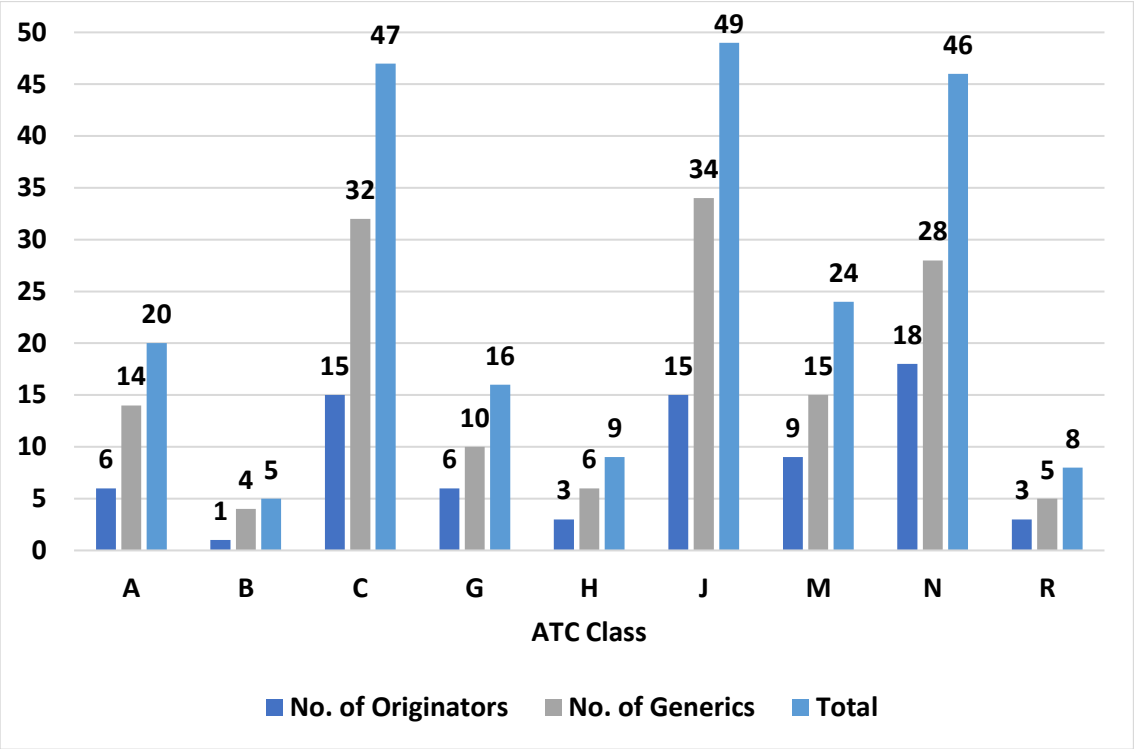

Figure 3.3 Comparison of the amount of originator and generic medicines per ATC class

A: Alimentary tract and metabolism, B: Blood and blood forming organs, C: Cardiovascular system, G: Genito urinary system and sex hormones, H: Systemic hormonal preparations, J: Anti-infective for systemic use, M: Musculoskeletal system, N: Nervous system, R: Respiratory system

3.2 Cost savings of generic medicines

Table 3.1 shows the percentage price differences between originator and generic medicines by ATC class. Drugs for blood disorders showed the highest average price difference from the originator (-51.93%), followed by drugs for cardiovascular disorders (-46.37%), and drugs for the alimentary tract and metabolism (-38.52%). Drugs for respiratory conditions had the lowest average price difference (-5.50%). The overall average price difference between originator and generic medicines across all ATC classes is -29.12%.

Table 3.1 Percentage price differences between originator and generics by ATC Class (N=148)

ATC Code	Description	n	Mean (%)	Std. Dev.
A	Alimentary tract and metabolism	14	-38.52	22.21
B	Blood and blood forming organs	4	-51.93	3.99
C	Cardiovascular system	32	-46.37	20.54
G	Genito urinary system and sex hormones	10	-32.00	17.02
H	Systemic hormonal preparations	6	-16.43	21.20
J	Anti-infective for systemic use	34	-14.78	41.38
M	Musculoskeletal system	15	-32.18	33.72
N	Nervous system	28	-23.16	36.19
R	Respiratory system	5	-5.50	34.65
Total		**148**	**-29.12**	**33.18**

Further investigation was conducted on the ATC subclasses of the drugs included in the study. Table 3.2 shows the differences in the prices of originators and generics within the ATC class for drugs used in the treatment of cardiovascular disorders. The subclass for calcium channel blockers (n=7) showed the highest percentage price difference (μ=-65.46%), followed by the drugs acting on the renin-angiotensin system (n=7, μ=-49.74%). The subclass which showed the lowest percentage price difference between originators and generics are the diuretic drugs (n=1, μ=-5.31), followed by drugs used as antihypertensives (n=3, μ=-17.62%).

Table 3.2 Percentage price differences between originator and generics in ATC Class C, drugs used for cardiovascular disorders (N=32)

ATC Code	Description	n	Mean (%)	Std. Dev.
C02	Antihypertensives	3	-17.62	3.40
C03	Diuretics	1	-5.31	.
C08	Calcium Channel Blockers	7	-65.46	11.73
C09	Agents Acting on the Renin-Angiotensin System	7	-49.74	15.10
C10	Lipid Modifying Agents	14	-44.23	17.54

In the class for anti-infectives used for systemic treatment, there were only two subclasses. The first class includes antibacterials used for systemic purposes, while the other class includes antivirals for systemic use. Analysis revealed that between the two subclasses, antivirals (n=5) showed a higher percentage price difference between originators and generics (μ=-69.83%) than the antibacterials (n=29, μ=-5.28%). Further analysis was done with the pharmacological subclasses of J01 – Antibacterials for systemic use. Quinolone antibacterials (n=8) have the highest mean percentage difference in price (μ=-19.81%), followed by other beta-lactam antibiotics (n=4, μ=-15.71%). Beta lactam antibacterials (n=4) and other antibacterials (n=1) showed an increase in price in the generic medicines compared to originators (μ=25.71%, μ=78.99%).

Table 3.3 Percentage price differences between originator and generics in ATC Class J, drugs used as anti-infectives for systemic use (N=34)

ATC Code	Description	n	Mean (%)	Std. Dev.
J01	Antibacterials for Systemic Use	29	-5.28	36.89
J01M	Quinolone Antibacterials	8	-19.81	16.11
J01D	Other Beta-Lactam Antibacterials	4	-15.71	19.03
J01F	Macrolides, Lincosamides and Streptogramins	12	-9.48	39.89
J01C	Beta-Lactam Antibacterials, Penicillins	4	25.71	38.38
J01X	Other Antibacterials	1	78.99	.
J05	Antivirals for Systemic Use	5	-69.83	12.69

Analysis was conducted for the therapeutic and pharmacologic subclasses under the ATC class for drugs utilised for nervous system disorders. Among the therapeutic subclasses, analgesics (n=3) showed the highest mean percentage difference between originator and generics (μ=-68.31%), and was followed by psycholeptics (n=6, μ= -30.83%). Antiepileptics (n=6), showed the lowest difference (μ =-6.76%) among the therapeutic subclasses. Two therapeutic subclasses had drugs which are classified in different pharmacologic subclasses and analysis was also conducted. Of the two pharmacologic subclasses identified under the class of analgesics, N02B or other analgesics and antipyretics (n=2) had a higher mean difference (μ=-80.65%) than N02C or antimigraine (n=1, μ=-43.63%). Analysis into the pharmacologic subclasses of psycholeptics showed that antipsychotics (n=1) had the highest mean difference

(μ=72.76%), followed by hypnotics and sedatives (n=1, μ=-36.27%), and anxiolytics (n=4, μ=-18.99%).

Table 3.4 Percentage price differences between originator and generics in ATC Class N, drugs used for nervous system disorders (N=28)

ATC Code	Description	n	Mean (%)	Std. Dev.
N02	Analgesics	3	-68.31	21.37
N02B	Other Analgesics and Antipyretics	2	-80.65	0.00
N02C	Antimigraine	1	-43.63	.
N03	Antiepileptics	6	-6.76	15.31
N05	Pyscholeptics	6	-30.83	41.10
N05A	Antipsychotics	1	-72.76	.
N05B	Anxiolytics	4	-18.99	45.09
N05C	Hypnotics And Sedatives	1	-36.27	.
N06	Psychoanaleptics (Antidepressants)	13	-16.77	36.76

Chapter 4

Discussion

4.1 Cost savings of generic medicines

Results reveal that there was a price decrease when generic medicines were compared with their originator medicines and a 29% average price decrease was observed across all ATC classes. From a consumer standpoint, this translates to money saved from a patient's regular expenses. A study in 2015 shows that in Europe, generic medicines tend to be 20 to 80% cheaper than originator medicines (Dylst et al., 2015). From a public health perspective, this translates to cost savings on government expenditure for essential medicines. In the case of Malta, the use of generic medicines greatly benefits the Pharmacy of Your Choice (POYC) scheme which provides government subsidised medications for most chronic conditions. The gain achieved in using generic medicines may help to increase the variety of therapeutic agents covered by the national health scheme. This concept becomes more relevant when looking at medicinal products where there is a considerably high price differential such as biosimilar drugs. A paper by the European Commission in 2012 suggests that by employing generic substitution, it is expected that there would be reduced public expenditure in European countries by at least 20% (Carone et al., 2012). This public expenditure allows more people to be included in a government funded healthcare program, as well as increasing benefits and coverage of its beneficiaries. In the context of Malta, strategic purchasing of generic medicines by the Central Procurement and Supplies Unity (CPSU), and rationalisation of patient entitlements leading to reduced unused medications by the POYC, may help to cut down on costs and allow more people to benefit from the national health scheme.

The ATC class which showed the highest percentage price difference between originator medicines and generics are drugs for blood disorders. It is worth noting that there is only one drug molecule in this ATC class, which is clopidogrel. The originator was compared to 4 generic counterparts, considered in this study, which resulted to a 52% price difference. This may imply that the presence of generic counterparts in the market led to a reduction in prices of clopidogrel. A study in Canada shows that generic clopidogrel was non-inferior to the originator brand, Plavix®, in terms of survival rates and recurrent hospitalisation for acute coronary syndromes, all leading to substantial healthcare cost savings (Ko et al., 2018). Clopidogrel is a drug which is available on the national health system for free in Malta according to a protocol for patients with ischaemic heart disease who either underwent a percutaneous coronary intervention or trans-catheter aortic valve implantation or were admitted for acute coronary syndrome. Patients must satisfy eligibility criteria for free medicines and duration of approval is for a period between 6 months to 1 year. There are patients who would fall outside these criteria and are required to pay out of pocket for the medication for the duration of the treatment or until their approval is granted.

The class which had the lowest price difference from the originator medicines are drugs used for respiratory diseases (5.5%). One factor contributing to this is that there is a generic product of cetirizine which is 51% higher per unit dose than the originator medicine, Zyrtec®. When this generic medicine was excluded from the data set, the price reduction for the ATC class turned out to be 19.69%. This means that in general, increased competition in the market through the entry of generic medicines contribute to beneficial price reductions. Most of the drugs included in this category are used for

allergic conditions. According to a published survey from Great Britain, drugs used for hay fever accounted for £114.7m (€131.5m) of the overall non-prescriptions medicines market in 2017 (Connelly, 2018). This means that many patients use these medications on a regular basis, hence when many alternative brands at a lower price are available, this results in long-term benefits to consumers.

4.1.1 Impact on cardiovascular drugs

Examining the mean differences of pharmacologic subclasses revealed the specific reduction in prices for each drug class. In the drugs for cardiovascular disorders, calcium channel blockers showed the highest price reduction, with 65% savings when using generic medicines. The only drug which is included in this subclass is amlodipine, a non-dihydropyridine calcium channel blocker. According to a market research, among the antihypertensives, calcium channel blockers holds the largest share in 2018, estimated to account for one-fourth of the global antihypertensive market. The same market study stated that angiotensin converting enzyme (ACE) inhibitors are manifesting to have the fastest annual growth rate in terms of market share. ACE inhibitors belong to a general class of medications which act on the renin-angiotensin system together with angiotensin II receptor blockers (ARB). [12]

Results of the current study reveal that drugs which act on the renin-angiotensin system have an approximate price reduction of 50% when generic alternatives are preferred. A

[12] Allied Market Research. Antihypertensive drugs Market to Garner $28.79 Billion by 2026 [Internet]. 2020 [cited 2020 Aug 14]. Available from: https://www.globenewswire.com/news-release/2020/02/19/1987190/0/en/Antihypertensive-drugs-Market-to-Garner-28-79-Billion-by-2026.html

study conducted in China, which employed probabilistic analysis, stated that implementing a low-cost essential antihypertensive medicines program has the potential to prevent 800,000 cardiovascular events (Gu et al., 2015). A study conducted in India which compared the prices of generic and innovator formulations of various antihypertensive drugs, showed that the innovator formulation of amlodipine was 1,750% expensive than the generic ones. The use of generic alternatives in this case may reduce the treatment expenditure of patients by many folds (Vadgama and Gaekwad, 2019).

4.1.2 Impact on anti-infective drugs

Generic alternatives of medicines used for infectious diseases had a 15% average reduction in prices when compared with originator products. Although these medicines are commonly used only for a short duration of time, prices of these products may contribute to low adherence to drug treatment regimens. An Indian study investigated the relative potency of generic brands of various antibiotics and compared them with originators. Researchers have observed that price and being an originator was not important indicators of quality and potency of a drug. The inexpensive generic brand performed as well as the originators on the market (Das et al., 2019). In contrast, some studies point out that chemical deviations among generic antibiotics may lead to non-equivalence. A study conducted in Colombia revealed that a certain salt form of meropenem made it less stable at room temperature. However, these generics are still compliant with the United States Pharmacopoeia standards and may not be seen by many regulatory agencies (Agudelo et al., 2014).

Among the antibacterial drugs analysed in the present study, the generic quinolones showed the largest price reduction of about 20% compared with the originators. A study in Colombia conducted an *in vitro* analysis on generic moxifloxacin, a fluoroquinolone antibiotic, regarding its effects against *E. coli* and *S. aureus*. The study found that the minimum inhibitory concentration of both generic and standard moxifloxacin are about the same for both strains of bacteria (Alviz-Amador et al., 2018).

The results of the present study show that generic antiviral medications offer superior price savings of about 70%. The only antiviral drug included in the analysis is oral aciclovir, which is mainly used for herpes simplex, varicella, and herpes zoster viral infections. This antiviral drug speeds up the healing process and may reduce the severity of symptoms.[13] A study in India determined the cost-effectiveness of using generic antivirals in treating hepatitis C infection. It showed that treatment with low-cost, generic antivirals will result in cost-savings, as cirrhosis and liver cancer may be prevented in the future (Aggarwal et al., 2017). In contrast, a study attempted to determine the level of bioequivalence of a generic oral form of aciclovir and the originator, Zovirax® in healthy volunteers. Bioequivalence metrics showed that the specific generic considered in the study was not bioequivalent to the originator (Amini et al., 2008).

[13] Institute for Quality and Efficiency in Health Care. How effective are creams and tablets for the treatment of cold sores? [Internet]. InformedHealth.org. 2018 [cited 2020 Aug 15]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK525789/

4.1.3 Impact on drugs acting on the nervous system

Analysis of data revealed that an estimated 23% price reduction can be benefited from using generic medicines for nervous system disorders. A study from the United States revealed that there is a shortage of generic drugs used for neurological conditions. There were around 21 medicines in shortage per month reported with a median shortage duration of 7.4 months. Among the reasons cited for the shortages included regulatory issues and business decisions, aside from the usual supply/demand issues (Omorodion et al., 2017). This shortage of generic medicines used for neurologic conditions not only deprives patients of access to affordable and bioequivalent medications, but this may also worsen the condition of some cases.

Among the therapeutic classes, analgesics which only included the drug paracetamol had the highest price reduction of 68%. A study in Nigeria assessed the quality and interchangeability of common brands of generic paracetamol. All 6 generic medicines analysed were interchangeable with one another (Ukwueze et al., 2008). A similar study was conducted in Palestine where 10 generic paracetamol products were tested. Results showed that 9 of the generic paracetamol products were comparable to the innovator. Locally produced generic medicines are possibly 2 to 3 times cheaper than the ones which are imported (Zaid et al., 2013).

Further analysis into the pharmacological subgroups under psycholeptics, it was observed that antipsychotics had the highest mean price reduction at 73%, while anxiolytics may offer the least savings with only 19%. In a ten-year period in Croatia, psycholeptics had the highest share of generic psychopharmaceuticals on the market,

with 83.6% in 2001 and 82.2% in 2010. Interestingly, hypnotics and sedatives had more generic alternatives and antipsychotics had least. The study suggested that mixing initiatives to lower generic medicine prices by enhancing their prescribing may improve utilisation and promote savings for the patient. [14]

Within the neurologics group, antiepileptics were seen to have the lowest mean price reduction at 7%. A study in India shows that there is an extensive variation in the prices of various generic antiepileptics on the market. Valproic acid had a 216.7% cost variation between the cheapest and the most expensive generic medicine, followed by lamotrigine with 150%. High costs of medications are seen to cause non-adherence leading to treatment failure of epilepsy (Shukla and Mehani, 2016).

4.2 Generic medicines availability in the market

Results from the present study show that drugs for blood disorders have the highest number of generic counterparts with four generics for every originator. This information may be a result of a lower sample size to work with as there is only one drug molecule in this class. Drugs for the genitourinary system and sex hormones have an average of one generic counterpart for every originator which may impact patients using drugs in this category. Considering all classes, for every originator medicine on the Maltese market, there is an average of two generic competitors.

[14] Polić-Vižintin M, Tripković I, Štimac D, Šostar Z, Orban M. Utilization of generic versus brand name psychopharmaceuticals during a ten-year period in Croatia. In: Annual Congress & Medicare Expo on Primary Healthcare [Internet]. 2016 [cited 2020 Aug 17]. Available from: http://dx.doi.org/10.4172/2167-1079.C1.003

In a study in the United States of America, which used a simultaneous equation framework to capture interactions between generic brand entry, prices, and market share, it was reported that generic competition is particularly intense for blockbuster drugs. These drugs have more generic entrants, price erosion, and generic penetration than other drugs. The same study revealed that originator drug prices react to generic competition as there is a decline in the average price of the originator drug by 0.2% (Saha et al., 2006). Competition plays a significant role in driving prices of both originator and generic medicines. However, as Malta is an island nation and has a relatively small market, importers may deem it impractical to compete at a limited market space. A study looking into the generic drug markets in Europe and the United States suggests that governments must prioritise convincing more physicians, pharmacists, and patients that generic drugs are bioequivalent to originator products (Wouters et al., 2017).

4.3 Limitations of the study

Since there are ATC classes which only have one or two drug molecules within the group, this may affect the reliability to draw definite conclusions from the data for these classes. During the data gathering process, it was observed that there are only few originator drug products sold in community pharmacies in Malta, thus limiting the point of comparison for prices of generic medicines. Second, the data generated was sourced from the database of a private community pharmacy which is part of a group of 19 pharmacy outlets. Lastly, since January 2020 when the data were collected, there have been a lot of changes in the prices of medicines due to supply issues as a result of Brexit and the COVID-19 pandemic. This new data was not included in the current study.

4.4 Recommendations

A similar study determining the utilisation and promotion of the advantages of generic medicines in Malta may be important to have a better perspective of the scenario. Increasing the number of medicines included in the study may be explored by future researchers. Data can be gathered at different points in a year to determine the average price of the product within the year.

4.5 Conclusion

The use of generic medicines potentially decreases a patient's cost of drug therapy. Also, generic alternatives are available in Malta for most of the commonly used medications.

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Appendices

Appendix 1 List of Publications and Abstracts

Accepted abstract for FIP Virtual 2020

Pharmaceutical practice:
Health and medicines information
FIPSUB-1580 /

Comparison of Prices of Originator and Generic Medicines

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My preferred method of presentation is: Poster Presentation
Please fill in the presenting author's organization: Department of Pharmacy, Faculty of Medicine and Surgery, University of Malta

Background: Generic medicines have gained popularity in recent years since they allow cost savings and create competition contributing to improved medicines access.
Purpose: To compare the prices of originator medicines with their generic counterparts available on the Maltese market

Methods: The study focused on solid oral dosage forms available from community pharmacy in Malta as of January 2020. A tally of originator medicines and their generic counterparts was generated. Each drug was classified based on the Anatomical Therapeutic Chemical (ATC) classification system. The ratio of originator to generic counterparts was identified. The prices of the originator and generic medicines were listed and compared. The percentage price difference for each class and the overall average percentage price difference were determined.
Results: The study included 76 originator medicines and their generic counterparts (n=148) covering 9 ATC classes. For every originator medicine, an average of two generic alternatives are available (1:2). The average percentage price difference for all classes indicates a price reduction. Drugs for blood disorders showed the highest average price difference (-52%), followed by drugs for cardiovascular disorders (-46%). Drugs for respiratory conditions had the lowest price difference (-6%). The overall average price difference between originator and generic medicines among all ATC classes is -29%.
Conclusion: The results infer that the generic alternatives are available with a varied price difference across pharmacological classes. Further study into reasons behind the difference could support strategies that increase access to medicines.

FIP VIRTUAL 2020 SEPTEMBER

Comparison of Prices of Originator and Generic Medicines

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INTRODUCTION

Increasing costs of medicines is a global challenge, especially in low- and middle-income countries, since this is seen as a deterrent for patients to gain access to vital treatment modalities.[1]

Improvements in the affordability of essential medicines are most important in countries where there are still high out-of-pocket payments which may lead to patients not receiving treatment.[2]

The United Nations laid out seventeen sustainable development goals to be met by 2030, where the third goal puts high priority in ensuring that every person has access to treatment through a universal health coverage and be able to have access to safe and effective medicines and vaccines.[3]

Generic medicines could play a vital role in addressing medicines access issues since they allow cost savings by creating competition with the originator medicines, while rendering the same therapeutic effect.[4]

AIMS

To compare the prices of originator medicines with their generic counterparts available on the Maltese market.

SETTING

Community Pharmacy

Acknowledgments

John Robert Omandac would like to acknowledge the support given by the Malta Medicines Authority through its International Fellowship Program for granting the opportunity to pursue further studies in Malta.

METHOD

The study employed a quantitative descriptive approach and focused on solid oral dosage form pharmaceuticals available on the Maltese market (January 2020). The methodology flow is shown in Figure 1.

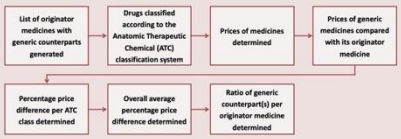

Figure 1. Methodology flowchart

RESULTS

Generic medicines availability in the market

There were 76 originator medicines and their generic counterparts (N=148) included in the study. The generated list encompasses drugs from 9 different ATC anatomic classes (level 1). Figure 2 shows the distribution of medicines included in the study based on marketing classification, resulting in a 1:2 ratio of originator (66%) to generic medicines (34%).

Figure 3 illustrates the distribution of originator and generic medicines for each ATC class. Among the ATC classes, the one which has highest number of generic medicines is the class for anti-infectives for systemic use (n=34), followed by the class of drugs for cardiovascular disorders (n=32). Both mentioned classes have the same number of originator medicines (n=15).

Cost savings of generic medicines

Table 1 shows the price difference of generic medicines compared with originators. Drugs for blood disorders showed the highest average price difference from the originator (-51.93%), followed by drugs for cardiovascular disorders (-46.37%), then drugs for the alimentary tract and metabolism (-38.52%). Drugs for respiratory conditions had the lowest average price difference (-5.50%). The overall average price difference between originator and generic medicines across all ATC classes is -29.12%.

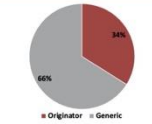

Figure 2. Percentage distribution of originator and generic medicines

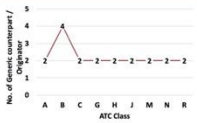

Figure 3. Number of generic counterpart(s) per originator medicine by ATC Class

Table 1. Percentage price differences between originator and generics by ATC Class

ATC Code	Description	N	Mean (%)	Std. Dev.
A	Alimentary tract and metabolism	14	-38.52	22.21
B	Blood and blood forming organs	4	-51.93	3.99
C	Cardiovascular system	32	-46.37	20.54
G	Genito urinary system and sex hormones	10	-32.00	17.02
H	Systemic hormonal preparations	6	-16.43	21.20
J	Antiinfective for systemic use	34	-14.78	41.38
M	Musculoskeletal system	15	-32.18	33.72
N	Nervous system	28	-23.16	36.19
R	Respiratory system	5	-5.50	34.65
	Total	148	-29.12	33.18

CONCLUSION

There was a price decrease when generic medicines were compared with their originator medicines across all ATC classes. From a consumer standpoint, this translates to money saved from a patient's regular expenses. From a public health perspective, this translates to cost savings on government expenditure for medicines covered by the National Health Services Scheme.

Generic alternatives are currently available in Malta for most of the commonly used medications, in the majority of a ratio of 1 originator: 2 generic medicines. More generics on the market translate to more competition, leading to driving prices down further.

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Appendix 2 Ethics Approval

FRECMDS_1920_186 - for RECORDS

FACULTY RESEARCH ETHICS COMMITTEE <research-ethics.ms@um.edu.mt> Mon, Jun 15, 2020 at 10:27 AM
To: John Robert Omandac <jrdomandac@gmail.com>, john.omandac.19@um.edu.mt
Cc: Francesca Wirth <francesca.wirth@um.edu.mt>, Lilian M Azzopardi <lilian.m.azzopardi@um.edu.mt>

Dear John Robert D. Omandac,

Documents received with thanks.

Since your self-assessment resulted in no issues being identified, FREC will file your application for record and audit purposes but will not review it.

You may proceed with your study. Any ethical and legal issues including data protection issues are your responsibility and that of your supervisor.

Regards,
Ms Ruth Stivala
B.A.(Hons)(Melit.),M.A.(Melit.)
Secretary
Faculty Research Ethics Committee

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