

Accessibility to Generic Medicines on the Maltese Market

*Submitted in partial fulfilment
of the requirements of the
Degree of Master of Pharmacy*

Louella Bianca Ignas

Department of Pharmacy
2020



L-Universit`
ta' Malta

University of Malta Library – Electronic Thesis & Dissertations (ETD) Repository

The copyright of this thesis/dissertation belongs to the author. The author's rights in respect of this work are as defined by the Copyright Act (Chapter 415) of the Laws of Malta or as modified by any successive legislation.

Users may access this full-text thesis/dissertation and can make use of the information contained in accordance with the Copyright Act provided that the author must be properly acknowledged. Further distribution or reproduction in any format is prohibited without the prior permission of the copyright holder.

Acknowledgements

This study would not have been possible without the guidance and direction of both my excellent supervisor Professor Lilian M. Azzopardi and co-supervisor Dr. Francesca Wirth, who I look up to for their dedication to research and pharmacy education.

I would also like to thank the questionnaire validation panel, Dr. Maresca Attard-Pizzuto, Dr. Stephanie Cassar, Dr. Konrad Zammit, Mrs. Bartolo and Alison Grech, as well as my managing pharmacists Hannah Flynn and Daniela Aquilina for helping me with the translations of the questionnaire.

I would like to acknowledge Malta Medicines Authority, headed by Professor Anthony Serracino-Inglott, for the fellowship program which granted me the opportunity to enrol in the Master of Pharmacy program.

And finally, my sincerest gratitude to my family, both in the Philippines and here in Malta, and to our Almighty Father for encouraging me and giving me strength to surpass all the challenges to finish the course.

Abstract

As the price of innovative and complex therapies increases, availability and access to generic medicines is critical for the sustainability of healthcare systems.

The aims of this study were to identify available generic medicines on the Maltese market and to develop and validate a questionnaire to assess the perception of the general public regarding accessibility to generic medicines.

Two drug classes were selected for the purpose of this study: drugs for oncology and drugs acting on the nervous system. Innovator drugs for oncology are expensive and nervous system drugs are widely prescribed in Malta and not broadly represented on the national health service scheme, requiring patient out of pocket payment. All authorised products as listed by the national competent authority were reviewed, and generic products available for each active ingredient and the corresponding dose and pharmaceutical forms were analysed. A questionnaire was formulated and validation with an expert panel was carried out.

For oncology, 159 generics for 15 originators are available, namely: Alkylating agents (n=16), antimetabolites (n=63), plant alkaloids (n=26), cytotoxic antibiotics (n=18), and other antineoplastic agents (n=36). The majority of generic oncology drugs are available as parenteral dosage forms (n=139). For nervous system drugs, 467 generics for 114 originators were available, namely: Antiepileptics (n=104), antipsychotics (n=146), hypnotics, sedatives and anxiolytics (n=65), antidepressants (n=128), central nervous system stimulants (n=8),

and drugs used in addictive disorders (n=16). The majority of generic drugs for nervous system disorders are oral preparations (n=435). There were 9 originators for oncology drugs and 60 for nervous system drugs which did not have generic counterparts. Results showed that for oncology drugs, antimetabolites had the most generics available, while alkylating agents had the least. Drugs for nervous system disorders were generally well-represented, with antipsychotics having the greatest number of generic products available. The questionnaire developed focused on assessing perception of access to generic medicines. Overall, the panel agreed that the questionnaire is concise, quick, and easy for the patients to reply.

Through this study the available generic medicines on the Maltese market for oncology drugs and for drugs acting on the nervous system were identified and a tool to understand the perception of generic medicines and accessibility by patients was developed.

Table of Contents

Abstract	iii
List of Tables	viii
List of Appendices	x
Chapter 1: Introduction	1
1.1.Generic Medicines	2
1.2.Generic Medicines and Sustainability of Healthcare Systems	3
1.3.Generic or International Non-proprietary Name (INN) Substitution and Prescribing	5
1.4.Public Perception of Generic Medicines	7
1.5.Setting	10
1.6.Rationale for the study	10
1.7.Aims	11
Chapter 2: Method	12
2.1. Study Design	13
2.2. Procedure for Data Collection	13
2.3. Development of Questionnaire	14
2.4. Validation of Questionnaire	17

2.5. Ethical Considerations	17
2.6. Dissemination	17
Chapter 3: Results	18
3.1. Generics and Originators for Oncology Drugs	19
3.1.1. Number of Generics by Sub-classification by Active Ingredient and Route of Administration	20
3.2. Generics and Originators for Drugs for Nervous System	24
3.2.1. Number of Generics by Sub-classification by Active Ingredient and Route of Administration	25
3.3. Questionnaire	32
Chapter 4: Discussion	33
4.1. Availability of Generic Medicines for Oncology and Nervous System Drugs in Malta	34
4.2. Questionnaire	35
4.3. Limitations of the Study	36
4.4. Further Research	37

4.5. Conclusion	38
References	39
List of Publications and Abstracts	49
Appendices	50

List of Tables

Table 3.1.	Number of Generics and Originators for Oncology by Classification	19
Table 3.2.	Number of Generics and Originators for Alkylating Agents by Active Ingredient and Route of Administration	21
Table 3.3.	Number of Generics and Originators for Antimetabolites by Active Ingredient and Route of Administration	22
Table 3.4.	Number of Generics and Originators for Plant Alkaloids and Natural Products by Active Ingredient and Route of Administration	23
Table 3.5.	Number of Generics and Originators for Cytotoxic Antibiotics by Active Ingredient and Route of Administration	23
Table 3.6.	Number of Generics and Originators for Other Antineoplastic Agents by Active Ingredient and Route of Administration	24
Table 3.7.	Number of Generics and Originators for Drugs for Nervous System by Classification	25
Table 3.8.	Number of Generics and Originators for Antiepileptics by Active Ingredient and Route of Administration	26
Table 3.9.	Number of Generics and Originators for Antipsychotics by Active Ingredient and Route of Administration	28
Table 3.10.	Number of Generics and Originators for Hypnotics, Sedatives and Anxiolytics by Active Ingredient and Route of Administration	29

Table 3.11.	Number of Generics and Originators for Antidepressants by Active Ingredient and Route of Administration	30
Table 3.12.	Number of Generics and Originators for CNS Stimulants by Active Ingredient and Route of Administration	31
Table 3.13.	Number of Generics and Originators for Drugs Used in Addictive Disorders by Active Ingredient and Route of Administration	32

List of Appendices

Appendix 1. Publication: Public Perception of Generic Medicines in Malta	51
Appendix 2. Questionnaire	55
Appendix 3. Ethics Approval: Correspondence from FREC	57
Appendix 4. Dissemination: FIP Abstract	58

Chapter 1

Introduction

1.1. Generic Medicines

According to the World Health Organization (WHO), a generic medicine is “a pharmaceutical product, usually intended to be interchangeable with an innovator product that is manufactured without a license from the innovator company and marketed after the expiry date of the patent or other exclusive rights”.¹ The European Medicines Agency (EMA) defines a generic medicine as a “product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies”.² The definition from the United States Food and Drug Administration (FDA) is “a drug product that is comparable to a brand/reference listed drug product in dosage form, strength, route of administration, quality and performance characteristics, and intended use”.³

Generally, generic medicines have the same dosage form, route of administration, efficacy, safety, indication for use and quality, but are largely cheaper compared to their reference proprietary counterpart (Babar et al., 2010; Dunne et al., 2013; Alrasheedy et al., 2014; Hassali et al., 2014a; Hassali et al., 2014b; Alfonso-Cristancho et al., 2015; Dunne & Dunne,

¹ The World Health Organization. WHO Expert Committee on Specifications for Pharmaceutical Preparation Forty-Eighth Report [Internet]. Geneva: WHO Technical Report Series, No. 986; 2014 [cited 2020 Aug 06]. Available from: <https://apps.who.int/iris/handle/10665/112733>

² European Medicines Agency (EMA). Questions and answers on generic medicines [Internet]. Canary Wharf: EMA; 2011 [cited 2020 Aug 06]. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Medicine_QA/2009/11/WC500012382.pdf.

³ US Food and Drug Administration (FDA). Approval of generic drugs [Internet]. In: Generic drugs. Silver Spring, MD: FDA; 2008 [cited 2020 Aug 06]. Available from: <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm127615.pdf>

2015; El-Dahiyat, 2017; Singh et al., 2020). The differences in the description of generic medicines in various regions reflects the divergence of the influence of policies that regulate their use, and in turn how they can contribute to the healthcare system (Dunne et al., 2013; Alfonso-Cristancho et al., 2015).

1.2. Generic Medicines and Sustainability of Healthcare Systems

Health care costs are one of the key concerns for many countries including out-of-pocket payments (Cameron et al., 2009; Jamshed et al., 2009; Al Ameri et al, 2013). A study in Pakistan demonstrated that consumers contribute to a significant percentage (77%) of the country's medical-related expenditure (Jamshed et al., 2009). This is also the scenario in other low- and middle-income countries where medications are predominantly procured privately despite being publicly provided for free or at lower prices (Cameron et al., 2012).

In 2007, yearly prescription drug spending in the United States reached \$286 billion (Shrank et al., 2009). Pharmaceutical spending in the United Kingdom increased over the recent decades which accounts to more than 10% of the total health service budget. In 2010, medicine consumption of the United Arab Emirates (UAE) increased to 4 billion UAE dirhams (Al Ameri et al., 2013). More than 78% of the New Zealand health system is also publicly subsidised, however medicine expenditures are still increasing (Babar et al., 2011; Tobin & Laing, 2015).

In Sweden, the total cost for medicine procurement more than doubled across a decade owing to an increase in bulk of pharmaceuticals, a transition to more costly drugs and related expenses with the entry of new pharmaceuticals (Andersson et al., 2007). Health care costs in Portugal in 2008 accounted to 10% of GDP, from which pharmaceuticals comprised 21.3%, one of the highest shares in the European Union (Quintal & Mendes, 2011). On a per capita basis, Ireland's medicine expenditure (€1.9 billion) was more than other European countries in 2010 and the spending was consistent for 3 more years (O'Leary et al., 2015).

As the price of innovative and complex therapies, and pharmaceutical expenditure increases, availability and access to generic medicines is critical for the sustainability of healthcare systems. Being therapeutically equivalent, generic medicine use translates into significant savings for both the government and the consumers, and in turn, improves availability and affordability of medicines (Jamshed et al., 2009; Babar et al., 2010; Cameron et al., 2012; Hassali et al., 2014a; Hassali et al, 2014b; El-Dahiyat, 2017).

From data between 1997 and 2000, a health economic research in the USA stated that generic substitution could have rendered savings up to \$2.9 billion for elderly populations and for those younger than 65 years old, \$5.9 billion (Haas et al., 2005). In the United States, the cost of generics is less than one-third of the originator, which translates into more effective patient health services (Alfonso-Cristancho et al., 2015). In Europe, generic medicine use renders an estimated savings of €25 billion per year for consumers and health care systems (Godman et

al., 2010). In a report of WHO in 2010⁴, generic substitution in a study involving 17 middle income countries resulted to an estimation of an average of 60% cost reduction for patients. Underutilization of generics was indicated as one of the primary causes of inefficiency in health care in the same report.

About 70% of the population in Yemen lack access to medicines and basic health services and there is no national level policy to improve or boost generic medicines use, along with negative perceptions and availability of counterfeit medicines (Al-Tamimi et al., 2013). Generic medicines contribute to the containment of escalating healthcare budgets if they are maintained on the market in large amounts and at reasonable prices (Dylst et al., 2013). Sustaining medicine access remains a challenge for government officials of developing countries (Simoens & De Coster, 2006; Kotwani, 2010; Dunne et al., 2013; Yousefi et al., 2015; Alam et al., 2017).

1.3. Generic or International Non-proprietary Name (INN) Substitution and Prescribing

Prescriptions from doctors greatly influence the medications their patients are taking and procuring and prescribing by generic name or the INN increases patient access to generic medications. Generic substitution is widely practiced in Europe. However, there are several

⁴ World Health Organisation. The World health report 2010: health systems financing: the path to universal coverage. Geneva, 2010 [cited 2020 Aug 29]. Available from: https://www.who.int/whr/2010/whr10_en.pdf

concerns being raised such as medication non-adherence when patients are switched across generic brands. Particularly for the elderly, confusion can arise due to differences in physical appearance since patients may receive different generic formulations for the same medicine every time they have their prescription refilled (Babar et al., 2010; Dylst et al., 2013). Another argument could be the opposite; that generic prescribing can improve medication adherence as patients can sustain to purchase them regularly being cheaper and accessible. This is evident especially at times when the branded medicine is not in stock (Al-Tamimi et al., 2013). The consumers' inclination to a particular brand, including in the case of branded generics, was pointed out as a vital parameter affecting generic substitution (Babar et al., 2010).

Various policies have been implemented to publicize the use of generic medicines which include generic substitution in the United States, obligatory generic substitution in Sweden and Finland, and generic prescribing in the United Kingdom (Dylst et al., 2013; Hassali et al., 2014a). Great Britain leads generic prescribing among many other European countries, including most prescriptions of NHS patients in England. The Pharmaceutical Benefits Scheme (PBS) scripts in Australia are filled with generics. In Canada, using generic drugs in supplying prescriptions translated to significant savings in 2009 (Babar et al., 2011).

In Malta, a proposal for international non-proprietary name (INN) or generic prescribing, instead of an originator product, was dismissed in 2006. The goal was to improve medicine access, giving patients cheaper options and increasing the exposure of generic products on

the market.⁵ Having been turned down, pharmacists are still given the opportunity to present generic counterparts to patients in accordance with Article 80 of the Medicines Act 2003⁶ except in cases where 'no substitution is allowed' is indicated (Azzopardi & Zarb Adami, 2012).

1.4. Public Perception of Generic Medicines

Globally, the levels of patient acceptance to generic medicines is variable (Dunne & Dunne, 2015; Tobin & Laing, 2015). In Jordan, 78% of consumers permit generic substitution, but this is likely owing to the high cost of medicines and not necessarily due to their understanding of generics (Tobin & Laing, 2015). The positive acceptance of generic medicines in Brazil does not subsequently lead to consumption as there are other factors such as cost, supply, or availability which affects a patient's choice (Guttier et al., 2017).

A Malaysian study on perceptions of the affordability of medicines resulted in more than 40% of respondents agreeing that there is an association between the price and quality of medicines (Babar & Ibrahim, 2003). This indicates that some consumers may relate cheaper medicines to inferior quality (Himmel et al., 2005; Thomas & Vitry, 2009). Previous

⁵ Farrugia M. Proposal to ban prescription of brand medicines turned down [Online]. Times of Malta; 2006 Sept 14 [cited 2020 Jul 30]. Available from: URL: www.timesofmalta.com/articles/view/20060914/local/proposal-to-ban-prescription-of-brand-medicines-turned-down.41494

⁶ Medicines Act 2003 [Internet]. Malta [cited 2020 Aug 28]. Available from: <https://legislation.mt/eli/cap/458/eng/pdf>

Malaysian studies reported patients' unacceptance of generics, with the majority having negative views on their quality, safety, and efficacy (Hassali et al., 2014a; Hassali et al., 2014b).

In a survey conducted in Japan in 2008, it was revealed that 40 % of respondents were unaware that generics were cheaper than branded drugs (Hoshi & Kimura, 2008). In studies carried out in South Africa and Auckland New Zealand, misconceptions about generics were reported to be quite prevalent (Tobin & Laing, 2015). In UAE, the variability and acceptability of generic medicine packaging appearance when compared to branded drugs contribute to lesser acceptance of generics (Sharif et al., 2016). Until the early part of the 21st century, Ireland has a conventional low level of generic medicine use. This is suggestively attributed to negative views both by prescribers and patients and the relatively minimal price differences between branded and generic medicines (O'Leary et al., 2015). Lebanon also has low recognition of the financial benefit which leads to patients' unacceptance to choose and procure them (Saleh et al., 2017).

In a survey disseminated to commercially insured people in the USA, minimal willingness to use generics was reported among the respondents despite their awareness of the advantage over branded medicines in terms of economic value and lack of differences in side effects (Shrank et al., 2009; Keenum et al., 2012; Alrasheedy et al., 2014). This was consistent in another study on the mismatch of patients' beliefs and their actual procurement of over-the-counter (OTC) generic medicines (Kohli & Buller, 2013). In Iraq, medicines dispensed for

free in the government sector are generally generics unlike in private pharmacies. Regulations which would enable pharmacists and physicians to promote use of generics to reduce consumer expenditures have not been implemented. Consequently, the consumers' understanding and acceptance of generic medicines solely determine the rate of generic medicine use (Sharrad & Hassali, 2011).

Various studies reported diverse correlations of sociodemographic profile of patients to the perception of generic medicines. A study conducted in Colombia, indicated that individuals with lower income and lower education level tend to be less knowledgeable and hold more negative attitudes toward generics (Shrank et al, 2009). This was parallel to literature reviews carried out which stated that acceptance of generic medicines appears to be low in patients from lower socioeconomic groups (Hassali et al., 2009; Dunne & Dunne, 2015). Studies from the UAE, Portugal and New Zealand suggested that the level of patients' approval to generics tends to increase with the level of education (Babar et al., 2010; Quintal & Mendes, 2011; Tobin & Laing, 2015). In contrast, a study in UAE revealed that some of highly educated respondents demonstrated uncertainty of generic medicines efficacy (Al Ameri et al., 2013). With a study population of lower socioeconomic status and education, a research in the USA showed that over half of the respondents are willing to use generics than branded drugs (Kohli & Buller, 2013). Most of the younger and wealthy patients in the USA reported preference for a generic over a brand name drug and belief of its superior safety (Shrank et al., 2009). This was not the case in a study in Brazil where the wealthiest populations are less willing to take generic drugs (Guttier et al., 2017).

1.5. Setting

The National Health System (NHS) in Malta is unique in which patients can be eligible to a nationwide pharmaceutical service called the Pharmacy Of Your Choice (POYC) scheme, which was launched in 2008. Patients are benefitting from free medicines procured by the government, which are distributed through private community pharmacies. These medicines are included on the Government Formulary List (GFL) for chronic conditions listed in the second part of the Fifth Schedule of the Social Security Act which includes a range of medicines for different indications and chronic diseases. Meeting the increasing number of beneficiaries and facilitating access to health care, entitled patients can collect their medicines from any pharmacy of their choice in which they register. Most of these medicines supplied are generic products. Along with the government service, private health services are also provided.⁷

1.6. Rationale for the study

In 2012, the generics market was described as still in its early stage, imposing the need for more awareness among the Maltese population (Azzopardi & Zarb Adami, 2012). In Malta, the experience gained by the authorisation and marketing of generics over the years implied that generic medicinal products are well-accepted, however the local accessibility of generics is yet to be explored (Borg et al., 2014).

⁷ Azzopardi-Muscat N, Buttigieg S, Calleja N, Merkur S. Health Systems in Transition: Malta Health system review. European observatory on health system and politics 2017; 19(1):16-18 [cited 2020 Aug 08]. Available from URL: http://www.euro.who.int/__data/assets/pdf_file/0009/332883/Malta-Hit.pdf?ua=1

Subsequently, data compiled during a World Pharmacy Day campaign to understand consumer perspective on generic medicines was available and prompted the rationale for this study. The data available was streamlined for publication (Appendix 1) and reported an overall positive perception of generic medicines, indicating improvement from the former study. In the 2020 data, respondents were knowledgeable on the definition of a generic medicine, had experience using generic medicines and would shift to a generic medicine if the innovator product was out-of-stock (Sammut Bartolo et al, 2020). Among the limitations of the Sammut-Bartolo et al research were the sampling method and size which limited the generalisation of the results and parameters that may influence use of generic medicines such as comorbidities and medicine currently taken by the patient, were not evaluated (Sammut Bartolo et al, 2020).

Against this background, this research was developed to focus on identifying availability of generic medicines and to establish a robust tool to measure consumer perspective.

1.7. Aims

The aims of this study were to identify available generic medicines on the Maltese market and to develop and validate a questionnaire to assess the perception of the public regarding accessibility to generic medicines.

Chapter 2

Method

2.1. Study Design

This study was a descriptive, quantitative study, focusing on the availability of generic products on the Maltese market for oncology drugs and drugs acting on the nervous system.

2.2. Procedure for Data Collection

Two drug classes were selected to identify the availability of generic medicines on the Maltese market namely drugs for oncology and drugs acting on the nervous system. The rationale for identifying these two classes were affordability and access on the NHS system.

Contemporary management of cancer is predicated on the availability and affordability of antineoplastic agents. Through time, these agents improved through research and development geared towards targeted therapy. However, these advancements have come at a very substantial cost (Meropol & Schulman, 2007; Siddiqui & S. Vincent, 2012).

Nervous system drugs are among the most widely prescribed medicines in Malta. This class of drugs is not broadly represented on the national health service scheme, requiring patient out of pocket payment.

All authorised products in Malta were reviewed by accessing the national database available on the Malta Medicines Authority website.⁸ Data compiled includes classification, medicine name, active ingredient, dosage, pharmaceutical form, Anatomical Therapeutic Chemical (ATC) code, Authorisation date and Marketing Authorisation Holder. The generic products available for each active ingredient, and their corresponding classification, dosage and pharmaceutical forms were analysed. The classification was based on the ATC code classification system and the British National Formulary classification⁹. Biological and biosimilar medicines were excluded from the analysis since interchangeability and substitution in this area is not at the same level as practiced with non-biologic drugs.

2.3. Development of Questionnaire

This descriptive quantitative study involved development of a questionnaire based on literature (Hassali et al., 2009; Kobayashi et al., 2011; Sharrad & Hassali, 2011; Azzopardi & Zarb Adami, 2012; Skaltas & Vasileiou, 2015; Sammut Bartolo et al, 2020) to understand the perception of generic medicines and accessibility by patients.

The developed questionnaire (Appendix 2) consisted of two sections. The first section is intended to gather the respondents' demographic information. The second section is

⁸ Medicines Authority. Medicines Authority Medicines Database [Internet]. Malta; 2020 [cited 2020 Jan 8]. Available from: <http://medicinesauthority.gov.mt/advanced-search>

⁹ Joint Formulary Committee. British National Formulary [Internet]. London: British Medical Association and Royal Pharmaceutical Society of Great Britain; [cited 2020 Aug 31]. Available from: <https://bnf.nice.org.uk/>

comprised of four multiple-choice questions and an open-ended question to assess accessibility to generics for medicines taken.

Question 1 surveys if the patient knows the correct description of a generic medicine. The use of generic medicines can be reflected from the patient's understanding of what they are (Azzopardi & Zarb Adami, 2012).

The second question explores the reasons why patients are using generic medicines. Related to the previous question, knowledge of generic medicines is investigated, asking if the rationale for use was because it was cheaper and whether they are confidently informed that generics are similarly effective and safe.

Some patients are already using generic products or may have been switched to a generic medicine from an innovator brand. There are also patients who do not take generic medicines or prefer branded products. The parameters affecting such instances are not included in the scope of the questionnaire.

The reasons for not using a generic product are probed in Question 3. The consumers' negative views about generic medicines may be correlated with lack of education and information (Dunne & Dunne, 2015; Sammut Bartolo et al., 2020). Healthcare professionals

have also reported negative perceptions which may influence the opinion of patients about generic medicines (Colgan et al., 2015; Toverud et al., 2015; Sammut Bartolo et al., 2020).

Purchase of medicines, especially those which are prescription-only (POM) is affected by the prescriptions from the doctors who have the choice to prescribe originator brands. In this case, the patient's preference towards generic counterparts would be limited. This in turn, can also affect whether the patients have been using the innovator brand from the time the medication was started. Furthermore, the patient could not be aware of the availability of generic alternatives for the medications being taken.

Question 4 posed a situation where the particular brand is not in stock and the possible actions for the patient. A generic counterpart could be an option, if available, some would wait for the medicine to be back in stock and another action which could be taken is seeking advice from the doctor or the pharmacist.

The final part of the questionnaire asks the patient to list all medications currently being taken and, whether the generic or originator brand is being taken. This is intended to identify comorbidities, number of medications taken and the potential of the patient to use generics so as to be able to correlate with the responses to the other questions.

2.4. Validation of Questionnaire

The questionnaire was validated by a panel of five persons, comprising a community pharmacist, an academic pharmacist, a general practitioner, and two lay persons. These persons were given the task to review the content of the questionnaire and to recommend any changes.

A pharmacist was selected by convenience sampling to translate the English questionnaire to Maltese, and another pharmacist was recruited to perform back-translation of the Maltese questionnaire to English.

2.5. Ethical Considerations

The University Research Ethics Committee (UREC) form was filled out and self-assessment resulted in no issues being identified. The form, together with the study protocol and proposal, were submitted to the Faculty of Medicine and Surgery Research Ethics Committee (FREC) for record and audit purposes (Appendix 3).

2.6. Dissemination

The dissemination activities pertaining to this study included the publication of the Sammut-Bartolo data (Appendix 1) and an accepted abstract at the 2020 FIP virtual conference (Appendix 4).

Chapter 3

Results

3.1. Generics and Originators for Oncology Drugs

The number of generic products and originators for oncology drugs by classification are presented in Table 3.1. The results indicate that the total number of generics for oncology drugs available in Malta is 159, representing 15 innovators. The number of generics available are: antimetabolites (n=63), other antineoplastic agents (n=36), plant alkaloids (n=26), cytotoxic antibiotics (n=18), and alkylating agents (n=16).

Table 3.1. Number of Generics and Originators for Oncology by Classification

CLASS	SUB-CLASS	GENERICS		ORIGINATORS	
		SUB*	CLA**	SUB*	CLA**
Alkylating Agents	Nitrogen Mustard Analogues	8	16	4	4
	Alkyl Sulfonate	1		0	
	Nitrosourea	1		0	
	Other Alkylating Agents	6		0	
Antimetabolites	Folic Acid Analogues	14	63	1	5
	Purine Analogues	3		3	
	Pyrimidine Analogues	46		1	
Plant Alkaloids and Natural Products	Vinca Alkaloids and Analogues	6	26	0	1
	Podophyllotoxin Derivatives	10		1	
	Taxanes	10		0	
Cytotoxic Antibiotics	Actinomycin	1	18	0	0
	Anthracyclines	9		0	
	Other Cytotoxic Antibiotics	8		0	
Other Antineoplastic Agents	Platinum Compounds	16	36	0	5
	Methylhydrazine	2		0	
	Protein Kinase Inhibitor	3		0	
	Other Antineoplastic Agents	15		5	
TOTAL		159		15	

* Total number per sub-classification

** Total number per classification

3.1.1. Number of Generics by Sub-classification by Active Ingredient and Route of Administration

The number of generic products and originators of the sub-classifications for oncology are tabulated by active ingredient and route of administration in Tables 3.2 to 3.6.

Route of administration are designated as oral, parenteral, topical, or rectal. The oral route includes tablets (coated, gastro-resistant, chewable, orodispersible, soluble, sublingual and modified-release), capsules (hard, soft, gastro-resistant and modified-release), liquid dosage forms (solution, drops, syrup and suspension) and others (oral lyophilisates and granules for oral solution). The parenteral route is comprised of powders and concentrates for solution, and emulsion for injection and infusion. The topical route includes creams and rectal solutions is assigned as rectal route.

Cyclophosphamide is only available on the market as originator products as both oral and parenteral dosage forms. The majority of the generic alkylating agents identified are parenteral formulations. Parenteral bendamustine has the highest number of generics (n=5) with no identified originators.

Table 3.2. Number of Generics and Originators for Alkylating Agents by Active Ingredient and Route of Administration

SUB-CLASS	ACTIVE INGREDIENTS	ROUTE OF ADMINISTRATION	GENERICS	ORIGINATORS
Nitrogen Mustard Analogues	Cyclophosphamide	Oral	0	1
	Cyclophosphamide Monohydrate	Parenteral	0	2
	Chlorambucil	Oral	1	1
	Melphalan	Oral	1	0
	Ifosfamide	Parenteral	1	0
	Bendamustine Hydrochloride	Parenteral	5	0
Alkyl Sulfonate	Busulfan	Oral	1	0
Nitrosourea	Lomustine	Parenteral	1	0
Other Alkylating Agents	Cisplatin	Parenteral	3	0
	Dacarbazine	Parenteral	3	0

Ralitrexed, oral fludarabine phosphate and topical fluorouracil do not have generic counterparts. Cytarabine has the greatest number of generics (n=18), followed by gemcitabine (n=14), both with no originators identified. Both mercaptopurine and parenteral fludarabine have 1 originator and 1 generic counterpart on the market. Only fluorouracil has a topical formulation among all drugs captured for this study. For this sub-class, there are more parenteral than oral formulations identified which are mostly generics.

Table 3.3. Number of Generics and Originators for Antimetabolites by Active Ingredient and Route of Administration

SUB-CLASS	ACTIVE INGREDIENT	ROUTE OF ADMINISTRATION	GENERICS	ORIGINATORS
Folic Acid Analogues	Methotrexate	Oral	1	0
	Methotrexate	Parenteral	11	0
	Raltitrexed	Parenteral	0	1
	Pemetrexed	Parenteral	2	0
Purine Analogues	Mercaptopurine	Oral	1	1
	Tioguanine Bp	Oral	1	0
	Fludarabine Phosphate	Parenteral	1	1
	Fludarabine Phosphate	Oral	0	1
Pyrimidine Analogues	Cytarabine	Parenteral	18	0
	Fluorouracil	Parenteral	7	0
	Fluorouracil	Topical	0	1
	Gemcitabine	Parenteral	14	0
	Capecitabine	Oral	7	0

Parenteral etoposide (n=10) and docetaxel (n=8) have the greatest number of generics. Oral etoposide is present on the market only as its innovator brand, which is also the only oral preparation and originator identified from the group.

Table 3.4. Number of Generics and Originators for Plant Alkaloids and Natural Products by Active Ingredient and Route of Administration

SUB-CLASS	ACTIVE INGREDIENT	ROUTE OF ADMINISTRATION	GENERIC	ORIGINATORS
Vinca Alkaloids and Analogues	Vincristine Sulfate	Parenteral	2	0
	Vinblastine Sulfate	Parenteral	1	0
	Vinorelbine Tartrate	Parenteral	3	0
Podophyllotoxin Derivatives	Etoposide	Parenteral	10	0
	Etoposide	Oral	0	1
Taxanes	Paclitaxel	Parenteral	2	0
	Docetaxel	Parenteral	8	0

All cytotoxic antibiotics are available on the market as generic parenteral products, led by mitomycin (n=5). Among the anthracyclines, mitoxantrone has the greatest number of generics (n=4).

Table 3.5. Number of Generics and Originators for Cytotoxic Antibiotics by Active Ingredient and Route of Administration

SUB-CLASS	ACTIVE INGREDIENT	ROUTE OF ADMINISTRATION	GENERIC	ORIGINATORS
Actinomycin	Dactinomycin	Parenteral	1	0
Anthracyclines	Doxorubicin Hydrochloride	Parenteral	1	0
	Epirubicin Hydrochloride	Parenteral	1	0
	Idarubicin Hydrochloride	Parenteral	3	0
	Mitoxantrone	Parenteral	4	0
Other Cytotoxic Antibiotics	Bleomycin Sulfate	Parenteral	3	0
	Mitomycin	Parenteral	5	0

Irinotecan is most widely available as generics (n=12) representing 3 originators. Amsacrine exists on the market as the reference product. Parenteral dosage forms comprise 30 out of 35 generics identified for this group.

Table 3.6. Number of Generics and Originators for Other Antineoplastic Agents by Active Ingredient and Route of Administration

SUB-CLASS	ACTIVE INGREDIENT	ROUTE OF ADMINISTRATION	GENERICS	ORIGINATORS
Platinum Compounds	Cisplatin	Parenteral	1	0
	Carboplatin	Parenteral	6	0
	Oxaliplatin	Parenteral	9	0
Methylhydrazine	Procarbazine	Oral	2	0
Protein Kinase Inhibitor	Everolimus	Oral	3	0
Other Antineoplastic Agents	Amsacrine	Parenteral	0	1
	Hydroxycarbamide	Oral	1	1
	Topotecan	Parenteral	2	0
	Irinotecan Hydrochloride Trihydrate	Parenteral	12	3

3.2. Generics and Originators for Drugs for Nervous System

Table 3.7 indicates the number of generic products and originators for nervous system drugs by classification. The number of generics available are: antipsychotics (n=146), antidepressants (n=128), antiepileptics (n=104), hypnotics, sedatives and anxiolytics (n=65), drugs used in addictive disorders (n=16) and Central Nervous System (CNS) stimulants (n=8). The total number of generics identified were 467 for 114 innovators.

Table 3.7. Number of Generics and Originators for Drugs for Nervous System by Classification

SUBCLASS	GENERIC	ORIGINATORS
Antiepileptics	104	33
Antipsychotics	146	34
Hypnotics, Sedatives and Anxiolytics	65	14
Antidepressants	128	16
CNS Stimulants	8	14
Drugs Used in Addictive Disorders	16	3
TOTAL	467	114

3.2.1. Number of Generics by Sub-classification by Active Ingredient and Route of Administration

In Tables 3.8 to 3.13, the number of generic products and originators of the sub-classifications for nervous system drugs are tabulated by active ingredient and route of administration. The same designation for route of administration as for oncology drugs was applied (section 3.1.1).

Among the antiepileptics, parenteral phenytoin, oral sodium valproate and vigabatrin are not represented with generic products. Pregabalin has the highest number of identified generics (n=28), followed by levetiracetam (n=16) and gabapentin (n=13), all of which do not have

originators. Oral oxcarbazepine and primidone have equal proportions of generics and innovators identified (n=1). Carbamazepine, lamotrigine and oral phenytoin have more originators than generics. Generic oral antiepileptics are about three times more than their originators.

Table 3.8. Number of Generics and Originators for Antiepileptics by Active Ingredient and Route of Administration

ACTIVE INGREDIENT	ROUTE OF ADMINISTRATION	GENERICS	ORIGINATORS
Pregabalin	Oral	28	0
Levetiracetam	Oral	16	0
Gabapentin	Oral	13	0
Topiramate	Oral	8	7
Clonazepam	Oral	7	0
Zonisamide	Oral	6	0
Lacosamide	Oral	4	0
Ethosuximide	Oral	3	1
Lamotrigine	Oral	3	6
Levetiracetam	Parenteral	3	0
Phenobarbital	Oral	3	0
Valproate Sodium	Parenteral	3	1
Carbamazepine	Oral	2	4
Phenobarbital	Parenteral	2	0
Oxcarbazepine	Oral	1	1
Phenytoin	Oral	1	3
Primidone	Oral	1	1
Phenytoin	Parenteral	0	1
Valproate Sodium	Oral	0	6
Vigabatrin	Oral	0	2

Oral risperidone (n=34), olanzapine (n=28), aripiprazole (n=24) and oral haloperidol (n=11) are among those which are well represented with generic products. There are no identified originators for olanzapine and aripiprazole considering their large number of available generics. Parenteral chlorpromazine hydrochloride, oral levomepromazine, oral flupentixol, oral and parenteral zuclopenthixol, pimozide, lithium carbonate and parenteral risperidone do not have generic counterparts on the market. There are more originators available than generics of fluphenazine decanoate, trifluoperazine and flupentixol decanoate. Parenteral levomepromazine, parenteral prochlorperazine mesylate and parenteral haloperidol have a 1:1 ratio of generics to originators. Among the generics from this group, there are a total 140 oral and 6 parenteral dosage forms. There are more originators (n=14) than generic parenteral preparations.

Table 3.9. Number of Generics and Originators for Antipsychotics by Active Ingredient and Route of Administration

ACTIVE INGREDIENT	ROUTE OF ADMINISTRATION	GENERICS	ORIGINATORS
Risperidone	Oral	34	4
Olanzapine	Oral	28	0
Aripiprazole	Oral	24	0
Haloperidol	Oral	11	1
Quetiapine	Oral	9	3
Clozapine	Oral	7	2
Quetiapine Fumarate	Oral	5	0
Amisulpride	Oral	5	0
Chlorpromazine Hydrochloride	Oral	4	0
Prochlorperazine Maleate	Oral	4	1
Ziprasidone	Oral	4	0
Sulpiride	Oral	4	0
Haloperidol	Parenteral	2	2
Levomepromazine	Parenteral	1	1
Fluphenazine Decanoate	Parenteral	1	2
Prochlorperazine Mesilate	Parenteral	1	1
Trifluoperazine Hydrochloride	Oral	1	2
Flupentixol Decanoate	Parenteral	1	2
Chlorpromazine Hydrochloride	Parenteral	0	1
Levomepromazine	Oral	0	1
Flupentixol	Oral	0	1
Zuclopenthixol Acetate	Parenteral	0	2
Zuclopenthixol Dihydrochloride	Oral	0	3
Pimozide	Oral	0	1
Lithium Carbonate	Oral	0	1
Risperidone	Parenteral	0	3

From the group of hypnotics, sedatives, and anxiolytics, there are more oral (n=47) than parenteral generic products (n=14). Bromazepam and parenteral midazolam have the most generics (n=7), while mexazolam, flurazepam, etifoxine hydrochloride and oral lormetazepam have none. Midazolam has no identified originator product. Parenteral lorazepam has 1 innovator and 1 generic on the market. Throughout this study, only diazepam has a rectal preparation and is available as a generic medicine.

Table 3.10. Number of Generics and Originators for Hypnotics, Sedatives and Anxiolytics by Active Ingredient and Route of Administration

ACTIVE INGREDIENT	ROUTE OF ADMINISTRATION	GENERICS	ORIGINATORS
Bromazepam	Oral	7	1
Midazolam	Parenteral	7	0
Diazepam	Oral	6	1
Diazepam	Parenteral	5	0
Lorazepam	Oral	5	1
Clobazam	Oral	5	1
Alprazolam	Oral	5	2
Diazepam	Rectal	4	0
Hydroxyzine Hydrochloride	Oral	4	1
Nitrazepam	Oral	4	1
Zolpidem Tartrate	Oral	4	1
Buspirone Hydrochloride	Oral	3	0
Temazepam	Oral	3	0
Lorazepam	Parenteral	1	1
Chloral Hydrate	Oral	1	0
Lormetazepam	Parenteral	1	0
Mexazolam	Oral	0	1
Etifoxine Hydrochloride	Oral	0	1
Flurazepam	Oral	0	1
Lormetazepam	Oral	0	1

For antidepressants, the ratio of generics to originators is 8:1. All dosage forms identified are oral. Bupropion, tianeptine and the combination preparation of flupentixol and melitracen do not have generics available. Among those which are well represented with generic products are escitalopram (n=22), duloxetine hydrochloride (n=16), amitriptyline hydrochloride (n=12) and fluoxetine (n=11). Amitriptyline hydrochloride and fluoxetine do not have identified originators.

Table 3.11. Number of Generics and Originators for Antidepressants by Active Ingredient and Route of Administration

ACTIVE INGREDIENT	ROUTE OF ADMINISTRATION	GENERICS	ORIGINATORS
Escitalopram	Oral	22	3
Duloxetine Hydrochloride	Oral	16	0
Amitriptyline Hydrochloride	Oral	12	0
Fluoxetine	Oral	11	1
Sertraline Hydrochloride	Oral	10	0
Mirtazapine	Oral	10	0
Venlafaxine	Oral	9	0
Paroxetine	Oral	8	1
Citalopram	Oral	7	0
Imipramine	Oral	4	0
Nortriptyline Hydrochloride	Oral	4	2
Trazodone Hydrochloride	Oral	4	0
Clomipramine Hydrochloride	Oral	2	3
Maprotiline Hydrochloride	Oral	2	0
Fluvoxamine Maleate	Oral	2	2
Moclobemide	Oral	2	0
Mianserin Hydrochloride	Oral	2	0
Agomelatine	Oral	1	0
Bupropion Hydrochloride	Oral	0	2
Tianeptine	Oral	0	1
Flupentixol/Melitracen	Oral	0	1

All CNS stimulants identified are oral preparations and unlike other sub-classes, there were more originators than generics. Methylphenidate has the highest number of generics (n=4) representing the same number of originators. Atomoxetine and piracetam are only marketed as innovators.

Table 3.12. Number of Generics and Originators for CNS Stimulants by Active Ingredient and Route of Administration

ACTIVE INGREDIENT	ROUTE OF ADMINISTRATION	GENERICS	ORIGINATORS
Methylphenidate Hydrochloride	Oral	4	4
Dexamfetamine Sulfate	Oral	3	0
Modafinil	Oral	1	1
Atomoxetine	Oral	0	8
Piracetam	Oral	0	1

Drugs used in addictive disorders are mostly available as generic products. Methadone hydrochloride has the greatest number of generics (n=6) having no originators. Disulfiram is available on the market as 1 generic and 1 innovator product. All generic products of the active ingredients in the group are for oral administration.

Table 3.13. Number of Generics and Originators for Drugs Used in Addictive Disorders by Active Ingredient and Route of Administration

ACTIVE INGREDIENT	ROUTE OF ADMINISTRATION	GENERICS	ORIGINATORS
Methadone Hydrochloride	Oral	6	0
Buprenorphine	Oral	5	2
Naltrexone Hydrochloride	Oral	4	0
Disulfiram	Oral	1	1

3.3. Questionnaire

Following questionnaire validation, comments put forward by the panel were taken into consideration. One suggestion was to add ‘other’ option for gender. Another amendment was the addition of “I do not take/ prefer taking branded medication” as an option to question 2. The panelist stated that patients may be buying medication which is not available as a generic or they prefer buying the originator brand. Asking for a healthcare professional’s advice when the particular brand is out-of-stock could also be an option for patients. This led to inclusion of “Ask doctor/pharmacists for opinion” to question 4. Overall, the panel agreed that the questionnaire is concise, quick and easy for the patients to reply.

Chapter 4

Discussion

4.1. Availability of Generic Medicines for Oncology and Nervous system drugs in Malta

The results showed that for oncology drugs, antimetabolites had the most generics available, while alkylating agents have the least. Folic acid and pyrimidine analogues were noted to be the most widely available as generic products, considering the number of originators on the market. All cytotoxic antibiotics identified were available as generics. Most of the identified generic drugs for oncology were parenteral dosage forms, with cytarabine having the greatest number. There were 9 originators for oncology drugs which do not have generic products for the following active ingredients; cyclophosphamide, raltitrexed, oral fludarabine, topical fluorouracil, oral etoposide, amsacrine. Bendamustine, cytarabine and gemcitabine had no identified originators.

Drugs for nervous system disorders were generally widely available as generics, led by antipsychotics. The majority of generic drugs for nervous system were oral preparations. Oral risperidone had the highest number of generics. Diazepam was well represented by generics in all its routes of administration. Antidepressants are shown to have several available generics for a relatively small number of originators. Parenteral antipsychotics had more originators available than generics. This was also the case of CNS stimulants, which however had the least among the sub-classifications. Risperidone was noted to have the greatest number of non-proprietary products available. There were no identified originators for antipsychotics such as olanzapine and aripiprazole, and antiepileptic pregabalin, considering their large number of available generics. Antiepileptics such as valproate sodium, modified-release carbamazepine, lamotrigine and vigabatrin, and antipsychotics similarly to parenteral dosage forms for haloperidol, flupentixol, zuclopenthixol and risperidone did not have

generic products available. Overall, there were 60 originators which did not have generic counterparts.

To the authors best knowledge, no similar published studies on generic availability of oncology drugs and drugs for nervous system in other countries are available.

4.2. Questionnaire

Despite the influence of healthcare professionals, patients now become more involved in decision-making on medicine use. Patients' prevailing perceptions on generic medicines greatly affect the extent of use of generic medicines. Evaluating views would indicate necessary interventions for public education to boost acceptance of generic medicines (Halme et al, 2009; Shrank et al, 2011; Sharif et al, 2016).

In Malta, the majority of elderly patients and patients entitled to medications from the POYC scheme are using generics distributed by the government. There are also instances where patients are being given originator medicines, depending on the present supply. Patients in the younger age group and those with a higher education level use generic medicines after recommendations by health care professionals or the media (Sammut Bartolo et al., 2020).

As an update from the Sammut-Bartolo et al study, the questionnaire included a part intended to identify comorbidities and the potential of the patient to use generics. Two studies showed the inverse relationship patient acceptance to generics and the severity of the disease (Figueiras et al, 2008; Al Ameri et al, 2013). In another study, patients with acute diseases are more likely to choose generic medicines (Chong et al, 2011). Physician respondents of a study in Guatemala stated that prescribing for a more complicated diseases would necessitate the use of a non-generic product. Prescribers greatly influence the use of generics in diabetes and hypertension (Flood et al, 2017).

In the management of cardiovascular disorders, one factor which contributes to generic medicine use is availability among drug classes or ATC groups (Gama et al, 2017). Generic medicines should be made available to sustainably provide low cost options for patients to have access to acute and chronic disease prevention and management (Mendis et al, 2007; Gama et al, 2017).

4.3. Limitations of the Study

Medicinal products can be registered on the Maltese market either by national procedures, European procedures or centralised procedures¹⁰. The national products list from the Malta

¹⁰ Medicines Authority. Registration [Internet]. Malta; 2020 [cited 2020 Aug 6]. Available from: <http://www.medicinesauthority.gov.mt/registration>

Medicines Authority website did not include products not registered through national procedures, excluding some of the innovator and generic products on the market.

4.4. Further Research

Reliability testing and dissemination of the questionnaire was not undertaken. The researcher recommends test-retest reliability of the questionnaire over a two-week period and the distribution of questionnaires to a large cohort, such as to patients in community pharmacies representative of each district in Malta.

Innovator products which patents already expired can be considered and availability of their generic counterparts on the market could be determined. Analysis of originators which do not have generic alternatives can also be explored. Another point of investigation is access to generics for special types of dosage forms like modified-release and parenteral preparations. Active ingredients can be segmented by dosage strengths and dosage forms, to be able to capture a larger aspect of generic medicine accessibility.

Further studies could broaden the scope of drug class to be analysed such as drugs for cardiovascular and endocrine disorders, which are also commonly prescribed in Malta and are used chronically. Availability of generic first-line medications for such morbidities can be indicative of accessibility to cost-effective pharmaceutical healthcare.

Related studies by Cameron et al. can also be conducted locally which could be focused on generic medicines. These studies explored the availability of medicines for acute and chronic diseases in the public and private sector, which would be reflective of the medicine accessibility of the population (Cameron et al, 2009; Cameron et al, 2011).

4.5. Conclusion

The study shows that there is an overall good representation of generic medicines for drugs for oncology and nervous system on the market. Antimetabolites and antipsychotics have the greatest number of generics available for each class. The study also identified products which are only marketed as their originator brands. A two-part questionnaire was developed which can be used to assess consumer perception of generic medicines and may serve as a measure to understand consumer feedback after patient education campaigns. Assessing the presence of co-morbidities can facilitate the determination of patients' inclination to generic medicine use.

To ensure access to healthcare, generic medications should be made available and efficiently implemented health policies can aid in promoting public acceptance of generics. As a primary health care provider, pharmacists play a major role in educating and assisting consumers to make informed decisions regarding generic medicine use.

References

Alam MM, Mittal A, Chawla D. Evaluating patients' perception towards generic and branded medicines: A segmentation approach. *Journal of Generic Medicines* 2017;13(4):184–192.

Al Ameri MN, Mohamed W, Makramalla E, Shalhoub B, Tucker A, Johnston A. Renal patients' views on generic prescribing and substitution: Example from the United Arab Emirates. *EMHJ - Eastern Mediterranean Health Journal* 2013;19(4):373 – 381.

Alfonso-Cristancho R, Andia T, Barbosa T, Watanabe JH. Definition and Classification of Generic Drugs Across the World. *Appl Health Econ Health Policy* 2015;13(Suppl 1):S5-S11.

Al-Tamimi SK, Hassali MA, Alrasheedy AA. Challenges to generic medicines utilization in Yemeni healthcare system. *GaBi J.* 2013;2(2):63-4.

Andersson K, Bergström G, Petzold MG, Carlsten A. Impact of a generic substitution reform on patients' and society's expenditure for pharmaceuticals. *Health Policy* 2007;81(2-3):376-384.

Azzopardi Y, Zarb Adami M. Public perception of generic pharmaceuticals in Malta. *Journal of EuroMed Pharmacy* 2012;(2):11-14.

Babar ZUD, Ibrahim MIM. Affordability of medicines in Malaysia - consumer perceptions. *Essential Drugs Monitor* 2003;33:18-9.

Babar ZUD, Stewart J, Reddy S, Alzaher W, Prateeka V, Nineweh Y, et al. An evaluation of consumers' knowledge, perceptions and attitudes regarding generic medicines in Auckland. *Pharm World Sci* 2010;32(4):440–448.

Babar ZUD, Grover P, Stewart J, Hogg M, Short L, Seo H, et al. Evaluating pharmacists' views, knowledge, and perception regarding generic medicines in New Zealand. *Research in Social and Administrative Pharmacy* 2011;7(3):294-305.

Borg JJ, Tomasi P, Pani L, Aislaitner G, Pirozynski M, Leufkens H, et al. Licensing of Generic Medicines: Are There Any Challenges Left? A Pharmaceutical Regulatory Perspective. *Scientia Pharmaceutica* 2014;82(4):847-856.

Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R. Medicine prices, availability, and affordability in 36 developing and middle-income countries: A secondary analysis. *Lancet* 2009;373:240–9.

Cameron A, Roubos I, Ewen M, Mantel-Teeuwisse A, Leufkens HGM, Laing RO. Differences in the availability of medicines for chronic and acute conditions in the public and private sectors of developing countries. World Health Organization. Bulletin of the World Health Organization 2011 06;89(6):412-21.

Cameron, A, Mantel-Teeuwisse AK, Leufkens HGM, Laing RO. Switching from Originator Brand Medicines to Generic Equivalents in Selected Developing Countries: How Much Could Be Saved? Value in Health 2012;15(5):664-673.

Chong CP, March G, Clark A, Gilbert A, Hassali MA, Bahari MB. A nationwide study on generic medicines substitution practices of Australian community pharmacists and patient acceptance. Health Policy 2010;99(2):139-148.

Colgan S, Faasse K, Martin L, Stephens M, Grey A, Petrie K. Perceptions of generic medication in the general population, doctors and pharmacists: A systematic review. BMJ Open 2015;5:e008915(10 pages).

Dunne S, Shannon B, Dunne C, Cullen W. A review of the differences and similarities between generic drugs and their originator counterparts, including economic benefits associated with usage of generic medicines, using Ireland as a case study. BMC Pharmacology & Toxicology 2013;14(1):1.

Dunne SS, Dunne CP. What do people really think of generic medicines? A systematic review and critical appraisal of literature on stakeholder perceptions of generic drugs. *BMC Med* 2015;13:173.

Dylst P, Vulto A, Simoens S. Demand-side policies to encourage the use of generic medicines: an overview. *Expert Review of Pharmacoeconomics & Outcomes Research* 2013 ;13(1):59-72.

El-Dahiyat F. Pharmacoeconomic evidence and policies to promote use of generic medicines in Jordan. *Pharmaceuticals Policy and Law* 2017;19(1-2):71-86.

Figueiras MJ, Marcelino D, Cortes MA. People's views on the level of agreement of generic medicines for different illnesses. *Pharm World Sci* 2008;30:590–594.

Flood D, Mathieu I, Chary A, García P, Rohloff P. Perceptions and utilization of generic medicines in Guatemala: a mixed-methods study with physicians and pharmacy staff. *BMC Health Serv Res.* 2017;17(1):27.

Gama H, Torre C, Guerreiro JP, Azevedo A, Costa S, Lunet N. Use of generic and essential medicines for prevention and treatment of cardiovascular diseases in Portugal. *BMC Health Serv Res.* 2017;17(1):449.

Godman B, Shrank W, Wettermark B, Andersen M, Bishop I, Burkhardt T, et al. Use of Generics-A Critical Cost Containment Measure for All Healthcare Professionals in Europe? *Pharmaceuticals* 2010;3(8):2470-2494.

Guttier MC, Silveira MPT, Luiza VL, Bertoldi AD. Factors influencing the preference for purchasing generic drugs in a Southern Brazilian city. *Rev. Saúde Pública* 2017;51:59.

Haas JS, Phillips KA, Gerstenberger EP, Seger AC. Potential Savings from Substituting Generic Drugs for Brand-Name Drugs: Medical Expenditure Panel Survey, 1997–2000. *Annals of Internal Medicine* 2005;142(11):891-897.

Halme M, Linden K, Kääriä K. Patients' Preferences for Generic and Branded Over-the-Counter Medicines: An Adaptive Conjoint Analysis Approach. *The Patient: Patient-Centered Outcomes Research* 2009;2(4):243-255.

Hassali MA, Shafie A, Jamshed S, Ibrahim M, Awaisu, A. Consumers' views on generic medicines: A review of the literature. *International Journal of Pharmacy Practice* 2009;17(2): 79-88.

Hassali MA, Alrasheedy AA, McLachlan A, Nguyen TA, Al-Tamimi SK, Ibrahim MI et al. The experiences of implementing generic medicine policy in eight countries: A review and recommendations for a successful promotion of generic medicine use. *Saudi Pharmaceutical Journal* 2014a;22: 491-503.

Hassali MA, Saleem F, Hanif AA, Tze Yinn CL, Pui Chee L, Fen TT et al. A survey assessing knowledge and perception of prescribers towards generic medicines in Hospital Seberang Jaya. *Journal of Generic Medicines* 2014b;11(1–2):4–10.

Himmel W, Simmenroth-Nayda A, Niebling W, Ledig T, Jansen RD, Kochen MM, et al. What do primary care patients think about generic drugs? *Int J Clin Pharmacol Ther.* 2005 ;43(10):472-9.

Hoshi S, Kimura H. Questionnaire on the Awareness of Generic Drugs among Outpatients and Medical Staff. *Drug Discoveries & Therapeutics* 2008;2(3):194.

Jamshed S, Babar Z, Ibrahim M, Hassali M. Generic medicines as a way to improve access and affordability: A proposed framework for Pakistan. *Journal of Clinical and Diagnostic Research* 2009;3(3):1596-1600.

Keenum AJ, DeVoe JE, Chisolm DJ, Wallace LS. Generic medications for you, but brand-name medications for me. *Research in Social and Administrative Pharmacy* 2012;8(6):574-578.

Kobayashi E, Karigome H, Sakurada T, Satoh N, Ueda S. Patients' attitudes towards generic drug substitution in Japan. *Health Policy* 2011;99(1):60-65.

Kohli E, Buller A. Factors influencing consumer purchasing patterns of generic versus brand name over-the-counter drugs. *South Med J.* 2013;106(2):155-160.

Kotwani A. Commentary: Will generic drug stores improve access to essential medicines for the poor in India? *Journal of Public Health Policy* 2010;31(2):178-184.

Mendis S, Fukino K, Cameron A, Laing R, Filipe A Jr, Khatib O et al. The availability and affordability of selected essential medicines for chronic diseases in six low- and middle-income countries. *Bull World Health Organ* 2007;85:279–88.

Meropol NJ, Schulman KA. Cost of cancer care: issues and implications. *J Clin Oncol.* 2007;25(2):180-6.

O’Leary A, Usher C, Lynch M, Hall M, Hemeryk L, Spillane S, et al. Generic medicines and generic substitution: contrasting perspectives of stakeholders in Ireland. *BMC Research Notes* 2015;8:790.

Quintal C, Mendes P. Underuse of generic medicines in Portugal: An empirical study on the perceptions and attitudes of patients and pharmacists. *Health Policy* 2011;104(1):61–68.

Saleh S, Abou Samra C, Jleilaty S, Constantin J, El Arnaout N, Dimassi H, et al. Perceptions and behaviors of patients and pharmacists towards generic drug substitution in Lebanon. *International journal of clinical pharmacy* 2017;39(5):1101–1109.

Sammut Bartolo N, Ignas L, Wirth F, Attard Pizzuto M, Vella Szijj J, Camilleri L, et al. Public perception of generic medicines in Malta. *J Pharm Health Services Research* 2020; 11(3):295-298.

Sharif SI, Chaar RJ, Albadrani ZZ, Shahwan JS, Badreddin MN, Charbaji MAK. Evaluation of the Knowledge and Perceptions of Patients towards Generic Medicines in UAE. *Pharmacology & Pharmacy* 2016;7:369-378.

Sharrad A, Hassali M. Consumer perception on generic medicines in Basrah, Iraq: Preliminary findings from a qualitative study. *Research in Social and Administrative Pharmacy* 2011;7(1):108-112.

Shrank WH, Cox ER, Fischer MA, Mehta J, Choudhry N. Patients' perceptions of generic medications. *Health Affairs* 2009;28(2):546-556.

Shrank W, Choudhry K, Liberman J, Brennan T. The Use Of Generic Drugs In Prevention Of Chronic Disease Is Far More Cost-Effective Than Thought, And May Save Money. *Health Affairs* 2011;30(7):1351-1357.

Siddiqui M, S. Vincent R. The High Cost of Cancer Drugs and What We Can Do About It. *Mayo Clinic Proceedings* 2012;87(10):935-43.

Simoens S, De Coster S. Sustaining Generic Medicines Markets in Europe. *Journal of Generic Medicines: The Business Journal for the Generic Medicines* 2006;3(4):257–268.

Singh AV, Dixit A, Kumar A, Pandey D, Singh CV, et al. *National Journal of Physiology, Pharmacy and Pharmacology* 2020;10(4):338-343.

Skaltsas L, Vasileiou K. Patients' perceptions of generic drugs in Greece. *Health Policy* 2015;119(11):1406-1414.

Thomas R, Vitry A. Consumers' perception of generic medicines in community pharmacies in Malaysia. *Southern Med Review* 2009;2(2):20-23.

Tobin MR, Laing R. Generic medicine: Boston University students' perceptions and surprising lack of knowledge. *Journal of Generic Medicines* 2014;11(3-4):136-145.

Toverud E-L, Hartmann K, Håkonsen H. A Systematic Review of Physicians' and Pharmacists' Perspectives on Generic Drug Use: What are the Global Challenges? *Applied Health Economics and Health Policy* 2015;13(Suppl 1):35-45.

Yousefi N, Mehralian G, Peiravian F, NourMohammadi S. Consumers' perception of generic substitution in Iran. *International Journal of Clinical Pharmacy* 2015;37(3):497-503.

List of Publications and Abstracts

Sammut Bartolo N, Ignas L, Wirth F, Attard Pizzuto M, Vella Szijj J, Camilleri L, et al.
Public perception of generic medicines in Malta. J Pharm Health Services Research 2020;
11(3):295-298. (Appendix 1)

Ignas L, Wirth F, Azzopardi, LM. Accessibility to Generic Medicines (Appendix 4)

Appendices

Appendix 1

Publication: Public Perception of Generic Medicines in Malta

Public perception of generic medicines in Malta

Nicolette Sammut Bartolo^a, Louella Ignas^a, Francesca Wirth^a,
Maresca Attard Pizzuto^a, Janis Vella Szijj^a,
Liberato Camilleri^b, Anthony Serracino-Inglott^a and
Lilian M. Azzopardi^a

^aDepartment of Pharmacy, Faculty of Medicine and Surgery, University of Malta, Msida, Malta and
^bDepartment of Statistics and Operations Research, Faculty of Science, University of Malta, Msida, Malta

Abstract

Objectives To assess the perception of generic medicines among the general public in Malta.

Methods A self-administered questionnaire was developed to assess knowledge, attitudes and use of generic medicines. The questionnaire was disseminated to a sample of the public recruited by convenience sampling in five localities in Malta. Descriptive statistics were undertaken.

Key findings A total of 228 participants completed the questionnaire; 54% were female, 42% were ≥60 years old, and 37% had up to secondary education level. Sixty-one per cent of the participants were aware of the correct definition of a generic medicine, and 55% stated that they had previously used generic medicines. Twenty per cent of the participants had never used generic medicines since they perceived them to be inferior in quality or less effective compared to their originator counterparts. Fifty-four per cent of the participants would switch to a generic medicine if the originator product was out-of-stock and 38% would pay between 1% and 20% less for a generic medicine compared to the originator product.

Conclusions Participants in this study exhibited a positive overall perception regarding generic medicines, demonstrating improvement in perception from a previous local study. The majority of participants were knowledgeable about generic medicines, had previously used generic medicines and would switch to a generic medicine if the originator product was not in stock.

Keywords cost of medicines; generic medicines; Malta; public perception

Introduction

The use of generic medicines has increased considerably over the past few decades in both developed and developing countries^[1]; however, generic medicines are still being used less compared to branded medications.^[2] Patients may have negative views about generics and perceive them to be inferior in quality and inappropriate for treating more serious conditions compared to branded counterparts.^[3] Pharmacists and physicians can contribute to inform patients on the equivalence of generic and originator medicines in terms of efficacy and quality.^[2]

In Malta, a study in 2012 concluded that the generics market was still in its infancy and that the Maltese population lacked awareness.^[4] The regulatory perspective indicates that over recent years, concerns with regard to generic medicines changed.^[5] The research question posed for this study was how has the perception of generic medicines by the Maltese public changed? The aim was to assess the evolution of the perception of generic medicines among the general public in Malta.

Methods

The study was registered with the Faculty of Medicine and Surgery Research Ethics Committee of the University of Malta.

This descriptive, cross-sectional study involved development of a self-administered questionnaire based on literature^[1–4,6–10] to assess public perception of generic medicines.

Correspondence: Nicolette Sammut Bartolo, Department of Pharmacy, Faculty of Medicine and Surgery, University of Malta, Msida, MSD 2080, Malta. E-mail: nicolette.sammut-bartolo@um.edu.mt

The questionnaire was reviewed by four pharmacists and four lay persons, and face validity was achieved. The questionnaire consists of two sections to collect participant demographic information and six multiple-choice questions in total to assess knowledge and use of generic medicines. A pilot study with 20 participants selected by convenience sampling was carried out. No changes to the questionnaire were made after the pilot study.

The questionnaire was distributed by pharmacy students at a public marketplace in four localities in Malta and at the University campus over a five-day period. The marketplaces were located in the Southern Harbour, Northern Harbour and South Eastern districts, and the University campus is located in the Northern Harbour area. Participants were invited to participate by convenience sampling on a voluntary basis.

Data analysis was carried out using SPSS version 24. Descriptive statistics were calculated, and the chi-square test was used to assess the association of each question with age, gender and level of education (0.05 level of significance adopted).

Results

A total of 228 participants completed the questionnaire. Participant demographics are shown in Table 1.

The majority of the participants, 61% ($n = 139$), were familiar with the term generic medicine and selected the correct definition 'cheaper version of the originator/reference product with the same active ingredient/s and action/s' (Table 2). The association between knowledge of the definition and age was statistically significant ($X^2(4) = 11.213$, $P = 0.024$), with the '18–39' and '40–59'-years age groups being more knowledgeable about the definition compared to participants ≥ 60 years. No statistically significant difference ($P > 0.05$) was observed with gender and level of education.

The majority of the participants, 55% ($n = 125$), stated that they had previously used generic medicines. The main reason for using generic medicines was that they were provided free-of-charge through the National Health Service (NHS) (50%, $n = 63$). A significant association was

observed with age ($X^2(6) = 31.60$, $P < 0.001$) and level of education ($X^2(6) = 28.059$, $P = 0.001$). A higher proportion of participants ≥ 60 years or with only primary education level stated that they use generic medicines since they are provided free-of-charge through the NHS.

Reasons for not using generic medicines included the belief that generic medicines are of inferior quality (42%, $n = 19$) and of lower effectiveness (41%, $n = 19$) compared to their originator counterparts.

When asked how much less they would be willing to pay for a generic medicine compared to the originator counterpart, 38% ($n = 87$) of the participants would be willing to pay between 1 and 20% less. A significant association was observed with age ($X^2(6) = 36.59$, $P < 0.001$) and level of education ($X^2(9) = 29.527$, $P = 0.001$), with participants ≥ 60 years and with primary and secondary education level being most willing to pay at least 40% less than the originator product.

The majority of the participants, 54% ($n = 123$), stated that they would switch to a generic alternative if the originator was out-of-stock. A significant association was observed ($X^2(4) = 16.430$, $P = 0.002$) with age, with participants aged '18–39' and '40–59' years being more willing to switch to a generic alternative, and participants ≥ 60 years more likely to check for any remaining originator stock or remain without the medication until the originator is back in stock.

Discussion

The majority of participants were aware of generic medicines and had a positive overall perception regarding their use. Improvement in the perception of generic medicines compared to the previous local study was observed.^[4]

Knowledge about generic medicines in other studies is reported to be variable^[3,7-10]. Negative perceptions towards generic medicines may be associated with lack of education and information provided to consumers.^[3] This was not observed in the elderly in Malta who, however, were using generics for the main reason that the product was made available on the NHS scheme for chronic medications. The NHS model adopted in Malta is relatively unique whereby entitled patients receive medicinal products procured by Government Pharmaceutical Services and which are distributed through private community pharmacies. Younger participants and those with a higher education level stated that they consider use of generic medicines following recommendation by a healthcare professional or as influenced by the media. The reasons for using generic medicines in these participants are because they are cheaper and due to confidence that generic medicines are identical in effectiveness, quality and safety to the originator product.

The difference observed between age groups and education levels with respect to the price they are willing to pay for a generic compared to the originator product may be attributed to financial limitations of elderly individuals and those with lower education levels. Elderly participants were also less willing to switch to a generic alternative if an originator is out-of-stock.

Table 1 Participant demographics ($N = 228$)

Demographic	Category	Frequency (n)	Percentage (%)
Age (years)	18–39	80	35
	40–59	50	22
	60+	96	42
Gender	Undisclosed	2	1
	Female	123	54
	Male	100	44
Level of education	Undisclosed	5	2
	Primary	50	22
	Secondary	84	37
	Postsecondary	34	15
	Graduate	53	23
	Undisclosed	7	3

Table 2 Participant responses

Question	Response	Frequency (n)	Percentage (%)
What is a generic medicine? (N = 228)	More expensive version of the brand-name product	18	8
	Cheaper version of the brand-name/reference product with <i>different</i> active ingredient/s and action/s	71	31
	Cheaper version of the brand-name product with the <i>same</i> active ingredient/s and action/s	139	61
Have you ever used a generic medicine? (N = 228)	Yes	125	55
	No	46	20
	Don't know	57	25
If yes, what are the reasons for using a generic medicine? (n = 180)	Confident that it is identical in effectiveness and safety to the brand-name product	35	28
	Cheaper	38	30
	Recommended (by pharmacist, physician, other health care professional, media, etc.)	44	35
	Given via the free medicines (POYC) scheme	63	50
If no, what are the reasons for not using a generic medicine? (n = 46)	More side effects compared to the brand-name product	8	17
	Less effective compared to the brand-name product	19	41
	Inferior quality compared to the brand-name product	19	42
What would you do if a particular brand-name medicine is out-of-stock? (N = 228)	Stay without the medication until the brand-name product is back in stock	14	6
	Go round various community pharmacies to check for any remaining stock	91	40
	Switch to a generic medicine	123	54
How much less are you willing to pay for a generic medicine compared to the brand-name product? (N = 228)	1–20%	87	38
	21–30%	41	18
	31–40%	34	15
	>40%	66	29

Limitations

Reliability testing of the questionnaire was not undertaken. The method for participant recruitment was by convenience sampling within a 5-day period from the identified public areas. The sample population of 228 is small in relation to the total population of Malta (estimated total population reported as 493 559 at the end of 2018 according to the Malta National Statistics Office), and this limits the generalisation of the findings.

Level of education was a parameter that was tested, which may reflect impact of occupation. Other parameters that may affect use of generic medicines namely health-related parameters, such as number and significance of comorbidities and number of medicines per day, were not assessed in this study. Further research with a larger cohort and exploring the impact of these parameters sheds light on the multifactorial reasoning behind acceptance of generic medicines.

Conclusions

Participants in this study exhibited a positive overall perception regarding generic medicines, demonstrating improvement in perception from a previous local study. Participants were knowledgeable on the correct definition of a generic medicine, have previously used a generic medicine and would switch to a generic medicine if the originator product was not in stock.

Declarations

Conflict of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Acknowledgements

The participation of Kurt Degabriele and Carla Esteve, pharmacy students in the research group at the time of the study, in the compilation of relevant literature and in data handling, is acknowledged. The authors acknowledge the Malta Pharmaceutical Students' Association, led by Health Campaigns Officer, Ms Renita Busuttil, for data collection during the World Pharmacists Day campaign.

Authors' contributions

Pharmacists Nicolette Sammut Bartolo, Francesca Wirth, Maresca Attard Pizzuto, Janis Vella Szijj, Anthony Serracino-Inglott and Lilian M Azzopardi designed the study and together with Master of Pharmacy student Louella Ignas contributed to the final draft of the article. Francesca Wirth,

Nicolette Sammut Bartolo and statistician Liberato Camilleri contributed in the analysis of data. All authors state that they had complete access to the study data that support the publication.

References

1. Colgan S *et al.* Perceptions of generic medication in the general population, doctors and pharmacists: a systematic review. *BMJ Open* 2015; 5: e008915 (10 pages).
2. Alrasheedy AA *et al.* Patient knowledge, perceptions and acceptance of generic medicines: a comprehensive review of the current literature. *Patient Intelligence* 2014; 6: 1–29.
3. Dunne SS, Dunne CP. What do people really think of generic medicines? A systematic review and critical appraisal of literature on stakeholder perceptions of generic drugs. *BMC Med* 2015; 13: 173 (27 pages).
4. Azzopardi Y, Zarb Adami M. Public perception of generic pharmaceuticals in Malta. *J EuroMed Pharm* 2012; 2: 11–14.
5. Borg JJ *et al.* Licensing of generic medicines: are there any challenges left? A pharmaceutical regulatory perspective. *Sci Pharm* 2014; 82: 847–856.
6. Sharrad AK, Hassali MA. Consumer perception on generic medicines in Basrah Iraq: preliminary findings from a qualitative study. *Res Social Adm Pharm* 2011; 7: 108–112.
7. Aivalli PK *et al.* Perceptions of the quality of generic medicines: implications for trust in public services within the local health system in Tumkur, India. *BMJ Global Health* 2018; 2(Suppl 3): e000644 (11 pages).
8. Babar ZU *et al.* An evaluation of consumers' knowledge, perceptions and attitudes regarding generic medicines in Auckland. *Pharm World Sci* 2010; 32: 440–448.
9. Hassali MA *et al.* Consumers' views on generic medicines: a review of the literature. *Int J Pharm Pract* 2009; 17: 79–88.
10. Toverud EL *et al.* A systemic review of physicians' and pharmacists' perspectives on generic drug use: what are the global challenges? *Appl HealthEcon Health Policy* 2015; 13(Suppl. 1): S35–S45.

Appendix 2

Questionnaire

Questionnaire

I am Louella Bianca Ignas, a Master of Pharmacy Student at the University of Malta. As a part of my course, I am currently conducting a study with the title: '**Accessibility to Generic Medicines on the Maltese Market**'.

PARTICIPANT DEMOGRAPHICS

Age	<input type="checkbox"/> 18 – 29 <input type="checkbox"/> 30 – 39	<input type="checkbox"/> 40 – 49 <input type="checkbox"/> 50 – 59	<input type="checkbox"/> 60 – 69 <input type="checkbox"/> 70 – 79	<input type="checkbox"/> 80+
Gender	<input type="checkbox"/> Male	<input type="checkbox"/> Female	<input type="checkbox"/> Other	
Level of Education	<input type="checkbox"/> Primary <input type="checkbox"/> Secondary	<input type="checkbox"/> Post-Secondary <input type="checkbox"/> Tertiary	<input type="checkbox"/> Post-Tertiary	
Locality of Residence				

1. What is a generic medicine? Choose one option

- a. Cheaper version of the brand-name product with different active ingredient/s and action/s
- b. Cheaper version of the brand-name product with the same active ingredient/s and action/s
- c. More expensive version of the brand-name product

2. What are your reasons for using a generic medicine? You may choose more than one option

- a. Cheaper than branded medicine
- b. Confident that it is identical in effectiveness and safety to the brand-name product
- c. Have been using a generic product for medication taken
- d. Given via the free medicines (POYC) scheme
- e. Recommendation
 - pharmacist
 - physician
 - family and friends
 - media
- f. I do not take/prefer taking branded medications

3. What are the reasons for not using a generic medicine? You may choose more than one option

- a. The doctor prescribed a branded product
- b. Have been using the branded product for medication taken
- c. Less effective compared to the brand-name product
- d. More side-effects compared to the brand-name product
- e. Not aware about its availability for the medicines I take

4. What would you do if a particular branded medicine is out-of-stock? Choose one option

- a. Switch to a generic product, if available
- b. Wait until the branded product is back in stock
- c. Ask doctor or pharmacist for opinion

5. List the medicines that you are currently taking

_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____

Thank you

Kwestjonarju

Jiena isimni Louella Bianca Ignas, studenta tal- Master of Pharmacy fl-Universita ta' Malta. Bhalta parti mil kors tieghi, qed imexxi studju bit-titlu: 'L-accessibilita tal-medicini generici fuq is-suq Malti'.

DEMOGRAFIJA TAL-PARTECIPANT

Eta'	<input type="checkbox"/> 18 – 29	<input type="checkbox"/> 40 – 49	<input type="checkbox"/> 60 – 69	<input type="checkbox"/> 80+
	<input type="checkbox"/> 30 – 39	<input type="checkbox"/> 50 – 59	<input type="checkbox"/> 70 – 79	
Sess	<input type="checkbox"/> Ragel	<input type="checkbox"/> Mara	<input type="checkbox"/> Ohra	
Livell t'Edukazzjoni	<input type="checkbox"/> Primarju	<input type="checkbox"/> Post-Sekondarju	<input type="checkbox"/> Post-Terzjarju	
	<input type="checkbox"/> Sekondarju	<input type="checkbox"/> Terzjarju		
Lokalita tar-residenza				

1. X'inhi medicina generika? Aghzel għazla waħda biss.

- a. Verżjoni irħas mill-prodott b'isem tad-ditta b'ingredjent/l attiv/l u azzjoni differenti
- b. Verżjoni irħas mill-prodott b'isem tad-ditta bl-istess ingredjent/l attiv/l u azzjoni
- c. Verżjoni oghla mill-prodott tad-ditta

2. X'inhuma ir-raġunijiet għalfejn tuża medicina generika? Tista tagħzel iktar min għazla waħda.

- a. Irħas mil-medicina tad-ditta
- b. Taħseb li għandha l-istess effett u sigurta bhal prodott tad-ditta
- c. Diġa kont qed tuża medicina generika
- d. Mogħti permezz tal-iskema ta'medicini b'xejn (POYC)
- e. Suġġerita minn:
 - spizjar/a
 - familja jew ħbieb
 - tabib/a
 - xandir
- f. Ma niehux – nippreferi niehu medicina tad-ditta

3. X'inhuma ir-raġunijiet għalfejn ma tuzax medicina generika? Tista tagħzel iktar min għazla waħda.

- a. It-tabib kien kitibli medicina tad-ditta
- b. Diġa kont qed niehu il-medicina tad-ditta
- c. Anqas effattiv meta mqabbel mal-prodott tal-isem tad-ditta
- d. Aktar effetti sekondarji meta mqabbla mal-prodott tad-ditta
- e. Mhux konxju li il-medicina generika teżisti għat-tip ta' medicina li niehu

4. X'tagħmel jekk medicina tad-ditta ma tkunx disponibbli? Aghzel għazla waħda

- a. Taqleb fuq medicina generika, jekk tkun disponibbli
- b. Toqgħod mingħajr medicina sakemm il-prodott tad-ditta jerga' jkun disponibbli
- c. Nistaqsi lit-tabib/a jew spizjar/a għal-opinjoni

5. Elenka il-medicini li-qed tiehu bhalissa

_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____

Grazzi

Appendix 3

Ethics Approval: Correspondence from FREC



L-Università
ta' Malta

Louella Bianca Ignas <louella.ignas.19@um.edu.mt>

FRECMDS_1920_180 - FOR RECORDS

1 message

FACULTY RESEARCH ETHICS COMMITTEE <research-ethics.ms@um.edu.mt> 9 June 2020 at 14:43

To: Louella Bianca Ignas <louella.ignas.19@um.edu.mt>

Cc: Lilian M Azzopardi <lilian.m.azzopardi@um.edu.mt>, Francesca Wirth <francesca.wirth@um.edu.mt>

Dear Louella Bianca Ignas,

Documents received with thanks.

Kindly note that 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 the supervisor.

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



L-Università
ta' Malta

Faculty of Medicine & Surgery
University of Malta Medical School
Msida.
t: 356 2340 **1214**

Appendix 4

Dissemination: FIP Abstract



Pharmaceutical practice:
Social and administrative pharmacy
FIPSUB-1520 /

Accessibility to Generic Medicines

Louella Bianca Ignas¹, Francesca Wirth¹, Lilian M Azzopardi¹

¹Department of Pharmacy, Faculty of Medicine and Surgery, UNIVERSITY OF MALTA, Msida, Malta

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: As the price of innovative and complex therapies increases, availability and access to generic medicines is critical for the sustainability of healthcare systems.

Purpose: To identify generic medicines available on the Maltese market

Methods: Two drug classes were selected for the purpose of this study; drugs for oncology and drugs acting on the nervous system. Innovator drugs for oncology are expensive and nervous system drugs are widely prescribed in Malta and not broadly represented on the national health service scheme, requiring patient out-of-pocket payment. All authorised products as listed by the national competent authority were reviewed, and generic products available for each active ingredient and the corresponding dose and pharmaceutical forms were analysed.

Results: For oncology, 159 generics for 15 originators are available, namely; alkylating agents (n=16), antimetabolites (n=63), plant alkaloids (n=26), cytotoxic antibiotics (n=18), and other antineoplastic agents (n=36). For nervous system drugs, 467 generics for 114 originators are available, namely; antiepileptics (n=104), antipsychotics (n=146), hypnotics, sedatives and anxiolytics (n=65), antidepressants (n=128), central nervous system stimulants (n=8), and drugs used in addictive disorders (n=16). There were 9 originators for oncology drugs and 60 for nervous system drugs which did not have generic counterparts.

Conclusion: Results show that for oncology drugs, antimetabolites have the most generics available, while alkylating agents have the least. Drugs for nervous system disorders are generally well-represented, with antipsychotics having the greatest number of generic products available.



FIP
VIRTUAL 2020
SEPTEMBER

Accessibility to Generic Medicines

Louella Bianca Ignias, Francesca Wirth, Lilian M Azzopardo
Department of Pharmacy, Faculty of Medicine and Surgery, University of Malta, Msida, Malta
email: louella.ignias19@um.edu.mt



L-Università ta' Malta
Faculty of
Medicine & Surgery

Department
of Pharmacy

INTRODUCTION

Health care costs are one of the key concerns for many countries. As the price of innovative and complex therapies increases, availability and access to generic medicines is critical for the sustainability of healthcare systems.¹ Globally, the level of patient acceptance to generic medicines is variable.²

In 2012, the generics market in Malta was still in its early stage, indicating the need for more awareness among the Maltese population.³ In Malta, the experience gained by the authorisation and marketing of generics over the years implied that generic medicinal products are well accepted, however the local accessibility of generics is yet to be explored.⁴

AIM

To identify available generic medicines on the Maltese market for oncology drugs and drugs acting on the nervous system

SETTING

The National drug regulatory agency, the Malta Medicines Authority (MMA). Within the Authority, the Licensing Directorate processes all applications for product pre- and post-authorisation activities through established national and European procedures. This includes the granting, withdrawal, variation, revocation or suspension for all product related licences and authorisations. The Directorate also processes applications for work-sharing of European procedures.

Acknowledgments

Louella Bianca Ignias would like to acknowledge the support given by the Malta Medicines Authority through the International Fellowship Program for granting the opportunity to pursue further studies in Malta.

METHOD

This study was a descriptive, quantitative study, focusing on the availability of generic products on the Maltese market for oncology drugs and drugs acting on the nervous system. Innovator drugs for oncology are expensive and nervous system drugs are widely prescribed in Malta and not broadly represented on the national health service scheme, requiring patient out of pocket payment.

All authorised products in Malta were reviewed by accessing the national database available on the MMA website.⁵

Data compiled includes classification, medicine name, active ingredient, dosage, pharmaceutical form, Anatomical Therapeutic Chemical (ATC) code, Authorisation date and Marketing Authorisation Holder.

The generic products available for each active ingredient, and their corresponding classification, dosage and pharmaceutical forms were analysed. The classification was based on the ATC code classification system and the British National Formulary classification.⁶ Biological and biosimilar medicines were excluded from the analysis since interchangeability and substitution in this area is not at the same level as practiced with non-biological drugs.

RESULTS

For oncology, 159 generics for 15 originators are available, namely: Alkylating agents (n=16), antimetabolites (n=63), plant alkaloids (n=26), cytotoxic antibiotics (n=18), and other antineoplastic agents (n=36) (Table 1). From the identified generic drugs for oncology, 139 are parenteral dosage forms, with cytarabine having the greatest number (n=18).

For nervous system drugs, 467 generics for 114 originators are available, namely: Antiepileptics (n=104), antipsychotics (n=146), hypnotics, sedatives and anxiolytics (n=85), antidepressants (n=328), central nervous system (CNS) stimulants (n=8), and drugs used in addictive disorders (n=16) (Table 2). The majority of generic drugs for nervous system are oral preparations (n=435). Oral risperidone has the highest number (n=34).

There are 9 originators for oncology drugs which do not have generic products for the following active ingredients: cyclophosphamide, raltitrexed, oral fludarabine, topical fluorouracil, oral etoposide, amiracrine.

There are 60 nervous system drugs which do not have generic counterparts. There are no identified originators for antipsychotics, such as olanzapine and aripiprazole.

Table 1. Number of Generics and Originators for Oncology by Classification

CLASS	SUB-CLASS	GENERIC		ORIGINATOR	
		NO.	%	NO.	%
Alkylating Agents	Mitomycin	8	0	4	4
	Procarbazine	1	16	0	0
	Other Antineoplastic	1	0	0	0
	Other Antineoplastic	4	0	0	0
Antimetabolites	Fluorouracil	14	1	1	1
	Capecitabine	3	63	1	1
	Pyrimethamine	46	1	1	1
	Other Antimetabolites	15	0	0	0
Plant alkaloids and Natural Products	Vincristine	19	26	1	1
	Docetaxel	19	0	0	0
	Docetaxel	1	0	0	0
	Other Plant alkaloids and Natural Products	9	18	0	0
Cytotoxic Antibiotics	Anthracycline	8	0	0	0
	Anthracycline	16	0	0	0
	Fluorouracil	16	0	0	0
	Other Cytotoxic Antibiotics	2	0	0	0
Other Antineoplastic Agents	Topotecan	3	96	0	0
	Other Antineoplastic Agents	1	0	0	0
	Other Antineoplastic Agents	1	0	0	0
	Other Antineoplastic Agents	1	0	0	0
TOTAL		159		15	

* % calculated on the total number of generic drugs for oncology (n=159).

** % calculated on the total number of originators for oncology (n=15).

Table 2. Number of Generics and Originators for Drugs for Nervous System by Classification

SUBCLASS	GENERIC	ORIGINATOR
Antiepileptics	104	31
Antipsychotics	146	36
Hypnotics, Sedatives and Anxiolytics	85	14
Antidepressants	328	16
CNS Stimulants	8	14
Drugs Used in Addictive Disorders	16	5
TOTAL	467	114

CONCLUSION

The study shows that there is an overall good representation on the Maltese market of generic medicines for oncology and drugs used in nervous system disorders. For oncology drugs, antimetabolites had the most generics available, while alkylating agents have the least. Drugs for nervous system disorders are generally well-represented, with antipsychotics having the greatest number of generic products. Antidepressants were shown to have several available generics for a relatively small number of originators. CNS stimulants have more available originators than generics, which however had the least among the subclassifications.

REFERENCES

1. Jurek J, Suber G, Savelko M, Farnell M. Generic medicines as a way to improve access and affordability: A proposed framework for Pakistan. *Journal of Clinical and Diagnostic Research* 2015;9(1):16-18.
2. Durrer M, Durrer LP. What do people really think of generic medicines? A systematic review and critical appraisal of literature on stakeholder perceptions of generic drugs. *BMC Med* 2013;11:213.
3. Azzopardo L, Ignias LB. Public perception of generic pharmaceuticals in Malta. *Journal of Clinical Pharmacy and Therapeutics* 2012;37(1):11-14.
4. Wong C, Ignias LB, Poon J, Azzopardo L, Louella B, Wirth F, et al. Licensing of Generic Medicines: Are There Any Challenges Left? *A Pharmaceutical Regulatory Perspective*. *Scientia Pharmaceutica* 2019;19(1):89-101.
5. Medicines Authority. Medicines Authority Medicines Database [Internet]. Msida, Malta: 2018. Item 10. Available from: <http://medicinesauthority.gov.mt/medicinesearch>
6. British National Formulary Committee. British National Formulary [Internet]. London: British Medical Association and Royal Pharmaceutical Society of Great Britain; [cited 2020 Aug 10]. Available from: <http://bnf.nps.org.uk/>