The Effect of Brexit on accessibility to Medicine

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To my beloved family and friends whose love, support and encouragement have inspired me to pursue and complete this research

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Abstract

According to article 12 of the International Covenant on Economic, Social and Cultural Rights Health is a basic human right and access to medicine is a fundamental means to ensure health. It recognizes the right of everyone to the enjoyment of the highest attainable standard of physical and mental health. Nearly 2 billion people have no access to basic medicines. This research aimed to develop a rational and prompt medicines accessibility issues. The objectives were to critically analyze the demand and supply of medicines in Malta by addressing the sourcing of medicines in Malta in relation to Brexit effect; to explore alternative solutions to accessing medicines and to review the current NHS formulary in relation to rational prescribing.

The research methodology involved analysing data collected from Central Procurement Supplies Unit and the Malta Medicines Authority. A focus group discussion and interviews were set up to identify challenges with accessing medicines and to generate ideas for the purpose of formulating recommendations to enhance access to medicine.

The data collected was analysed in terms of therapeutic area and different alternatives for sourcing. The focus group reviewed the Government Formulary List (GFL) and private list of medicines and identified challenges with accessing medicines as Brexit; the UK ban on export of medicines; Lack of cooperation in the regulation of medicines between the EU and the UK post Brexit; Licensing and registration of medicines; Shortages; serialisation-FMD; Problems with drugs in GFL; Patients' perspective. The focus group gave examples from patients within their practices and the implication of access, and the risk posed to the patients.

The focus group recommended that a list of best options for medicines were duly compiled, and the following are examples:

a. GFL: Atenolol tablets 50mg x 2 was suggested instead of atenolol 100mg tablet.

b. Private market list: Atorvastatin tablets 100mg – Different brand of generic in other country not the UK was suggested.

An innovative way to detect, address and mitigate challenges to access medicines was developed to proactively enhance accessibility to medicines.

The lack of cooperation in the regulation of medicines between the EU and the UK post Brexit has proven to be more difficult to address because it requires co-operation between other countries. Partnership, consultation, collaboration between the health system and pharmaceutical industry is important to avoid and control medicines accessibility challenges.

Keywords

Brexit- Access -Barriers to medicine - Public health - Regulatory and Consequences

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List of Abbreviations

AHCBC	Advisory Health Care Benefits Committee
API	Active Pharmaceutical Ingredient
BREXIT	United Kingdom withdrawal from the European Union
CMA	Conditional marketing authorization
COVID-19	Coronavirus Disease 2019
CPSU	Central Procurement and Supplies Unit
EC	European Commission
EMA	European Medicines Agency
EML	Essential Medicines List
EU	European Union
FDA	Food and Drug Administration
FREC	Faculty Research Ethics Committee
GDPR	General Data Protection Regulation
GFL	Government Formulary List
GFLAC	Government Formulary List Advisory Committee
HIV	Human Immunodeficiency Virus
HMA	Heads of Medicines Agencies
INN	International Non-proprietary Names

MA	Marketing Authorization
MAA	Centralized Marketing Authorisation
MDH	Mater Dei Hospital
MMA	Malta Medicines Authority
MHRA	Medicines and Healthcare Products Regulatory Agency
MIAU	Medicines Intelligence and Access Unit
PICO	Population, intervention, comparator, and outcome
POYC	Pharmacy of Your Choice Scheme
PM	Prime Minister
R&D	Research and Development
TRIPS	Trade-Related Aspects of Intellectual Property Rights
UK	United Kingdom
UREC	University of Malta Research and Ethics Committee
WHO	World Health Organisation

Chapter 1: Introduction

1.1 Access to Medicines

The international Covenant on Economic, Social and Cultural Rights article 12 states that ‘’Health is a basic human right and access to medicine is a fundamental means to guarantee well-being. It acknowledges the right of everybody to the pleasure of the achievable standard of physical and mental health”[1]. In 2017, it was reported that approximately 2 billion persons had no access to essential medicines[2]. Inaccessibility to basic medications results in a lot of public health issues such as preventable misery and suffering.

Essential medications are thereby unobtainable, unaffordable, less accessible, undesirable or of little value for more than a quarter of the people of the world (Ahmadiani and Nikfar, 2016). Access to inexpensive, high quality crucial medications is vital to minimising the financial burden of care, avoiding bigger discomfort and grief, shortening the length of sickness, preventing unnecessary incapacities and losses globally (Gannedahl et al, 2018).

The World Health Organisation (WHO) prequalification plan is strongly established as a device for enhancing accessibility to secure, essential, high-quality medicines (Bermudez, 2017). Essential medications are important to the Sustainable Development Goals and are central to the goal of achieving Universal Health Coverage (Ahmadiani and Nikfar, 2016).

[1] United Nation Human Rights Office of the High Commissioner (OHCHR). International Covenant on Economic, Social and Cultural Rights. OHCHR; 1996-2020 [cited 2020 Nov 30] Available from URL: [http://www.ohchr.org/EN/ProfessionalInterest/Pages/CESCR.aspx]

[2] World Health Organization (WHO). Ten Years in Public Health, 2007-2017—Access to Medicines: Making Market Forces Serve the Poor. Geneva: WHO; 2017 [cited 2020 Nov 08] Available from URL: https://www.who.int/publications/10-year-review/chapter-medicines.pdf.

According to WHO evaluations, up to 90% of the people in small- and middle-income nations procures medications through patients paying out of their own pockets. When a household is forced to trade properties, example family cow, or remove its children out of school, this expense can be the beginning of intergenerational family poverty[2]. This is the chains of poverty where there are no systems of societal protection, such as those offered by universal health coverage are accessible and even low-cost generic products are a substantial monetary problem (Ahmadiani and Nikfar, 2016).

World Health Organisation has fought to provide accessibility to medications during its approximately 70-years of existence. Decent healthiness is not possible without accessibility to medicinal materials. Universal health coverage relies on the accessibility of excellence secure cheap health technologies in adequate amounts (Ahmadiani and Nikfar, 2016).

The United Nations (UN) created eight objectives in 2000 as Millennium Development Goals and 190 nations decided to support and attain these goals by 2015. Three of these goals including decrease in children's death, improvement of motherly health, battling HIV/AIDS, malaria, and other sicknesses were enormously reliant on availability and inexpensive medications. The part played by pharmaceutical companies is evidently stated in the millennium declaration: Produce a worldwide corporation for growth in co-operation with pharmaceutical companies, deliver accessibility to inexpensive, vital medicines in developing nations; people with accessibility to cheap crucial medicines on a continuous basis[3].

[3] United Nations. Millenniums Development Goals and Beyond 2015.Goal 8: Develop a global partnership for development. United Nations; 2015 [cited 2020 Nov 30] Available from URL: http://www.un.org/millenniumgoals/global.shtml

According to a right described by article 25 in the 1948 Universal Declaration of Human Rights (United Nations, 1948). A viable healthcare system ensures accessibility to all patients. Availability of healthcare is not constrained to adequate health services but also the vital medicine to avert, sustain, cure, or detect a disease. To accomplish this right, healthcare should be able to manage its funds sensibly, to be able to maintain itself (Cassar, 2020).

The 21st century has seen a variety of developments being made throughout numerous spheres of studies: an integration of engineering, chemistry, biology, regulatory science, and medicine to form into the healthcare system that we have today which aids access to medicine (Zeugolis and Pandit, 2015). Advancement in technology might be a grip to safeguarding accessibility by avoiding and managing conditions through improved monitoring. Stephen Oesterle detailed during a conference in Paris, that one third of American hospitalised patients with heart failure may well be discharged if their filling pressure could be monitored; a procedure which may well be carried out by means of implantable sensors [4].

1.1.1 Definition of access to medicine

Saurman (2016) and Peters et al (2018) state that accessibility allows a patient wanting to obtain the correct care at the right time from the right provider and in the correct environment. Access to medicines is achieved when the characteristics of consumers correspond to the aspects of the service such as location of pharmacies and cost of

[4] Heitner S, Spencer A, Fajadet J, Wijns W. Value-based healthcare, innovation and the future of interventional medicine: defining our place at the centre of the debate. EuroIntervention. 2017 [cited 20 Nov 17];13(5):e508-e512. Available from: https://eurointervention.pcronline.com/article/value-based-healthcare-innovationand-the-future-of-interventional-medicine-defining-our-place-at-the-centre-of-thedebate

medicines (Whitehead, 1992). This ensures that individuals are capable to obtain medicines when facing the need for care (Muscat, 2020).

1.2 Evolution of medicines

Medicine knows its origin in 460 BC from the birth of Hippocrates, the Greek father of medicine (Hajar, 2015). Hippocrates described scientifically typical illnesses and their treatment and prescribed a tree extract, 'salycasia' a derivative of aspirin for pain relief (Grammaticos and Diamantis, 2008). Natural products and healing methods were used to alleviate symptoms and treat diseases in traditional medicine (Yuan et al, 2016). Modern medicine emerged after the Industrial Revolution in the 18th century through scientific discoveries and inventions as characterised by aspirin which became a global commercial success[5] . In 1921, Sir Frederick Banting and his colleagues isolated the hormone insulin. This revolutionised the treatment of diabetes which was a fatal illness (Rosenfeld, 2013). A breakthrough was the first antibacterial, penicillin discovered in 1928 by serendipity by Sir Alexander Fleming (Fleming, 1929). In 1943, clinical trials showed that penicillin was an effective antibiotic, and its production was scaled up to be available to treat wounded soldiers during World War II[6] . Modern medicine has effectively reduced mortality from common infections and extended the lives of millions of patients with chronic diseases. Since the mass manufacturing of penicillin in the 1940s, the pharmaceutical industry has continuously progressed to provide access to medicines to optimise patient health outcomes[7] manufacturing of penicillin in the 1940s, the

[5] Medical News Today. What is modern medicine? 2018 [cited 2020 May 18] Available from: URL: https://www.medicalnewstoday.com/articles/323538

[6] 2 Mailer JS, Mason B. Penicillin: Medicine's wartime wonder drug and its production at Peoria, Illinois. 2001 [cited 2020 May 18] Available from: URL: https://www.lib.niu.edu/2001/iht810139.htm

[7] Walsh R. A history of the pharmaceutical industry. 2010 [cited 2020 May 18] Available from: URL: https://pharmaphorum.com/articles/a_history_of_the_pharmaceutical_industry/

pharmaceutical industry has continuously progressed to provide access to medicines to optimise patient health outcomes[6].

1.2.1 The right to health

"*The enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition" –*

World Health Organisation 1946 Constitution World Health Organisation. Constitution of the World Health Organisation. American Journal of Public Health. 1946; 36(11):1315-1323.

The right to health promotes accessibility to medications in a global manner, ensures equality in distribution independent of race, age, beliefs, orientation, and other factors that could distinguish between one member of society and another (Muscat, 2020). The right to health was emphasised in the Constitution of the World Health Organisation (WHO), the Universal Declaration of Human Rights and the International Covenant on Economic, Social, and Cultural Rights. The Doha Declaration on Trade-Related Aspects of Intellectual Property Rights (TRIPS) and Public Health confirmed that every individual has the right to accessibility to medications which are determined to be essential[8] . Accessibility to medicines is an essential element in the continuum of healthcare provision to promote the wellbeing of all individuals[9].

[8] World Trade Organisation. Declaration on the TRIPS agreement and public health. Doha. 2001 [cited 2020 May 18] Available from: URL: https://www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_trips_e.htm

[9] United Nations. The Sustainable Development Goals Report 2019. New York. 2019 [cited 2020 May 18] Available from: URL: https://doi.org/10.18356/55eb9109-en.

1.3 Challenges to medicine accessibility

Inaccessibility to medications is one of the greatest intricate and perplexing challenges that prevents healthiness. The plan for enhancing accessibility is extremely wide. To afford medicines is the foundation of accessibility, but several additional elements also ascertain if a person can get the medications, they need (Cameron, 2009). Disparities in local health systems and organizations hinder the supply of medications to lots of individuals. Accessibility also relies on purchasing habits, tax, and tariff procedures, mark-up along the supply chain, and the strength of nationwide medicine regulatory establishments. Besides being able to purchase inexpensive and decent quality medications. There must also be harmless scheme for monitoring drug safety and supply chain management to protect the public from substandard or fake medical products[10].

Inaccessibility to medications results in a cascade of sadness and sorrow, from no relief for the agonising discomfort of a child's earache, to women dying during childbirth because of bleeding, to deaths from illnesses that are easily treatable, not expensive, avoidable and can easily be cured (Chan, 2018). Inaccessibility to medications is one disparity that can be weighed by a completely obvious benchmark: amounts of avoidable deaths (Arcaya et al, 2015). Endeavor to enhance accessibility to medications are determined by a convincing moral obligation. Nobody should be denied access to treatments that can save life or promote health for unfair reasons, such as people with financial or social reasons (Sheiham, 2009). Yearly childhood deaths from illnesses that could have been avoided or treated with present therapeutic products would be inconceivable in an impartial and just world (Petersen, 2003).

[10] House of Commons, Business, Energy and Industrial Strategy Committee. Ninth Report of Session 2017–19. The impact of Brexit on the pharmaceutical sector. London: House of Commons; 2018 [cited 2020 Nov 30] Available from URL: https://publications.parliament.uk/pa/cm201719/cmselect/cmbeis/382/382.pdf

Another problem to accessibility to medicines is international conventions for the control of narcotic drugs. They place a double responsibility on governments: to avoid abuse, diversion, and trafficking, but also to protect the accessibility of controlled substances for medical and scientific purposes (Gilson, 2011). Many controlled substances play a crucial role in medical care, for instance the management of pain, or use in anaesthesia, surgical procedure, and the cure of mental disorders (Tompkins, 2017) Regrettably, the duty to avoid abuse has become far more interesting than the obligation to safeguard accessibility for medical care. There is less access to controlled medicines for easing moderate to severe pain. Efforts to promote accessibility are complicated by various financial problems. Affordability is important for families and health resources (Hurst, 2000).

Letting commercial benefits outweigh health interests would result to even bigger inequalities in accessibility to medications, with catastrophic life-and-death consequences. However, pharmaceutical companies are a business, not a charity (Hurst, 2000). When prices are so minimal, they prevent gains, businesses leave the market and leave behind a vacuum in the accessibility of quality products, for instance what happened with the anti-snakebite venom. Economic concerns are another disturbing public health problem (Srinivasan, 2003). Several illnesses primarily common in impoverished inhabitants have no health countermeasures or have outdated and ineffective ones. Inaccessibility to medicines suffers from the unavailability of medicines tailored to operate well in less resource environment with a hot climate[11].

Research and development (R&D) with its market-driven encouragements, empowered by the patent system, has traditionally refused to participate in new products for deprived populaces with practically have no procurement power, leading to a lack of R&D

[11] World Trade Organization (WTO) Overview: The TRIPS agreement. WTO;1995 [cited 2020 Nov 30] Available from URL: [https://www.wto.org/english/tratop_e/trips_e/intel2_e.htm

propelled by the exclusive wellbeing of the poor (Owen, 2003). Aside from having limited new products that deals with their priority sicknesses, the poor are penalised a second time: the shared practice of recovering the costs of R&D through high cost protected by patents implies that people who cannot pay high charges do without spending on contemporary long-lasting illness and overlooking other sicknesses such as tropical infections for example leishmaniasis, is evidently unfair and can widening the gap between the rich and the poor. This socioeconomic disparity is a worry to be detected and should be prevented (Owen, 2003). This can only be possible with significant involvement of pharmaceutical companies. Although R & D is awfully expensive in rare diseases, cost and revenue should be a major consideration. Although words have it that pharmaceutical companies spend about $60 billion for R&D, Nevertheless the yearly income of these companies surpasses 300 billion[12].

The poverty map poses additional difficulties with the recent changes. It is predicted that about 70% of the world's deprived currently live-in middle-income countries which are gradually losing their entitlement for funding from organisations such as the Global Fund to Fight AIDS, Malaria, Tuberculosis, Gavi, and the Vaccine Alliance. Are the governments of these countries going to compensate for the gap in accessibility to medications and vaccines? If they do not, enormous amounts of poor persons living in these countries that are swiftly getting rich will be left to take care of themselves[11].

Difficulties in accessibility to medication has also been because of copyright law and its problems. Even though copyright law has been used generally for so many years (Hulme, 1896). When the World Trade Organization (WTO) Agreement on Trade-Related

[12] World Health Organization (WHO). Pharmaceutical Industry. Trade, foreign policy, diplomacy and health . Geneva: WHO; 2020 [cited 2020 Jan 08] Available from URL: http://www.who.int/trade/glossary/story073/en/

Aspects of Intellectual Property Rights (TRIPS) was done in 1994 it took the copy right law to a new level thereby compelling the World Trade Organization (WTO) representatives to play a vital role in the safeguarding of intellectual property rights of any copyright product that is imported, manufactured, used, or traded, with the consent of the patent owner. Medicines were included in this deal that is why the manufacture of any medication has a period that the patent holder has control over the product in the market and can sell at any price and most cases the maximum price that is conceivable (Kesselheim et al, 2016). Within this time frame generic medications that are more affordable cannot be produced or available in the market after an agreement has been signed by a state with the patent holder thereby only the very expensive branded products will be available making it unaffordable for most patients to access the medicine if they cannot pay out of their pockets or if they cannot afford to buy or use insurance. This situation is worse when it comes to a small country like Malta with a small population and many needing medications (Fitzmaurice, 2018). Countries such as Malta with increased needs and reduced economic power, affordability and accessibility becomes a problem when branded products must be provided for the populace resulting in a big load of expenses for the states and devastating disbursements for the patients (Gelband, 2004). This can give rise to higher rates of diseases, mortality, and morbidity because of inaccessibility to medication. Additionally, any member or partners of TRIPS that manufactures, offers, or makes a production of a product that has a patent holder. The patent holder can take legal action against the government or a member state or request for a fine to make up for the loss of profit that has affected the company. This happened in the late 90s in South Africa when the pharmaceutical medicines production giant company GlaxoSmithKline prosecuted the South African government for importing of

the generic version of some antiretroviral medications used for the treatment of HIV/AIDS (Ncayiyana, 2001).

Another problem is the prolonged delay in the addition of new pharmaceutical ingredients and products into the World Trade Organisation list that is hurting worldwide accessibility to medication already and does not profit organisations, pharmaceutical companies, and nations. This issue must be handled by World Trade Organisation negotiators and not Brexit talks. Nevertheless, going back to the WTO rules may result in expensive tariffs for new and innovative medications and ingredients that is imported and exported between the UK and EU (Dunt, 2016).

Healthcare services are currently influenced by increasing costs of technology and medicine, demographic modifications, and the move in the direction of a more patient-centred health plan all these factors are contributing to medicine accessibility problems (Daughton and Ruhoy, 2010; Braithewaite et al, 2017; Muscat, 2020). The ageing population is contributing immensely to the increasing costs of healthcare services therefore healthcare must be able to acclimatise to meeting the rising demands of the age patient populace (Bennett, 2019).

As with most industries, the pharmaceutical industry is demonstrating a commitment to sustainable growth, transitioning innovation rooted from a ‘what is new’ concept to a ‘what is best school of thought. This approach is known as Corporate Social Responsibility (CSR), a de facto standard brought about by the Global Reporting Initiative which uses sustainable reporting to fund such decisions (Cassar, 2020). Companies using such standards exercise better judgment in their decision-making whilst also being transparent. CSR encourages advancements made in information technology,

personalised medicine, medical genetics, green chemistry, management of medicines and care in pharmaceuticals (Daughton and Ruhoy, 2010).

Problems with access to medicines is a danger to the health of individuals. Obstacles to access occurs from factors associated to the distribution and the demand of medications (Ensor and Cooper, 2004). Demand restraint factors affect the ability of people to access medicines while distribution restrictions are related to inadequacies of the healthcare services (Bigdeli et al, 2013) characterised by problems to access medicines in five different levels of the health system: health service delivery, individual level, health sector level, public policies, international and regional level. Barriers to access medicines at the individual level captures the demand from patients and their attitude to seek health services which depends on the social and cultural characteristics of the individual (Ensor and Cooper, 2004; Peters et al, 2008; Jacobs et al, 2012; Muscat, 2020). The other stages comprise the access difficulties associated to the supply of medicines in the healthcare organisation. Health service delivery includes aspects related to the irregular availability and high prices of medicines, irrational prescribing, dispensing and quality of medicines (Muscat, 2020). Barriers at the health sector level arise from the pharmaceutical governance functions including regulatory affairs, procurement and supply practices, inspections, and post-marketing surveillance. Public policies at national level may influence trade, industry, or legal sectors of the pharmaceutical industry. Barriers to medicines access in international markets incorporates pharmaceutical research and development, patents, and intellectual property rights (Bigdeli et al, 2013).

Perceptions related to access

Access is a broad, dynamic, and important component in the range of healthcare provision. Diverse determinates of access are presented in literature that consider the demand and supply characteristics of healthcare system operations as well as the processes involved for consumers to obtain care and benefit from healthcare services (Levesque et al, 2013; Muscat, 2020).

1.3.2 Scopes of access

1.3.2.1 Access dimensions according to WHO

The WHO impartial framework for access to essential medicines presents four scopes to steer pharmaceutical policy formulation and integrate activities to improve access to medicines[13]. The structure specifies four factors that are vital to ensure accessibility to medicines in national health systems (Bigdeli et al, 2013; Muscat, 2020):

i. **Essential medicine use** through the evolvement of drug formularies and treatment guidelines leading to more planned prescribing and enhanced patient safety (Muscat, 2020).
ii. **Fair prices** of medicines for healthcare systems and patients which is pursued through price competition, bulk procurement, and generic medicine policies (Muscat, 2020).
iii. **Pharmacoeconomics** which takes into consideration adequate funding levels and equitable financing systems to lessen the burden of the patients who spend

[13] World Health Organisation. Equitable access to essential medicines: a framework for collective action. WHO policy perspectives on medicines. Geneva. 2004 [cited 2020 May 18] Available from: URL: https://apps.who.int/iris/bitstream/handle/10665/68571/WHO_EDM_2004.4.pdf?sequence=1

out of their own pockets and exorbitant expenditures on medications (Muscat, 2020).

iv. **Availability of medicines** which must be supported through organised acquisition of medicines, reasonable application of regulatory sciences and the use of digitalised technology (Muscat, 2020).

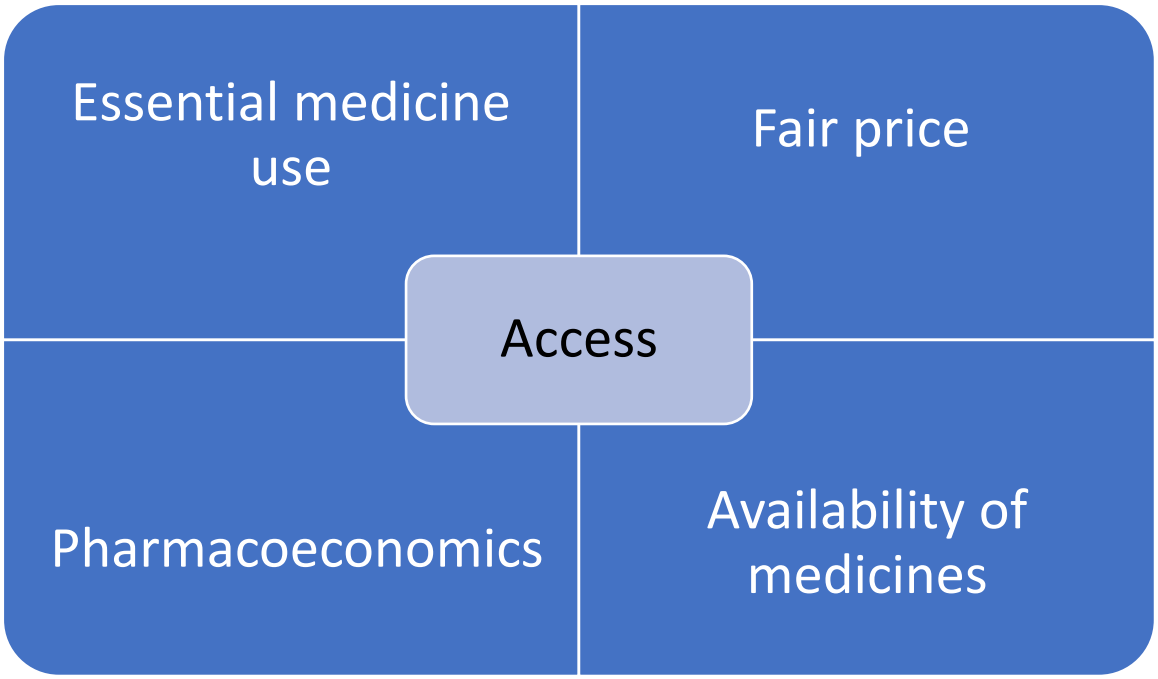

Figure 1.1: Access based on WHO principles

Figure based on: World Health Organisation. Equitable access to essential medicines: a framework for collective action. WHO policy perspectives on medicines. Geneva. 2004 [cited 2021 Mar 18] Available from:URL:https://apps.who.int/iris/bitstream/handle/10665/68571/WHO_EDM_2004.4.pdf?sequence=1

1.3.2.2 Introducing six A's of access

Penchansky and Thomas (1981) defined taxonomy of accessibility based on elements of use suggested by utilisation theorists. Five scopes of access to care were recognised in the theory of access which described the expectations of the patient related to their needs and desires. Saurman (2016) indicated that awareness is also a crucial element of access and should be applied when applying the concept to monitor, assess and improve access to healthcare (Muscat, 2020).

The idea of access is intricate and multidimensional. There are six dimensions of access: acceptability, accessibility, adequacy, affordability, availability, and awareness (Penchansky and Thomas, 1981; Saurman, 2016; Muscat, 2020). Each dimension is essential, interdependent, and interrelated to the other aspects in promoting or hindering access to medicines (Muscat, 2020).

i. Acceptability

Acceptability considers the predisposing and enabling factors of the individual in seeking healthcare services. This dimension focuses on communication and cultural relationships between the giver of the service and the receiver of the service (Goodson, 2010). Patient health outcomes are optimised when there is concordance rather than patient compliance with the pharmaceutical care plan (Chatterjee, 2006; Cousin et al., 2012; Cushing and Metcalfe, 2007; Muscat, 2020).

ii. Accessibility

Accessibility is determined by how services are effectively available for utilisation which is dependent on the acceptability of services, proximity, and the adequacy of supply. A

case example is the time it takes for patients to obtain the necessary healthcare (Muscat, 2020).

iii. Adequacy

Adequacy reflects the relationship about what the patient needs and the way supply sources are coordinated to meet the expectations of the patient. While medicines may be physically available, affordable, and acceptable to consumers, the adequacy dimension evaluates convenience and patient-centred aspects (Muscat, 2020).

iv. Affordability

This refers to a measure of the economic ability of patients to afford expenses for healthcare services without financial burden. Indirect costs, opportunity costs and the perception of value of the patient are also measured in the affordability dimension of access (Muscat, 2020).

v. Availability

Availability is determined by adequate provision by way of healthcare professionals and healthcare amenities such as pharmacies, clinics and hospitals that are available in reasonable time and proximity for patients to benefit from the health services (Muscat, 2020).

vi. Awareness

Awareness reflects the importance of effective communication and information strategies on healthcare services to curate the health needs of patients. The awareness dimension supports the empowerment of healthcare professionals and patients to understand and apply robust information to make health-related decisions (Muscat, 2020).

Access is a major concern in healthcare policy. Actions to enhance access are effective if the interrelationship between the different magnitudes of accessibility is recognised and effective measures of these dimensions are adopted in the basis of healthcare policy changes (McLaughlin and Wyszewianski, 2002). As described in the theory of access of Penchansky and Thomas (1981), the better the relation between the desires and needs of the patient and the healthcare system, the better is the access (Muscat, 2020).

Figure 1.2: The six dimensions of access

The six dimensions of access concept is based on the following publications: Penchansky R, Thomas WJ. The concept of access: definition and relationship to consumer satisfaction. Medical Care. 1981; 19: 127-140.

Saurman E. Improving access: modifying Penchansky and Thomas's Theory of Access. Journal of Health Services Research & Policy. 2016; 21(1):36-39.

1.3.2.3 Access in terms of utilisation

According to Bradshaw utilisation of medicines as a health need is in the Taxonomy of social need. Bradshaw describes four categories of need: comparative need, normative need, felt need and expressed need (Bradshaw, 1972). The normative need relates to the healthcare system policies which determine which medicines are included in the drug formulary list in relation to access to medicines. The felt need refers to the need recognised by the consumer after being prescribed or influenced to administer medicines. The expressed need corresponds to when a person goes to the pharmacy to obtain the medicine and the comparative need is linked to the capacity of the health system to provide an equitable response to the medical needs of the consumers (Vargas-Pelaez et al, 2017). Access to medicines results when all four perceptions of medications as a health need corresponds. Otherwise, inaccessibility to medications occurs (Muscat, 2020).

1.3.2.4 Access to healthcare in Malta

Malta has an exceptionally long history of medical care and associated social services (Godfroid, 2005). The values behind certain laws and policies that are in force today have been shaped over the years at least since before the coming of the Knights of St. John (Eade, 1991). The Knights Hospitaller's rule has left a mark on the Maltese healthcare system because the Knights considered the caring of the sick their most important role in society and took it very seriously (Riley-Smith, 2012). A particularly important principle is the fact that the distribution of free medicines started strictly as an act of charity. The concept that free medical treatment is charity and not a right continued well into the 20th century under British rule (Barry and Jones, 2002). The words charitable reappeared frequently in the names of services and the titles of their coordinators and chairpersons.

However, these were not only names, and they influenced the way each service was managed (Liebler and McConnell, 2020). In 1937 the post of Comptroller of Charitable Institutions was eradicated and swapped with that of the Chief Government Medical Officer (Leuchtenburg, 1996).

Some disease conditions that were considered to have been brought about through the patient's own actions, especially if these were immoral, were discriminated against by some institutions in the 1700s (Grob, 1973). For example, around 1710, the Santo Spirito Hospital in Rabat refused admission of syphilis cases. Sailors with syphilis were discriminated against and made to pay for their own medicinal care while after 1766, surgeons could charge fees for services to these patients, which was not always the case at the time (Francis, 2001). The values that have been gained by the present healthcare system from two meetings held by the Venerable Council and the Chapter General of the Order of St. John in June 1629 and May 1631 during the time of Antoine de Paule (Borg, 1967). The policies agreed upon called for a more carefully running of the hospital in Vittoriosa to prevent misuse of the process but at the same time treating the sick in a universal approach (Mitchell, 2002). From 1743 onwards it was decided that the hospital pharmacy should change the method used to obtain medicines to ensure good quality. Therefore, while cost was already considered to be an important issue when procuring drugs, it was not the only factor taken into consideration (Griffith, 2004).

In 1839, the Civil Hospital Drug Formulary was revised to conform with a standard list that was aimed at managing cost (Biehl, 2016). Then, economic considerations were being given more consideration. There was an event where a patient needed a costly T.B. drug that was justified on the fact that he would otherwise remain a perpetual financial burden on the State and not for some humanitarian reason (Rose et al, 2008). It is known

that in 1631 when a women's hospital was abolished, some prostitutes were issued mercurial treatments for use at home and free items of food until they got better (Siena, 2014). This can be considered one of the first instances of entitlement to free medicines in Malta that was not necessarily due to the patient's financial condition but to benefit the general population (Matthews, 2004).

Another practice that benefitted the general populace was the issue of free medicines to those who decided not to be admitted to hospital during cholera epidemics of the 1800s (Hamlin, 1998). Free medicines were given to the poor together with food rations. In 1865, an independent Relief Committee was formed for this purpose (McKeown, 2014).

In the 1840s, under the British rule, free medicines were given to underprivileged women, nuns, and other religious leaders. This practice has remained till the present day (Jayawardena, 2014). Even during the time of the Knights, the Commissioners of the Poor supplied medicines to sick women in their homes (Chadwick, 1942). Doctors not only prescribed free medicines but also made recommendations for financial relief (Kravitz, 1993). This helped to emphasise the strictly charitable nature of distribution of free medicines.

The first Government pharmacy that was not attached to a hospital started its operations in 1832 and it was called Farmacia. dei poveri or Albergo dei poveri (Cassar, 1965). The aim of the dispensary was to relief pressure on demand from the main government hospital on the island (Lucas, 2012). This value has not changed over the years. Although it was called a farmacia, there were doctors and surgeons as well as pharmacists operating the place, so it was more like the modern-day health centre than just a pharmacy as other services were provided (Cutler and McClellan, 2001).

Technology has supported the transition of healthcare to e-health through telemedicine, online health records and electronic prescriptions (Marva, 2014; Charlesworth et al, 2015). These prospects can be achieved via enormous extent of data collection regarding health for example through clothing devices and electronic health records which could be used to examine, protect, and sustain healthcare and access issues in Malta (Charlesworth et al, 2015). Notwithstanding the advantages, the move to digitalisation is extremely expensive and takes a lot of time and resources for instance within three years, the United Kingdom invested £510 million to implement e-Prescribing and online patient record keeping (Lichtner et al, 2016).

1.4 National Health Service (NHS) Malta

The fewest number of people in any Island of the EU is Malta. It has 417,432 residents living in it the total area in terms of land is 315 km2. They joined EU as a member state in 2004 (Pace, 2002). Its healthcare scheme is typically acquired from the UK, apart from the fact that it is to some extent more continental than the UK healthcare organisation. Malta's NHS is largely sponsored by national insurance contributions and general tax proceeds (Azzopardi et al, 2016). Usually, no charge is paid when using the system except for if the person is not eligible to healthcare benefits. However, it is different from the UK system of entitlement in the sense that eligibility is dependent on if a person is affected by the social security regulation. Compared to the UK, the scheme is not depended on you living in Malta. Even if you do not live in Malta, you can get healthcare benefits, However, you must be working and pay national social security contributions (Holzmann, 2005). Additionally, there is an increasing number of private healthcare sector as most Maltese inhabitants made their decision to use private healthcare services. The percentage of public healthcare expenses as a proportion of total expenses has lately

reduced in Malta to about 65% while it has remained increased in the UK about 83% (Dieleman, 2017).

Sustaining of the Malta healthcare scheme has turn out to be known as a crucial trial and has been beneath the examination of a cycle of economic and fiscal policy coordination within the European union. Malta obtained Country Specific Recommendations (CSRs) asking for a thorough transformation of the health system to enhance the competence and justifiable use of existing incomes in 2013 and 2014 (Azzopardi et al, 2015).

Malta's NHS offers its services without a charge to all citizens. It is funded out of general taxation therefore charges are not applicable, a system of co-payments or a repayment system. Mater Dei Hospital is the main government education hospital that offers accident and emergency, patients in the wards care, dedicated, ambulatory, and serious care services (Azzopardi et al, 2017). Maltese Primary health care is offered communally between private and public bodies that is managed autonomously. After discharge patients are given three days medicines supply as a to take home medicines free of charge depending on what they are prescribed. If the treatments are to be continued the medicines are purchased privately[14].

Malta has seven community Wellbeing Centres functioning 24 hours for 7 days in the week providing dedicated services. Public hospitals primarily offer dedicated secondary and tertiary care. Caring for health treatment is supplemented by the private hospitals and clinics (WHO, 1999).

The National Health System in Malta has been importing medications from the United Kingdom for so many centuries mainly due to English language being Malta's second

[14] Cordina G, Borg A. Pensions, health and long-term care – Malta country document. Analytical support on social protection reforms and their socio-economic impact. 2014 [cited 2020 May 20]. Available from: URL: file:///C:/Users/muscc156/Downloads/MT_asisp_CD14.pdf

most spoken language after the Maltese language, therefore, there is no need for translations or over-label when medicines are imported from the UK [15]. Also, most of the prescribers in Malta are UK trained and are used to UK pattern of prescribing. Medicines obtained in the UK contribute an important element on the supply of medicines in Malta because of reliance on the British market which emerged from registration and control limitation, specifically because of the use of English language in packaging and labelling of the pharmaceutical products sold in the European Union[15].

According to a report written by Inġ. Karl Farrugia in the Malta independent on Saturday, 30 March 2019; information for 2017 illustrates that 85% of the pharmaceutical goods obtained by the NHS were either registered in the UK or provided by UK companies[15].

1.4.1 The Malta Medicines Authority (MMA)

The MMA is an entity that is responsible for safeguarding and improving the health of people through the guidelines of medicinal products, medical devices, and pharmacological and therapeutic events (Azzopardi et al, 2017). They are core brilliance in evolving efficient and novel guideline and helping eminence and systematic excellence for the interest of patients and stakeholders. The agency is universally recognised, efficient and promotes individual's advancement and sustainable growth (Azzopardi et al, 2017).

They carry out responsibilities entrusted to the MMA by the Licencing Agency by means of the Medicines Act. They support and inform the Licensing organisation on any issue concerning to the control of therapeutic products and pharmaceutical events (Espín et al,

[15] The Malta Independent (THI). The impact of Brexit on the national health system in Malta in respect of treatment availability. Malta. 2019 [Cited Nov 2020]. Available from: URL: https://www.independent.com.mt/articles/2019-03-30/newspaper-opinions/The-impact-of-Brexit-on-the-national-health-system-in-Malta-in-respect-of-treatment-availability-6736205886

2016). They safeguard the public using up-to-date therapeutic and systematic information, about therapeutic goods sold in Malta and the EU to ensure that they of excellent value and have a positive risk to benefit profile by using autonomous, science-based assessment, post-approval schemes and involvement in making decision at EU level (Azzopardi et al, 2016). They methodically assess applications and monitor clinical trials conducted in Malta. To make sure that the medicines sold in Malta via the standardized distribution chain are of decent condition. They ensure superior feature examining and assessing of facilities for pharmaceutical activities (Espín et al, 2016). To supervise the wellbeing of medicinal products. They investigate and implement the important regulation by inquiry of possible violations of procedures and an array of other measures (Muscat, 2020).

They promote the efficient, secure, and logical usage of therapeutic products by providing of unbiassed and impartial knowledge that enables medical practitioners, healthcare experts and people in hospital and the public make educated informed choices on how to take their medications. They promote the accessibility of therapeutic products in the places where medicines are sold in Malta (Muscat, 2020). They promote competition of the Maltese marketplace via systematic monitoring, guidance, and the execution of principles of SMART Regulation (Azzopardi et al, 2017). They employ and create devices, guidelines, and methodologies to evaluate and guarantee the protection, value and efficacy of therapeutic products and pharmaceutical events (Muscat, 2020). They develop the specification of medicinal products and pharmaceutical activities for medicines for human use in the local market (Azzopardi et al, 2015). They contribute to European conferences of EMA, Council and the Commission and provide evaluation and offer systematic and monitoring situations in several regions. The system also supports

efficient stock control at the community pharmacies to reduce excess stocking or shortages (Muscat, 2020).

1.4.2 The Maltese Medicines Entitlement System

The Medicines Approval Section (MAS) has a duty for the putting together of the eligibility process to safeguard the conformity and assures that benefits are universal in application[16]. They are accessed by the symptoms, medical doctor's benchmarks, circumstances qualifying patients for getting therapy, examinations necessary before starting treatment, objective indicators of effectiveness and any need for any other assertions and then approved or rejected (West, 2015). In circumstances where an application for an item is denied a not entitled form letter is sent to the patient giving the reason why the application was rejected[17].

Maltese citizens are entitled to free medicines if they have a disease. Another way to get entitlement outside a Maltese government hospital setting is by the principle of social solidarity and happens through a system that requires a measure related to disease by the feature of the Social Security Act Cap 318 Article 23 and the amendment of this Act no. 1 of 2012 and the Fifth Schedule of the same Act. If a patient is diagnosed with a condition that is accessible on the GFL (Muscat, 2020). The patient can have their medicines free of charge. Sick persons experiencing long-lasting illnesses normally come under Schedule V (Yellow Card), whereas those with low income usually fall under the Schedule II (Pink Card). The Department of Social Security performs a means testing assessment for a patient to qualify for entitlement. The GFL has a list of pink positive

[16] Malta Medicines Authority. Introduction to medicines regulation. 2020 [cited 2020 May 20]. Available from: URL: http://www.medicinesauthority.gov.mt/introductionmedicinesregulation

[17] Malta House of Representatives. Social Security Act. 1987 [cited 2020 May 20]. Available from: URL: http://www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=8794&l=

medicines and medical devices for both acute and chronic use. Patients with the pink cards are entitled to the pink positive medicines only which are limited to a few medicinal products on the Government Formulary List (Muscat, 2020). Patients that are not entitled to free medicines procure their medicines through out-of-pocket payments from private community pharmacies. Patients with low income may be entitled to free medicines through the Second Schedule of the Social Security Act also known as the Pink Card based on means as part of non-contributory aids that offer social and medical support (Muscat, 2020).

International visitors in Malta can get free medical treatment but they must register with the Entitlement Unit immediately except if they are just a temporary visitor (Muscat et al, 2006). However, if a patient needs a complicated surgical procedure that are not available in Malta, they will have to travel abroad and such a therapy would have to be charged except for a citizen Maltese (Muscat et al, 2006). On the other hand, Australian nationals visiting Malta for the first six months of their stay can get free healthcare services in Malta. This mutual accord is merely applicable only if an Australian citizen is in Malta when a medical emergency occurs (Azzopardi et al, 2017).

As an EEA expert coming to Malta briefly, you will be required to make an application for a European Health Insurance Card (EHIC) in your country of origin prior to visiting Malta (Bertinato et al, 2005). EHIC is meant to allow you the right to use free general healthcare facilities without a charge on the same grounds as Maltese citizens. The EHIC can only be used for medical emergencies occurring at the same time or when you are in Malta. The EHIC is only intended for short-term journey, and the EU fervently advises that you bring private health insurance together with an EHIC (Bertinato et al, 2005).

A lot of EU expatriates in Malta, for example retired persons or employees on second assignment, could put in an application for a portable document S1 in their state of origin. This is applicable to workers who are contributing towards social insurance in their state of origin, and not in the Maltese island. You must apply for a certificate of entitlement from the Entitlement Unit if you hold or are in possession of a portable document S1, patients must present the certificate of entitlement in other to access free healthcare services at no additional cost in Malta (Bertinato et al, 2005).

With the Reciprocal Health Agreement (RHA) between British citizens and Maltese citizens, UK citizens working as experts in Malta that can demonstrate that they are normally inhabitants of the Maltese island are eligible to some form of healthcare services without a charge. They will be able to make a claim for an RHA entitlement card. The RHA entitlement card does not make them eligible for a free NHS service in the UK, not even for a surgical treatment that is not available in the Maltese island (Bertinato et al, 2005).

1.4.2 Malta National Healthcare Service Procurement System

The Central Procurement Union (CPSU) inside the Ministry for Health is accountable for processing medications through Article 126a of the EU Directive 2000/83/EC if there is lack of interest from the pharmaceutical corporations. The registration process requires a pharmacovigilance (PV) framework (Muscat, 2020). The body oversees the purchasing of medicinal products, medical devices, and similar items across the nationwide healthcare facilities[18].

[18] Government of Malta. Central Procurement and Supplies Unit – Corporate identity. 2019 [cited 2020 May 20]. Available from: URL: https://deputyprimeminister.gov.mt/en/cpsu/Pages/About-Us/CorporateIdentity.asp

The medicines, medical devices and pharmaceutical products distributed through the free health system are acquired through the Central Procurement and Supplies Unit (CPSU) (Azzopardi et al, 2017). The request for quotations or estimates for medical supplies are circulated using the Electronic Public Procurement System. Medical supplies are obtained through awarded tenders then supplied to sectors of the general health sectors as well as the public hospitals and the central POYC unit (Muscat, 2020). The central POYC unit receives the medical supplies from CPSU and is tasked with distributing the products to the community pharmacies according to patients registered with the pharmacy for the POYC scheme (Azzopardi et al, 2017). They are assigned a yearly budget from the federal government to purchase medicines, medical devices, pharmaceuticals, and other related items (West, 2015). The medicines purchased are those from the Government Formulary List (GFL) (Bugeja, 2008). They utilise community purchasing proposal techniques to guarantee impartiality in the procurement of medicines and allow competition to promote improved value and reduced cost. As a result of failure in local access to supply, the CPSU had to accept the role of importers responsibility to safeguard and gain access to products with minimal utilization (Muscat, 2020).

1.4.3 The Pharmacy of Your Choice Scheme in Malta (POYC)

The Pharmacy of Your Choice (POYC) programme gained establishment in 2007 to provide patients with free medicines. POYC is a system run by the Maltese ministry of Health committed to giving of eligibility to medical products free of charge and all associated benefits (West, 2015). POYC is a patient centred service that provides pharmaceutical services and allows persons that are sick to receive their eligible permitted medicine from a private community pharmacy of the persons that is sick's choice, thereby

avoiding unnecessary cues and saving precious time in comparison to when patients had to receive their medicines from general provincial pharmacies (Azzopardi et al, 2017).

Over 140,000 patients through the 219 community pharmacies are enjoying free medicines, medical devices, and related services through the Maltese ministry of Health POYC program under the Schedule V legislation (Vella, 2007). There is a restricted production area requiring the repackaging into patient package size, from government products purchased in large amount. The repackaged product is then circulated through the POYC Programme and the Government NHS hospital pharmacies stores. One Stop Shop Service consist of the Schedule V Medicines Approval, the POYC Registration and the Renewal of the Dangerous Drugs Control Card (Azzopardi et al, 2017).

The development of the POYCs scheme was intended to reduce waiting time, travelling distances and overall inconvenience to the patient's collecting medication under the national pharmaceutical scheme. Patients are entitled for free chronic or acute medication outside the hospital setting according to a government formulary (Muscat, 2020).

The medications and medical devices supplied through the free health system are obtained via the Central Procurement and Supplies Unit (CPSU), a Call for quotations for medical supplies are issued utilizing the Electronic Public Procurement System. Medical supplies are obtained through then supplied to sectors of the public health system including the public hospitals and the central POYC unit (Azzopardi et al, 2017). The central POYC unit obtains the medical supplies from CPSU and is tasked with disseminating the products to the community pharmacies with respect to patients registered with the pharmacy for the POYC scheme (Cassar, 2020).

The patient needs to go for an appointment with a medical practitioner or consultant specialist to get a prescription for 56 days except medications where dosing may be changing rapidly such as warfarin (Muscat, 2020).

The 56 days prescription may be received from the preferred community pharmacy registered under the POYC Scheme. Every 8 weeks the patient to has to have their medicine entitlement extended under the chosen Schedule (Azzopardi et al, 2017). To improve patient, care the dose of treatment for non-protocol regulated medicines can be changed because medicines specified for chronic conditions under the Schedule V Scheme requires monitoring for a long period of time (Muscat, 2020).

The POYC has a pharmacy IT unit within the Health Centres in Pharmacies located at Paola help to assist in the dispensing of medicines electronically of free Government's pharmacy stock to entitled people who are sick under the Schedule II Regulation, it is used in the dispensing of pharmaceuticals to entitled NHS staff, for patients injured on duty, The Police Corp in Malta, Armed Forces Corp, Malta, Detention Services Corp and the Third Country Citizens (Cassar, 2020).

1.5 Essential medicines

The WHO describes necessary medications as medications that fulfil the important health care demands of the people[19]. Essential medicines are meant to be always accessible within the perspective of operating health systems in sufficient amounts, in the suitable dosage forms, with guaranteed value, and at a cost the individual and the public can manage to pay for (Manikandan, 2015; Bigdeli et al, 2018; Muscat, 2020).

[19] World Health Organisation. Essential medicines and health products. 2020 [cited 2020 May 18] Available from: URL: https://www.who.int/medicines/services/essmedicines_def/en/

1.5.1 The WHO essential medicines list (EML)

The List of Essential medicines was first established in 1977, 208 individual medications were identified which collectively may possibly deliver secure, efficient therapy for many infectious and non-infectious diseases[15]. Its aim was to serve as a forward-looking global guidance for the development of healthcare system formularies. Medicines included in the EML are determined by their estimated present and future public health importance, clinical effectiveness, protection, and price efficiency. The EML list is to renew each two years and embodies the need to frequently update the selection of medicines to reflect novel options for emerging diseases, varying therapeutic patterns, and evolving healthcare needs (Haddix, 2003). The 2019 EML includes 460 medicines in contrast to the 212 medicines published in the 1977 EML[20] . These medicines are viewed essential for tackling the most vital world-wide public health needs (Muscat, 2020).

The notion of essential medicines has progressed through the years outside the selection of off-patent medications to incorporate innovative medicines, viable stock chains, impartiality in access, effectiveness, rational use of medications and economical for both patients and healthcare schemes [21]. Around 2001, antiretroviral medicines indicated in human immunodeficiency virus (HIV) were included in the EML even though that the medicines were deemed too expensive to be included in the EML of 1999. The listing on the EML triggered the pharmaceutical industry to reduce the cost and higher accessibility to antiretroviral medications. Since then, pioneering treatments have been included in the EML for the therapy of life-threatening illnesses including tuberculosis, hepatitis C and

[20] World Health Organisation. World Health Organisation Model List of Essential Medicines 21st List. Geneva. 2019 [cited 2020 May 18] Available from: URL: https://www.who.int/medicines/publications/essentialmedicines/en/

[21] Bigdeli M, Peters D, Wagner A. Medicines in health systems: Advancing access, affordability and appropriate use. Alliance for Health Policy Systems and WHO. Geneva. 2014 [cited 2020 May 18] Available from: URL: https://www.who.int/alliance-hpsr/resources/FR_webfinal_v1.pdf

cancer[22]. The scale behind including high-cost medicines is to encourage positive negotiation between countries and pharmaceutical stakeholders to reduce cost and improve access to innovative medicines (Muscat, 2020).

1.6 Drug formularies

Formularies are lists of permitted evidence-based medicines that direct medicine prescribing in healthcare systems (Woodhouse, 1994). The aim of a medication formulary is to deliver increased level value care utilising the greatest economical medicines which are easily accessible through the healthcare system. The formulary has a limited number of medicines listed according to the international non-proprietary names (INN) which have been selected on measures associated to proven quality, safety, efficacy, and cost (Van et al, 2016). When a medication is not listed on a formulary, the patient will suffer out-of-pocket costs to be able to administer the approved medicine. To reflect changing therapeutic needs, formularies should be reviewed regularly and updated by adding new medicines and deleting medicines which are no longer deemed to be cost-effective [23] .

A comprehensive and active formulary offers many advantages in improving patient care at reduced cost via enhanced variety, good practice guidance for prescribers and rational use of medicines [24]. The formulary system also supports financial management and expenditure on medicines by making procurement and inventory management more efficient (Jones and Cronin, 2000; Morgan et al, 2009).

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[22] Lo C. WHO's Essential Medicines List: discussing innovation and access. Pharmaceutical Technology. 2019 [cited 2020 May 18] Available from: URL: https://www.pharmaceuticaltechnology.com/features/who-essential-medicines-lis

[23] The Kennedy Forum. A consumer guide to drug formularies: Understanding the fundamentals of behavioural health medications. 2017 [cited 2020 May 18] Available from: URL: https://www.paritytrack.org/issue_briefs/a-consumer-guide-to-drug-formularies-understanding-thefundamentals-of-behavioral-heal

[24] Management Sciences for Health and World Health Organisation. Drug and Therapeutics Committee Training Course. 2007 [cited 2020 May 18] Available from: URL: https://www.who.int/medicines/technical_briefing/tbs/02-PG_Formulary-Management_final-08.pdf

1.7 The background of Brexit

The method of the UK leaving the European Union (Brexit). The UK voted in its ongoing union with the European Union in June 2016 signified a revolving moment in the association between the United Kingdom (UK) and the EU (Bulmer and James, 2018). The Prime Minister (PM) had encouraged the nation to cast their vote to Stay in the union instead she was beaten by 52% to 48% votes regardless of London, Scotland and Northern Ireland supporting remaining in the union (Sloat, 2018). The PM David Cameron accepted the result as a defeat on 24th of June 2016 and announced that he would resign on October 2016 (Smith, 2018). In March 2017, the UK government under the leadership of the PM Theresa May's government incited Article 50 of the Treaty on European Union, formally starting the discussions of UK departure from the EU. On the 31st of December 2020, Great Britain and Northern Ireland finally exited the EU (Prosser, 2021).

United Kingdom's (UK) departure from the European Union (EU) is perhaps the highest test that the British and the EU has ever encountered (Nick et al, 2017). The UK intension to depart the European Union (EU) and the EU's only trading place might come up with extreme implications for sick persons and accessibility to medications and therapeutic technologies (Menon, 2016). It could result in the interruption in market, and also in the event of absence of collaboration in the control of medications and medical procedures between the EU and the UK after Brexit (Fahy et at, 2017). This will have profound consequences for medicine supply in the UK and across Europe especially in small countries like Malta. After 45 years of membership in the European Union (EU), UK voted in a referendum in June 2016 to exit the EU. The United Kingdom became a tertiary country to the European Union On 31 January 2020, the UK has embarked on the transition period to leave the EU (Alexiadou, 2019). This has constitutional, communal,

and technical concerns for the control of health care markets. The effectiveness, protection, and value of medications in the United Kingdom will no longer be questioned by the regulatory framework of the EU (Jackson et al, 2017).

1.7.1 Challenges of Brexit

The UK is a key venue for scientific investigation and the production of medicines and medical devices Brexit has imposed harmful unique changes within the pharmaceutical industry affecting drug advancement, drug regulation and transaction within the EU causing less access to medicine There will be key changes in the way medicines and medical devices are tested, examined, and controlled within the UK and EU because of Brexit (Song, 2016).

These would result in possible serious outcomes of Brexit for the efficiency of pharmaceutical investigation in the UK and the rest of the EU. Together with the USA, the EU are the leaders of medications studies and have provided immensely to previous and present innovations in medication treatments (Kazzazi et al, 2017).

Even Though several ancient innovations go before the creation of the union, most or all of the European studies have remained inspired and enabled by the union, through permitted migration of persons, possessions and facilities, and prospects for sponsored studies like the Horizon 2020, All of these might completely be compromised by Brexit (Fahy et al, 2019). The UK and EU pharmaceutical corporations are battling to employ brilliant scientists after the referendum. There is departure of researchers and healthcare specialists from both the UK and EU since the Brexit vote (Golding and Waring, 2018). These might be partially as a result of misunderstandings regarding the intentions for the Brexit vote and also due to nervousness concerning what the imminent could be embracing. Nevertheless, UK occupation strategies has not yet transformed, and it is

unimaginable that appropriately skilled individuals might be prevented from employment in the UK after Brexit although people are disturbed in general and requires to be alleviated[25].

The UK is a very appealing place for competent personnel and for companies to embark on R & D (Papadopoulos, 2004). Presently, the industry can supply talents differences throughout the industry through international staffing, intra-corporation allocations and high-quality scientists in business and in UK research organizations (George et al, 2012). The UK has profited extremely from EU financial support for its R & D, resulting in a substantial percentage of developments and safeguarding both community and private financing to help them (Murray and Marriott, 1998). Because the sector is cooperative, there are advantages to both the EU and UK for ongoing obtaining of financing such as Horizon 2020 and its predecessors and to schemes like the Innovative Medicines Initiative (Saric et al, 2021).

1.7.1.1 Regulatory Consequences of Brexit

There will be monitoring implications of Brexit for the EMA and the EU. The Medicines and Healthcare Products Regulatory Agency (MHRA), UK. The authority that is regulating medicines in the UK, presently holds a significant amount of the projects of the EMA and nearly 30% of the requests for European marketing authorizations are evaluated by the MHRA (Golding and Waring, 2018). The UK participate in a vital part within the invention of both the EU clinical trials regulations and the EU Pharmacovigilance procedures. Practically all the boards of the EMA are managed by British delegates. Dissociating the MHRA from the EMA will cause a reduction of the

[25] British Medical Association (BMA). Press release. BMA. 2017 [cited 2020 Nov 14]. Available from: URL: www.bma.org.uk/news/media-centre/pres-releases/2017/november/almost-a-fifth-of-eu-doctors-have-made-plans-to-leave-uk-followings-brexit-vote).

prudence, proficiency, and resources of the MHRA (Golding and Waring, 2018). Before the UK's departure from the EU, MHRA supplied extensive systematic contribution to EMA marketing authorisations of new medications (Wouters, 2020). Around 2016, once the Brexit referendum occurred, a huge part of EU clinical trials was conducted in the UK, and UK professionals performed a significant responsibility in EMA assessments. The impending EMA without the MHRA may not be as powerful (Avery et al, 2011). This will result to a lose-lose situation. If there is a regulatory cooperation between UK and the EU, pharmaceutical companies could follow other agreement measures and meet various quality assurance measures to get a marketing authorisation in the UK and the EU resulting to needless disruptions in medicines accessibility and repetition of experimental studies (Kazzazi et al, 2017). Medicines could face restrictions at borders and might face severe intense re-testing requirements that can implicitly extend procedures and result in interruptions in access to medicine (Van et al, 2019).

Pharmaceutical companies located in the United Kingdom have been urged by EMA and the European commission (EC) to implement the essential stipulations to conform with EU law and safeguard access to medicines pro Brexit (McHale et al, 2018). The EC and EMA have been working diligently to promote regulatory procedures after Brexit for marketing authorisations of medicines approved under the national, decentralised, and mutual recognition (Breckenridge and Feldschreiber, 2019). They have put measures in place such as moving market authority owners who want to sell their products in the EU to another EU location, Testing and batch release should be done in an EU country, the master file of the UK Pharmacovigilance System should be moved to an EU location and the UK Qualified Persons for pharmacovigilance should be repositioned to the EU (Lipton, 1990). It is very vital for patients needs for supply of medicines to be continuously met after Brexit (Jackson et al, 2017).

The EMA is one of the EU decentralised organisations presently established in the UK, it is scheduled to exit the UK as soon as the UK departs from the union (Hopkin, 2017). The EMA's leaving for Amsterdam in 2019 poses a substantial concern for government, the EU, and the UK. Before the UK's departure from the EU, the MHRA provided substantial scientific input to EMA marketing approvals of new drugs[26] .

European law is one industry that continues to be exposed to issues. Cross-European pharmaceutical regulation commemorated its 50th ceremony in 2015, and the EMA now operates in a population of over 500 million EU nations (Jackson et al, 2017). In the background of more and more specific original therapeutic products, subject to pioneering initial authorising programmes, there is power in numbers. On the other hand, a severe threat to the health of the public from isolation that will result from Brexit[27]. Close connections between the MHRA and the EMA, such as the coordination of monitoring processes, might decrease the predictable interruptions coming from Brexit. UK officials and analysts have claimed that it will benefit both parties. But the EU is legitimately and constitutionally restricted from close cooperation with a nation that has decided to deviate from the alliance's regulations [28].

One of the very overwhelming financial concerns arises from the reality that the study-based pharmaceutical is a massive enterprise (Taylor, 2015). Global pharmaceutical

[26] European Medicines Agency. European authorities working to avoid shortages of medicines due to Brexit – questions and answers. 2020 [cited 2020 May 20] Available from: URL: https://www.ema.europa.eu/en/documents/other/european-authorities-working-avoid-shortagesmedicines-due-brexit-questions-answers_en.p

[27] Wellcome Trust. Regulation of clinical trials: Brexit and beyond [cited 2021 Jan 26] Available from: URL:https://wellcome.ac.uk/reports/regulation-clinical-trials-brexit-and-beyond.

[28] Luigetti R, Bachmann P, Cooke E, Salmonson T. Regulatory collaboration: collaboration, not competition: developing new reliance models. [cited 2021 Jan 26] Available from: URL:https://apps.who.int/medicinedocs/documents/s23135en/s23135en.pdf

firms, located in North America, Europe, and Japan, are strong financial operators. Strong Financial power swiftly turns into strong political power (Rifkin, 2013). When techniques to enhance accessibility to medicines are discussed at WHO, a typical diverging friction emerges, Questions such as who priority is given to, financial interests, or the health of the public concerns occurs (Van et al, 2012).

1.8 Risk and access to medicine

The definition of risk is the likelihood that any action or activity might occur to cause damage (Calman and Royston, 1997). Practically everything has an associated risk and zero risk does not exist. Normally the benefits of an action should outweigh the risks. In the field of medicine, risk modulates the occurrence of a disease and its prognosis in patients (Costa and Carneiro, 2011). Daily, health care professionals are faced with decisions on risk where the benefit-risk ratio needs to be considered in the process of making decisions (Conti et al, 2010).

Risk may be assessed and quantified through a structured approach to identify and understand risks associated with specific activities. Risk may be quantified using a three-dimensional approach by the Risk Circle. The Risk Circle considers three dimensions to risk; the probability of an event occurring, and the severity of the consequences represented by two equal sides, and detectability of an adverse event before taking place which rests on the base of the circle and has a shorter length. Detectability mitigates risk by reducing the probability of adverse events. It is not always given equal importance as probability and severity, but it should be considered for an accurate estimation of risk (Attard, 2016; Muscat, 2020).

Risk to patients in access to medicines, may be decreased by proactively addressing barriers to accessibility to minimise negative effects on the medicines needs of patients

(Attard, 2016). The process involves recognising and defining the risk problem and its structural analysis followed by gathering necessary intelligence and selecting a course of action that minimises risk (Tounsi and Rais, 2018).

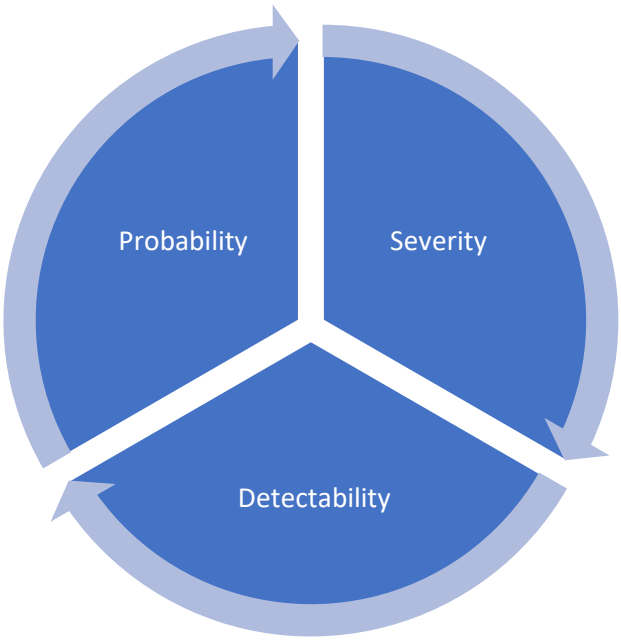

Figure 1.3: The Risk Circle

Attard Pizzuto M. Innovative Tools to Investigate Risk in Pharmaceutical Processes. 2016; Muscat C. Drug Intelligence and Access to Medicine;2020.

1.9 The Novel corona virus (COVID-19)

On the 30th of January 2020 WHO confirmed the novel coronavirus (COVID-19) as a public health disaster (Jee, 2020) and on the 11th of March 2020 COVID-19 was

proclaimed as a Global Pandemic that has a very high global risk of spread[29]. Data shows that the spread of a β coronavirus from animals, possibly pangolins or bats to humans largely owing to near body communication and inadequate sanitation habits in live products and illicit sales in natural world (Xiao et al, 2020). The corona virus spread of disease has a harmful effect on individuals, civilization, health services, countries, and living worldwide. It has caused disruptive effects and placed enormous strain on the global supply of medicines (Nicola et al, 2020).

Globally organised endeavour with instant immediate alert and radical lockdown procedures influences pandemics therefore additional efficient warning scheme requires to be done, as well as other measures, that would safeguard the against concealment, hindering or distribution of information (Attard, 2020).

The EU network has been observing closely the impacts of the pandemic on the EU medicine supply chains (Golan et al, 2020). Lack of access to medicines may result from several pharmaceutical reasons which include absence of the qualified personnel either because they cannot work from home or they are indirectly monitoring the pandemic, lack of provision of active pharmaceutical ingredients (API) required for the manufacturing of medicines which are mainly sourced from China and India where exports were restricted, financial problems encountered by different stakeholders, difficulties in the transportation of medicines from one country to another, higher request for medications vital to relieve COVID-19 sick persons and hoarding by healthcare systems and consumers[30]. The EU Executive Steering Group on Scarcities of Medicines Caused by Major Events was

[29] World Health Organisation. WHO timeline – COVID-19. 2020 [cited 2020 Jun 26] Available from: URL: https://www.who.int/news-room/detail/27-04-2020-who-timeline---covid-19

[30] 19 European Medicines Agency. Availability of medicines during COVID-19 pandemic. 2020 [cited 2020 Jun 26] Available from: URL: https://www.ema.europa.eu/en/human-regulatory/overview/public-healththreats/coronavirus

established to lead coordinated actions within the EU to avoid and alleviate interruptions in the supply of medicines and medical technologies[31].Ongoing discussions with the goal to improve the mechanisms for predicting the future demand of medicines and provide guidance on how to match the estimated demand with the available supply to ensure access to vital medicines[32]. The pharmaceutical industry has positively responded to the global need for action to treat COVID-19, from repurposing existing medicines, to developing vaccines, to searching for innovative ways to attack coronaviruses. The benefit of COVID-19 vaccines far outweighs the risk of side effect and contracting the COVID-19 virus with a possibility of hospitalisation and death (Chakraborty and Parvez, 2020).

Global accessibility to efficient vaccines and treatments is crucial to building herd immunity and eradicating the virus and free up beds in intensive care hospital wards[33]. The fight against the threat of COVID-19 is won when an approved vaccine or therapy would be accessible to all individuals (EMA, 2017). When the world collaborates and every single person in the world has been vaccinated and develop immunity against the virus (Golan, 2020).

[31] European Medicines Agency. EU authorities agree new measures to support availability of medicines used in the COVID-19 pandemic. 2020 [cited 2020 Jun 26] Available from: URL: https://www.ema.europa.eu/en/news/eu-authorities-agree-new-measures-support-availability-medicinesused-covid-19-pandemic

[32] European Medicines Agency. EU actions to support availability of medicines during COVID-19 pandemic – update 7. 2020 [cited 2020 Jun 26] Available from: URL: https://www.ema.europa.eu/en/news/eu-actions-support-availability-medicines-during-covid-19-pandemic-update-7

[33] Edwards DJ. New products alone are not enough. Pharma can do more to halt COVID-19. Access to medicine foundation. 2020 [cited 2021 Feb 28] Available from: URL: https://accesstomedicinefoundation.org/media/uploads/downloads/5e95d85128fb9_ATMF_Viewpoint_Role_for_pharma_in_C-19_200414%20(1).pdf

1.10 Rationale for the research

To gather information and data using a scientific approach to enhance the accessibility to medicines, through application of knowledge assembled by critically analyzing the demand and supply of medicines in Malta with relation to Brexit.

For a health system to be highly effective access to medicine and the continuous delivery of inexpensive medicines with enough quality, safety, efficacy, and effectiveness must be an important consideration. Inaccessibility to medicines is still one of the greatest serious international public health issues. In effect, access to medicines is on the global plan to advocate greater international cooperation to eradicate discriminations and injustices. WHO formulated a four-part framework to guide and coordinate cooperative activity on the accessibility to medications. Important activities of the agenda include rational selection and the usage of medications by advancement of nationwide therapy strategies and a nationwide list of medications, affordable prices pursued through price competition, bulk procurement, implementation of generic policies and price negotiation for new medicines, maintainable funding and dependable wellbeing and source schemes that assures the value, protection, and effectiveness of medicines by regulatory control.

The potential impact of Brexit on medicine accessibility is substantial affecting how medical products are licensed. The development of a proactive and targeted approach should allow improved accessibility to medications and reduce the impact of Brexit on accessibility to medications by stockpiling up to six months and change in registration. Integration of wealthy and complex analysis strategies in a multidisciplinary setting may lead to new routes for access to medicines.

A lot of development has been made, but many concerns continue to encourage worldwide R & D of access to medications that predominantly impact on the general

public. By understanding how medicines are accessed, the potential impact of Brexit on medicine accessibility can be better understood.

Co-operation, partnership, consultation and management between patients' group, healthcare professionals and the pharmaceutical industry is important to avoid and control medicines accessibility challenges. Malta health system must constantly empower members of staff to uninterruptedly endeavor for brilliance and to increase in value in the reputation of development and continuous supply of medicines for the benefit of all. Proactively addressing the barriers to accessibility to minimize negative effects on the medicines needs of patients.

1.11 Aim and objectives.

The research is aimed to gather information and data using a scientific approach to enhance the accessibility to medicines through application of knowledge assembled.

The objectives are:

1) To critically analyze the demand and supply of medicines in Malta by addressing the sourcing of medicines in Malta in relation to Brexit effect

2) To explore alternative solutions to accessing medicines

3) To review the current NHS formulary in relation to rational prescribing

Chapter 2: Methodology

2.1 Overview

The research employed a qualitative research design, using a wide range of literature review search utilizing HyDi, medicine complete, Micromedex, University of Malta discovery search gateway, Google Scholar online literature database, Medline, Embase, Medical Subject Heading (MeSH) phrases in PubMed. Relevant books, scientific documents, reports, and dissertations were reviewed. Appropriate keywords such as Brexit, access, barriers to medicine, public health, regulatory and consequences were used. The snowball method (Wohlin, 2014; Badampudi et al., 2015) was adopted to expand the literature review with innovative aspects. Robust relevant documents on Brexit and accessibility to medicines were retrieved by applying backward and forward snowballing to the reference list of reviewed articles (Muscat, 2020). The legislative framework related to the accessibility of medicines was consulted. This includes EU Directive 2001/83EC38 which was transposed in the Maltese legislation as the Medicines Act Chapter 45839 of the Laws of Malta (Muscat, 2020). Pertinent books, reports and dissertations were reviewed.

For the next best option outside the Government Formulary List (GFL), Micromedex was used to check for the alternative medicine according to the Pharmacological indication if there is none then a combination of the equivalent of the drug is then considered if there is still no match a generic brand of the drug is used. The GFL was first arranged according to the pharmacological indication in alphabetical generic order. The GFL list was then given a scale of 1 to 10. One (1) being the closest alternative option with an example and 10 being the last resort. Each option includes an example. Some of the drugs in the GFL were replaced with a different dosage form of the same medication when a suitable alternative could not be found.

To find alternative drugs for the private medicines in Malta using the list from MMA. The drugs were arranged in generic alphabetical order and then classified under cardiovascular, Central nervous system, Anti-infectives etc. The EMC and the BNF were used to check for alternative generic product. The generic version of the drug was considered. The list was then cross checked against UK ban drugs. Combination of the strengths in the list was also considered. Micromedex was used looking at FDA uses and cross checking with UK uses and then comparing the efficacy (comparable efficacy) to determine the drug classification. Google search was then made to check the dose equivalent of the brand name and then EMC and BNF were used to check UK uses and availability or discontinuation.

Data collected from CPSU, and the MMA was assessed. Issues related to accessibility such as drug shortages, sourcing issues, effect of UK in Malta, supply verse demand, formulary and alternative solutions was considered. The research entails the evaluation of accessibility of medicine problems documented at the Central Procurement Supplies Unit (CPSU) and the Malta Medicines Authority (MMA). A focus group and a series of interviews was used to examine and discuss obstacles to access medicines and the information gathered highlighting concerns related to accessibility. This includes review of the accessibility issue to analyse the implication of threats, opportunities, and outcomes on medication accessibility.

2.2 Research Design

Systematic gathering of information collected from Central Procurement Supplies Unit (CPSU) and the Malta Medicines Authority (MMA) was performed. A pragmatic approach was adopted for the comprehensive extraction and systematic classification of data on problems of accessing medicines. The information gathered was corroborated.

An integrated procedure was outlined, endorsed, and implemented to sustainably improve accessibility to medicines. These were assessed by qualitative research methods by a team of four (4) expert panel in a focus group discussion and a series of interviews from the director of licencing in MMA, a member of staff from the Medicines Intelligence and Access Unit (MIAU) MMA, and the managing director of CPSU.

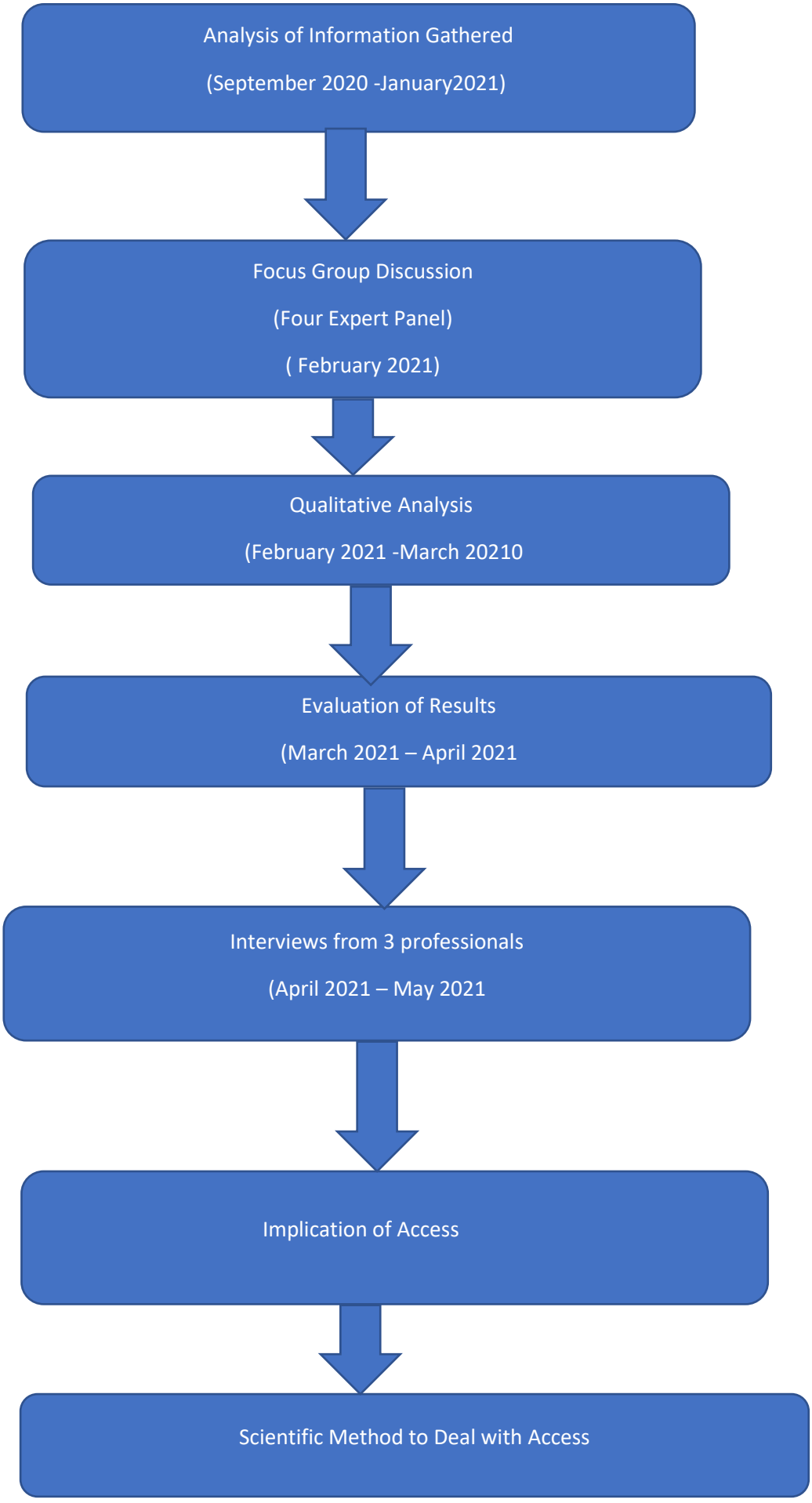

Figure 2.1: Flowchart of research methodology

2.3 Research Setting

The research was conducted at CPSU and the MMA in line with General Data Protection Regulation (GDPR) to ask for permission, which operates within a regulatory infrastructure based on best practices. The Malta Medicines Authority addresses health and pharmaceutical concerns as part of the goal of the Malta Medicines Authority to safeguard and improve public health as a result of the control of pharmaceutical products and therapeutic activities[34] .

The MMA facilitates access to medicines through the gathering of information and data using a scientific approach to enhance the accessibility to medicines, through application of knowledge assembled by critically analyzing the demand and supply of medicines in Malta with relation to Brexit for the benefit of the patients [35]. The data gathered from the CPSU, and the MMA was analysed**.**

All the data collected from CPSU and the MMA within the identified timeframe was assessed. Issues related to accessibility such as drug shortages, sourcing issues, effect of UK in Malta, supply verse demand, formulary and alternative solutions was considered.

2.4 Ethics approval

Approval of ethics from the University of Malta Research and Ethics Committee (UREC) was sought to take part in the research[36]. The UREC self-assessment form indicated that the research proposal required review of the Faculty Research Ethics Committee (FREC).

[34] 5 Malta Medicines Authority. Mission and Objectives. Malta: Malta Medicines Authority; 2020 [cited 2020 Oct 20]. Available from: URL: http://www.medicinesauthority.gov.mt/missionobjectives?l=1
[35] Malta Medicines Authority. Medicines Intelligence and Access Unit. Malta: Malta Medicines Authority; 2020 [cited 2020 Dec 10]. Available from: URL: http://www.medicinesauthority.gov.mt/directoratesunits?l=1#Medicines%20Intelligence%20and%20Access%20Unit
[36] University of Malta. Research Ethics & Data Protection – UM research. Malta: University of Malta; 2020 [cited 2021 Mar 10]. Available from: URL: https://www.um.edu.mt/research/ethics/forms

The research proposal was evaluated by the Faculty Research Ethics Committee (FREC). An institutional approval to take part in the research at the Malta Medicines Authority and CPSU was taken from the Chairman and a data protection statement was signed. An approval to take part in the research at the CPSU was also taken from the Managing Director. These were submitted to the FREC together with the CV of the researcher, email from the chairman of MMA, email from the managing director of CPSU, the research proposal and study protocol. The University of Malta Medicine and Surgery FREC granted ethical approval for the research, ‘’The effect of Brexit on accessibility to medicine’’ on the 10th of May 2021 following a presentation of the research proposal (Appendix 1).

2.5 Systematic analysis of data extracted

Triangulation of data gathered from MMA and CPSU. A focus group and series of interviews were used to gather robust, well-developed data and minimise bias.

2.5.1 Comprehensive extraction and systematic classification of data

A comprehensive extraction and systematic classification of data collected from MMA private drug list and CPSU GFL was carried out to extract and identify issues related to accessibility to medicines. Microsoft Excel® was used as a platform to document the alternative drugs for the private list, the next best option of the GFL and the outcome of the intervention. Explorative analysis of alternative routes was undertaken using Micromedex®, EMC and international regulatory authorities related to access to medicines such as Brexit, UK ban on export of medicines, Licensing and registration of Medicines, Absence of collaboration in the directive of medicines between the EU and the UK after Brexit, Drug shortages, Falsified medicines- serialisation-FMD, Problems

with drugs in GFL, Patients' perspective, drug recalls, medicine safety, pharmaceutical manufacturing issues and high prices of medicines were noted.

2.5.2 Focus group

Qualitative methods of research are experimental in the way it is conducted and lets the investigator obtain knowledge on subject wherever slight is already established (Liamputtong and Ezzy, 2005). Qualitative research approaches give the chance to understand around a variety of thoughts, encounters, and attitudes that individuals have about a certain subject, but they are not planned to be illustrative of the opinions of the wider populace (Llewellyn et al,1999; Liamputtong and Ezzy, 2005). Qualitative method of research was chosen because Brexit is a new and novel topic therefore had limited information/scientific based evidence to be able to include a quantitative method of research. These led to the decision to gather the information/data through interviews and focus groups. The focus group and interviews were used as tools to obtain knowledge and produce qualitative data from prominent healthcare professionals. A team of four expert panel consisting of two (2) general practitioners, an academic pharmacist, a clinical pharmacist from the focus group and two (2) regulatory pharmacist and the managing director of CPSU from the interview were organised to scientifically discuss the data gathered from the comprehensive extraction and systematic classification of data on challenges with accessing medicines and generate ideas for the purpose of devising recommendations to enhance access to medicine.

2.5.2.1 Focus group protocol

The focus group was led by a moderator who prompted a facilitated discussion and maintained a balanced input of participation from all members of the expert panel. The researcher followed the focus group and notes of the discussion outcomes were recorded

in writing by a minute taker who was a community pharmacist. The focus group protocol was adapted from (Dawson et al,1993) and included four main sections:

1. Introduction (Approximately 10 minutes)

The expert panel introduced themselves after being asked by the moderator and the moderator introduced the main topic the effect of Brexit on accessibility to medicines. The overall research question was then introduced (Appendix 2).

2. Rapport building stage (Approximately 10 minutes)

A set of leading questions were prepared for the expert panel and used to guide the open discussion (Appendix 2).

3. In-depth discussion (Approximately 60 minutes)

The moderator focused on the main questions and prompted an in-depth discussion to reveal the thoughts and ideas of the expert panel.

4. Closure (Approximately 10 minutes)

The moderator provided a summary of the main outcomes of the discussion and thanked the participants.

2.5.3 Qualitative analysis

Qualitative analysis was performed according to the outcomes of the focus group (Figure 2.1). This involved:

1. Systematic gathering of information and data using a scientific approach to enhance the accessibility to medicines.
2. A comprehensive extraction of data on challenges with accessing medicines collected from MMA private drug list and CPSU GFL was carried out.

3. A systematic classification of data on challenges with accessing medicines collected from CPSU GFL was carried out.
4. Systematic categorisation of data collected from MMA private drug list according to the barriers to access medicines was established and then scored on a scale of 1 to 10 by the focus group.
5. Qualitative analysis of data collected from MMA private drug list and CPSU GFL by using Microsoft® Excel.
6. Explorative analysis of alternative routes was undertaken using Micromedex®, EMC and international regulatory authorities by the focus group.
7. Examples of real patients with access to medicine issues in the practice of the participants from the focus group.
8. Qualitative analysis of the determination of risk imposed by access issues on the patient medicines need.

2.6 Step-by-step guide

A step-by-step guide was developed to clearly indicate the best practices which are recommended to proactively detect, address, and mitigate access issues to the benefit of patients. Explorative analysis of alternative routes using Micromedex®, EMC and international regulatory authorities to investigate access issues, based on examples of real patients with access to medicine issues in the practice of the participants from the focus group was done.

2.6.1 Patients with access to medicine issues

Each patient with access to medicine issues in real practice from the experience of the participants in the focus group made of four (4) experts in their area of specialty was described in three sections namely, examples of real patients with access to medicine

issues, Consequences to accessibility to medicines, Ways to mitigate the risk posed by inaccessibility to medicines (Table 2.1). The rationale pertinent to the case was illustrated through Patients with access to medicine issues in real practice. The real case examples of patients with access to medicine issues method was adopted to conduct in-depth investigations of access issues in the everyday context in which they take place (Crowe et al, 2011).

The first section describes the background information of real patients with medicine issues which gave rise to the respective access issue. Consequences to accessibility to medicines were assessed in the second section of the real case example. In the third section, Ways to mitigate the risk posed by inaccessibility to medicines were recommended to rectify the access implications and enhance medicines access for the benefit of patients.

Table 2.1: Patients with access to medicine issues sections

Section	Section title
1	Examples of real patients with access to medicine issues
2	Consequences to accessibility to medicines
3	Ways to mitigate the risk posed by inaccessibility to medicines

2.7 The interview process

An electronic invitation was sent through email to the three (3) professionals to confirm their availability to participate in an interview to discuss the effect of Brexit on accessibility to medicine. The interview was led by the principal researcher who

introduced herself to put the interview participant at ease, explained the purpose of the interview and how long the interview will last. The researcher then asked a set of prepared questions (Appendix 2) by paying attention, listening actively, and avoiding interrogation.

Chapter: 3 Results

3.1 Overview

The result involved two stages:

1. Analysis of data collected from Central Procurement Supplies Unit and the Malta Medicines Authority, the outcomes of the focus group outlining the barriers of accessibility to medications and the risk imposed on the medicines needs of patients and generation of ideas for the purpose of formulating recommendations to enhance access to medicine. This is based on real life experiences from the participants of the focus group in their areas of expertise.

2. A description to enhance access to medicines by explorative analysis of alternative routes using Micromedex® and international regulatory authorities. Step-by-step guide (Figure 3.1) to address concerns by patients and healthcare professionals through a risk-based approach.

3.2 Step-by-step guide to deal with access issues

The research identified an innovative method to deal with issues regarding access to medicines.

Step 1: Gathering of information from Central Procurement Supplies Unit and the Malta Medicines Authority using Microsoft excel®.

Step 2: Analysis of data collected from Central Procurement Supplies Unit and the Malta Medicines Authority.

Step 3: A description of ways to enhance access to medicines by explorative analysis of alternative routes using international regulatory authorities.

Step 4: Example of patients with access issue and the risk posed by inaccessibility to medicines. These are cases experienced by the focus group participants in their areas of expertise and they proposed ways to mitigate the risk posed by inaccessibility to medicines.

Step 5: Assesses the implications imposed by the inaccessibility to medicines issues. This clearly describes the access issues resulting from the experience of the patients and process to support access to medicines.

Step 6: Ways to mitigate the risk posed by inaccessibility to medicines. The innovative scientific methods provide tailored recommendations to assist in added-value personalised care by supporting safe, effective, good quality and rational use of medicines.

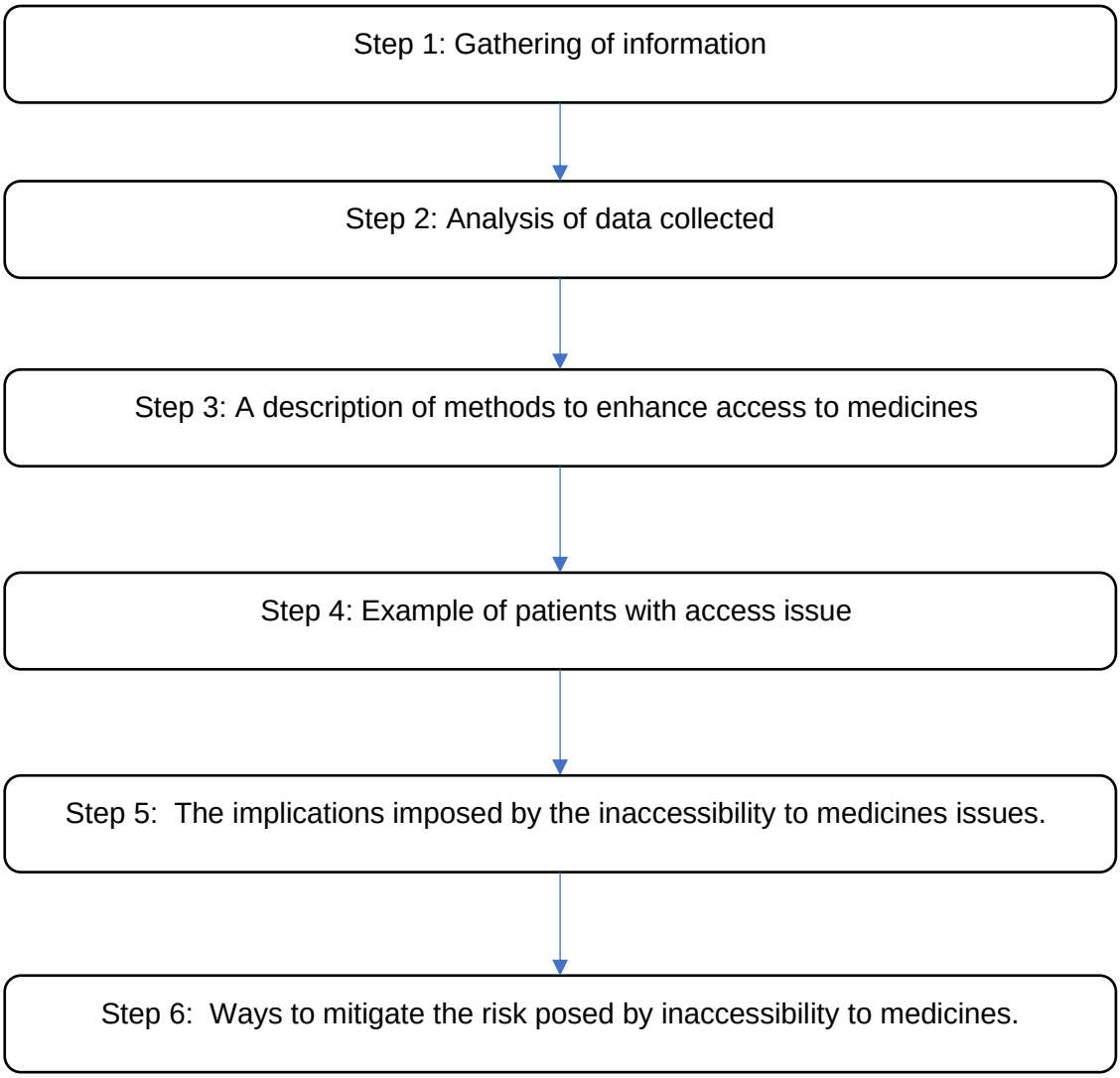

Figure 3.1 Schematic flow diagram of the risk-based scientific methods to address access issues

3.2.1 Results of analysis

Qualitative analysis of the list in the Government Formulary list (GFL) approved for use within the local NHS and the private list of medicines in MMA were carried out to examine challenges of accessibility to medications encountered in Malta. For the GFL one thousand four hundred and eighty (1480) medicines were listed and 47% (n=690) medicines were analysed. The scales were used as a basis for comparison for illustration purpose. In the GFL the next best option was considered by combining of two strengths

of the same medicine to make up for the desired dose – this was undertaken for 50% (n=345) medicines. Thirty three percent (n=230) were substituted by generics and 12% (n=80) were swapped with other alternative medicines from the same pharmacological class. Five percent (n=35) were exchanged with different dosage forms of the same medicines.

From the one thousand six hundred and fifty (1,650) medicines from the medicines authority list of medicines purchased privately in Malta 59% (n=780) medicines were analysed. Forty six percent (n=360) medicines were replaced with generics, twenty nine percent (n=225) were combined with different strengths of the same medicine to make up the required dose while 25% (n=195) were substituted with other alternatives.

3.2.1.1 The government formulary list (GFL)

Table 3.1 List of medicines within the government formulary list (GFL)

Best Option Inside Government Formulary List	Dosage Form	Dosage Strength	Disease Category/ Pharmacological Class	Next Best Option Outside Government Formulary List	Dosage Form	Dosage Strength	Brand Name	Scale of 1 to 10	References
Adenosine	Solution for Injection	6mg	class V antiarrhythmic agent/ Cardiovascular System	Adenosine	Injection	3mg/Lx 2	Adenocor	1	BNF, EMC
Amlodipine	Tablet	5mg	Calcium channel blockers Cardiovascular System	Nifedipine	Tablet	5mg	Adalat	10	Micromedex
Amlodipine	Tablet	10mg	Calcium channel blockers Cardiovascular system	Amlodipine	Tablet	5mg x 2	Amlodipine TEVA	1	BNF, EMC
Amitriptyline	Tablet	10mg	Tricyclic antidepressants	Nortriptyline	Tablet	10mg	Nortriptyline Kent	8	BNF, Micromedex
Atorvastatin	Tablet	10mg	HMG-CoA reductase inhibitors (statins) Cardiovascular system	Rosuvastatin	Tablet	10mg	Crestor	8	EMC, Micromedex
Bromazepam	Tablet	6mg	Long-acting benzodiazepine	Bromazepam	Tablet	3mg x 2	Lexotan	1	BNF, EMC
Gabapentin	Tablet	100mg	Anticonvulsants	Carbamazepine	Tablet	100mg	Tegretol	7	Micromedex
Valsartan	Tablet	80mg	Angiotensin II receptor antagonists (Cardiovascular)	Candesartan	Tablet	8mg	Atacand	2	BNF, EMC
Simvastatin	Tablet	20mg	HMG-CoA reductase inhibitors (statins)Cardiovascular system	Simvastatin	Tablet	10mg x 2	Zocor	1	BNF, EMC

After a review of certain medicines approved for use within the NHS and procured by CPSU, a selection of 10 medicines from the GFL was discussed by the focus group participants. They were then classified according to Disease Category/Pharmacological Class and the Next Best Option Outside the Government Formulary List was identified using a scale of 1 to 10 to find alternative medicines including generics and different dosage form (Table 3.1).

3.2.2 Private list of medicines in Malta medicine authority (MMA)

Table 3.2 List of medicines purchased through the private sector

Trade Names of Private Drugs Sold in Malta	Active Ingredient	Dosage Strength	Dosage Form	Pharmacological Class	Alternative Drugs	Alternative Generic Drugs	Dosage Form	Dosage Strengths	References
Amlodipine	Amlo TAD Besilat	10mg	Tablet	Cardiovascular	Amlodipine 5mg x 2	Amlodipine Teva	Tablet	5mg, 10mg	Google BNF, EMC
Atenomel	Atenolol	100mg	Tablet	Cardiovascular	Atenolol 50mg x 2	Atenolol Teva	Tablet	25mg, 50mg, 100mg	Google BNF, EMC
Lipitor	Atorvastatin	80mg	Tablet	Cardiovascular	Atorvastatin 40mg x2	Atorvastatin Accord	Tablet	10mg. 20mg, 40mg, 100mg	Google BNF, EMC
Cardura	Doxazosin	4mg	Tablet	Cardiovascular	Doxazosin 2mg x 2	Doxazosin Dexcel	Tablet	1mg, 2mg, 4mg	Google BNF, EMC
Amirol Fc	Amitriptyline	50mg	Tablet	Central Nervous system	Amitriptyline 25mg x 2	Amitriptyline Teva	Tablet	10mg, 25mg, 50mg	Google BNF, EMC
Lyrica	Pregabalin	300mg	capsule	Central Nervous system	Pregabalin 150mg x 2	Pregabalin Woockhart	Capsule	25mg, 50mg, 75mg, 100mg, 150mg, 300mg	Google BNF, EMC
Mirap Distabs	Mirtazapine	45mg	Tablet	Central Nervous system	Mirtazapine 30mg + 15mg	Mirtazapine Accord	Tablet	15mg, 30mg, 45mg	Google BNF, EMC
Klacid	Clarithromycin	250mg/ 5ml	Suspension	Anti- Infectives	Clarithromycin 125mg/5ml x 2	Clarithromycin Sandoz	Suspension	125mg/ 5ml 250mg/5ml	Google BNF, EMC
Augmentin	Amoxicillin / clavulanic acid	250mg/ 5ml	Suspension	Anti- Infectives	Amoxicillin/ Clavulanic acid	Co-Amoxiclav Mylan	Suspension	125mg/5ml 250mg/5ml	Google BNF, EMC
Ciprinol	Ciprofloxacin	500mg	Tablet	Anti- Infectives	Ciprofloxacin	Ciprofloxacin Dr Reddy's	Tablet	250mg, 500mg	Google BNF, EMC

After the review and systemic categorization of the private list of medicines in Malta Medicines authority the data gathered by the focus group and interview was done by first listing the private medicines from the MMA list according to disease category for example cardiovascular (CVS), central nervous system (CNS), anti-infective etc and then suggesting alternative drugs such as different brands and generics (Table 3.2).

3.3 Evaluation of results from focus group

The GFL list and the private list of Malta was evaluated and analysed to describe the cause of the issues leading to lack of access to medicines. Seven patient case examples from the experience of the experts of the focus group were identified and these were evaluated by assessing the implications of access issues on patient medicines needs and proposing patient-centred medicines interventions to mitigate the risk posed by inaccessibility to medicines.

3.3.1 Case example 1: Medicine is not accessible on the Government Formulary List

There is an existing problem and would even be made worse by the effect of Brexit since Malta is not able to purchase drugs directly from the UK anymore. The medicinal product may be sourced from other EU countries but since it is not available in English since it cannot be sourced from the UK after Brexit and relabelling expenses are not viable when considering the low demand in the Maltese market being a small island, example Visanne® (dienogest) tablets used in the treatment of endometrioses[37].

The Government Formulary List (GFL) includes a list of cost-effective medicines indicated for specific conditions which are supplied through the National Healthcare Service free of charge. Patients may be prescribed medicines which are not included in the GFL either due to lack of funding or the medicine may be too expensive as government are trying to save money and they are only available on the private market.

[37] Malta Medicines Authority. Summary of product characteristics – Visanne® tablets. 2015 [cited 2020 May 28] Available from: URL: http://www.medicinesauthority.gov.mt/medicine-details?id=84693

3.3.1.1 Consequences to accessibility to medicines

Lack of access of these medicines through the GFL results in financial burden on the patient who must pay the full price of the medicine to access the prescribed treatment. This can lead to increased stress level on the patients and even make their conditions worse. It may result in non-compliance and complications of the respective medical condition.

3.3.1.2 Ways to mitigate the risk posed by inaccessibility to medicines.

a. The drugs can be combined from a lower strength in the formulary to make up the higher dose. Example to give atenolol 100mg tablets, two (2) strengths of the 50mg atenolol can be combined to make up atenolol 100mg tablet.

b. The Government should consider sourcing medicines from other EU countries after Brexit.

c. Private arrangement could be made with the UK and other non-EU countries.

3.3.2 Case example 2: Shortages

Shortages could occur because of contamination of active pharmaceutical ingredients such as with nitrosamines. Several batches of valsartan-containing medicinal products from different manufactures were found to be produced from an active pharmaceutical ingredient contaminated with nitrosamine impurities. This produced a huge shortage of valsartan-containing medicines. Shortages could cause a reduction to access to medicine especially after Brexit.

3.3.2.1 Consequences to accessibility to medicines

The existence of nitrosamines in medicines caused a worldwide concern to patient safety. Access to these medicines was hindered due to drug recalls resulting in unavailability, lack of accessibility and inadequacy. Patient safety was compromised when patients on

valsartan-containing medicines stopped suddenly the intake of valsartan resulting in unanticipated cardiovascular complications such as stroke. This contaminated active pharmaceutical ingredient would even be worse after Brexit due to more bureaucracy and other negative consequences due to Brexit.

3.3.2.2 Ways to mitigate the risk posed by inaccessibility to medicines

a. Candesartan, an angiotensin receptor blocker should be provided instead of valsartan.
b. Patients should be educated on the implications of the contamination of medicines with nitrosamines.
c. other alternative cardiovascular medicines should be considered after Brexit.

3.3.3 Case example 3: Licencing of medicines

The marketing authorisation of a pharmaceutical product may be withdrawn by marketing authorisation holders or pharmaceutical companies due to marketing cessation, safety reasons and licencing of medicines issues which can be a consequence of the UK leaving the EU. Brexit has caused the discontinuation of several medicines which originate from the UK affecting the Maltese medicines supply chain in a negative manner. Examples of medicines which were discontinued include Zoely® (nomegestrol, estradiol) oral contraceptive pill, Zovirax® (aciclovir) eye ointment used in the treatment of herpes simplex keratitis[38] and Palexia® (tapentadol) tablets indicated in the management of severe chronic pain[39].

[38] Electronic medicines compendium (EMC). Summary of product characteristics - Zovirax® eye ointment. 2017 [cited 2020 May 28] Available from: URL: https://www.medicines.org.uk/emc/product/5469

[39]Electronic medicines compendium (EMC). Summary of product characteristics - Palexia® 100mg prolonged-release tablets. 2019 [cited 2020 May 28] Available from: URL: https://www.medicines.org.uk/emc/product/11410/smpc

3.3.3.1 Consequences to accessibility to medicines

The discontinuation of medicines results in lack of accessibility, availability and inadequacy causing several consequences on patient medicines needs including an increased risk of adverse effects related to the change in treatment. Awareness should be raised among patients to seek healthcare professional advice when changing medicines. Discontinuation of drugs would cause a bigger problem accessibility to medicines after Brexit.

3.3.3.2 Ways to mitigate the risk posed by inaccessibility to medicines

a. After Brexit, the Government of Malta should source medicines containing the same active pharmaceutical ingredient/s and formulation as the medicines which were discontinued.
b. Alternative medicines which were available on the market and may be prescribed for the respective condition should be used in place of the previous one. Example atenolol can be used in place propranolol.
c. Combination of two (2) strengths to make up a higher dose or drugs can be halved to make up a lower dose.
d. Alternative dosage forms could be used. Example switching paracetamol tablets to the capsules

3.3.4 Case example 4: High cost of medicines

This is an existing problem and would even be made worse by the effect of Brexit since Malta is not able to purchase drugs from the UK anymore thereby having to reply on more expensive alternatives. This could be due to bureaucracy, border control and lack of co-operation between the UK and the EU because of Brexit or because of pandemics leading to shortages of medicines and increased risk to public health. It could also be because of the price of medications in Malta which is more expensive than in nearby nations or

greater than the cost of other data collected from the Malta Competition and Consumer Affairs Authority. Examples: the price of Xarelto® (rivaroxaban) anticoagulant tablets, Bexsero® (Neisseria meningitidis group B) vaccine, and Lyrica® (pregabalin) tablets indicated in neuropathic pain, epilepsy, and generalised anxiety disorder[40]**.**

3.3.4.1 Consequences to accessibility to medicines

The high cost of medicine limiting access to medicines result in lack of affordability and accessibility causing patients to be left without the required medicines. Xarelto® was not accessible because of the high consumer price. Patients who cannot afford it used warfarin which has a cheaper price but requires compliance with regular international normalised ratio (INR) monitoring. If INR monitoring is missed, bleeding episodes may result. Lyrica® (pregabalin) tablets is an originator medicine which was expensive. Bexsero® vaccine was launched on the private market with a high price resulting in individuals not affording to purchase and vaccinate against the bacteria Neisseria meningitidis group B which can lead to deaths.

3.3.4.2 Ways to mitigate the risk posed by inaccessibility to medicines

a. To change to alternative generic medicines Example instead of Lyrica change to pregabalin Teva which is cheaper.

b. To obtain a fair price for the Maltese market relative to the price sold in other countries.

b. The possibility of sourcing the same medicine through parallel importations from countries where the price is cheaper than that sold in Malta such as Italy, Belgium, and Greece.

[40] Electronic medicines compendium (EMC). Summary of product characteristics – Lyrica® hard capsules. 2020 [cited 2020 May 28] Available from: URL: https://www.medicines.org.uk/emc/product/10303/smpc

3.3.5 Case example 5: Registration of medicines

Shortages could occur for a lot of reasons. Example medicine may not be marketed in Malta for several reasons:

a. The medicine is not registered, example Flixonase® (fluticasone) nasule drops used for the cure of nasal polyps and associated signs of nasal obstruction[41].

b. The medicinal product may be sourced but it is available in languages other than English since it cannot be sourced from the UK after Brexit and relabelling expenses are not viable when considering the low demand in the Maltese market being a small island, example Visanne® (dienogest) tablets used in the treatment of endometrioses[42].

3.3.5.1 Consequences to accessibility to medicines

The subsequent access consequences of medicines which are not marketed in Malta include limitations related to availability, accessibility, and adequacy. Availability is hindered since the medicine is not supplied by wholesale distributors and distributed to pharmacies resulting in lack of accessibility and inadequacy as patients cannot obtain the medicine at their convenience. These impacts would be felt more in Malta after Brexit. Flixonase® nasule drops and Visanne® tablets are indicated for specific conditions and there is no direct alternative medicine available on the Maltese market.

3.3.5.2 Ways to mitigate the risk posed by inaccessibility to medicines

a. The EMA and MHRA should collaborate and work together to avoid bureaucracy.
b. Malta and the UK could mutually recognise each other's products

[41] Electronic medicines compendium (EMC). Summary of product characteristics – Flixonase® nasule drops. 2019 [cited 2020 May 28] Available from: URL: https://www.medicines.org.uk/emc/product/5503/smpc

[42] Malta Medicines Authority. Summary of product characteristics – Visanne® tablets. 2015 [cited 2020 May 28] Available from: URL: http://www.medicinesauthority.gov.mt/medicine-details?id=84693

c. Consultants could request to supply the unlicensed medicines; Flixonase® nasule drops and Visanne® tablets on a named patient basis for specific patients.

3.3.6 Case example 6: Adverse effects related to a change of the medicinal product by manufacturer

The National Healthcare Service procures medicines according to the active pharmaceutical ingredient resulting in medicines which are supplied from different manufacturers this will become worse after Brexit since Malta can no longer purchase medicine from the UK thereby changing manufacturers. Changes from a proprietary medicinal product to a generic medicine may affect negatively patients stabilised on a specific medicine, often a proprietary product. Example: Patients who were stabilised on Concerta® (methylphenidate) prolonged release tablets indicated for attention-deficit/hyperactivity disorder[43] experienced adverse effects and uncontrolled symptoms when they were transferred to the generic methylphenidate medicine. This impact would be felt more after Brexit due to lack of co-operation between the UK.

3.3.6.1 Consequences to accessibility to medicines

Lack of acceptability and inadequacy were the implications of access caused by changes from the proprietary medicine to the generic medicine resulting in adverse effects and inconvenience to the patient. Brexit would add more to undesirable impacts associated to a swap of the pharmaceutical product by the producer because most medicines are procured from the UK before Brexit and after Brexit they have to be sourced from somewhere else. Attention-deficit/hyperactivity disorder patients are difficult to stabilise because of the characteristic of the disease. In this case, psychiatrists found it difficult to

[43] Malta Medicines Authority. Summary of product characteristics – Concerta® prolonged-release 18mg tablets. 2018 [cited 2020 May 28] Available from: URL: http://www.medicinesauthority.gov.mt/medicinedetails?id=8626

determine if the uncontrolled symptoms were due to a case of relapse or a change in the product manufacturer[44].

3.3.6.2 Ways to mitigate the risk posed by inaccessibility to medicines

a. The UK and the EU should co-operate on the awareness of adverse drug reaction reporting was raised to report adverse effects caused by medicines.
b. The EU and the UK should work together in clinical studies to take place to assess the uncontrolled symptoms being experienced by the generic medicine as compared to the proprietary medicinal product.
c. Patient's that are stabilised on Concerta® should remain on the proprietary medicine while new patients should be started on the generic medicine**.**

3.3.7 Case 7: Disruption of medicine supply

The UK ban on export of medicines would cause a disruption on medicine supply to patients. Disruption may result due to manufacturing issues or bureaucracy, border control because of Brexit or because of pandemics leading to shortages of medicines and increased risk to public health. Example: Aciclovir is on the UK ban list which is an agent used against viral infections. Aiciclovir is predominantly used for the indication of herpes simplex virus infections, chickenpox, and shingles. Further indications are for the avoidance of cytomegalovirus infections after transplantation and serious problems of Epstein-Barr virus infection.

3.3.7.1 Consequences to accessibility to medicines

The UK ban on export of medicines as a result of Brexit would cause a disruption to medicine supply and negatively affect medicine availability, accessibility and adequacy

[44] Malta Medicines Authority. Summary of product characteristics – Concerta® prolonged-release 18mg tablets. 2018 [cited 2020 May 28] Available from: URL: http://www.medicinesauthority.gov.mt/medicinedetails?id=

imposing critical risk on patient medicines needs. Example in the event of shortage of acyclovir this could lead to unnecessary inconveniences to patients and can result to progression of disease, avoidable hospitalisation and even death.

3.3.7.2 Ways to mitigate the risk posed by inaccessibility to medicines

Famciclovir can be given in place of aciclovir

3.3.8 Evaluation of results from interviews with the experts in MMA

Problems of lack of real time intelligence: This would affect accessibility to medicines especially after Brexit. Increase in demand in products registered in the UK because of marketing withdrawal/discontinuation due to Brexit which wholesalers are not prepared for because it is unprecedented. Example enalapril 5mg and 10mg tablets and timolol eye drops 0.025mg and 0.05mg are also out of stock. It is only found out when agents are contacted that the product is pending withdrawal, but it would still look registered. Products could be pending without withdrawal for as long as a month. Having a legal framework that must inform the MIAU about pending withdrawals or medicines not being available in the Maltese market before they are withdrawn would be helpful to mitigate medicine accessibility after Brexit. By checking the availability of a product if there is enough stock to cover the increase in demand due to the withdrawal of a product because of Brexit. Many companies stockpiled to cover a year due to Brexit it would be good to know the plans of the companies after the products that were stock pilled finishes after Brexit. If they would have an Irish pack or if they are considering replacing them with a new product from other EU member state. These may help in gathering of intelligence. Presently, companies are not legally obliged to report to MMA.

3.3.8.1 Evaluation of results from interviews with the managing director of CPSU

Because of the dependant of Malta on the UK market due to language barrier Brexit has a big impact on accessibility to medicine in Malta. But Malta still largely depends on the UK for its medicine supplies due to the legislation which requires packaging of medicines to be in English language and English language packs across the EU are only produced in few countries mainly the UK and Ireland. But there are accessibility problems with Ireland mainly because there is no good transport connection between Malta and Ireland. Flights from Malta to Ireland only operates once or twice a week whereas flights from Malta to the UK operates one or 2 flights per day. The logistics of purchasing from other EU countries are also very difficult due language barriers and registration. There are also registration issues such as with MMA which requires that if another product is locally registered medicines should be sourced from that company but unfortunately not all companies registered with MMA supplies the Maltese market therefore reliance is still on the previous suppliers most of which are from the UK. Due to Brexit patients might go without treatment because of regulatory issues, lengthy registration processes, relabelling and translations not just because of the issues of availability of stocks. The main medicine shortages are the injectables because of the difficulties in transporting them, especially the refrigerated items.

Medicine shortages resulted from the export ban even within which the EC had to intervene to reduce, countries were stockpiling for their own needs. Materials are not supplied. Malta stockpiled because of Brexit and COVID to help in a short while however the stocks are finishing and there is accessibility problems and problems with sourcing. There is a problem with the article 126a.

3.3.9 Result from GFL and private list

This study looked at the existing private list of drugs sold in Malta and the government formulary list (GFL) it was discovered that there is a problem with accessibility to medicine;

3.3.9.1 Brexit effect on medicine access

The United Kingdom (UK) departure from the European Union (EU) is perhaps the ultimate difficulty that the UK and the EU has yet encountered (Nick et al, 2017). The UK's leaving the European Union (EU) and the EU's only trading place might have severe consequences for patients' availability to treatments and therapeutic terms.

3.3.9.2 UK ban on export of medicines

The British administration declared a sanction on certain medicine exportations to safeguard the NHS patients' availability to medications. These bans occurred after a study of community pharmacists observed scarcities of a lot of most important forms of medications. The leadership controls will prevent exporters trading certain medications intended for people that are sick in the UK for a greater cost in a different nation, probably resulting or aggravating distribution crises. The government argued that the threat of the UK exiting the European Union with no a departure treaty in order is not the basis for the latest strategy, as scarcities do arise from time to time in the medication trading places. Although that is undoubtedly the scenery to the latest exportation injunction, as governments resolve action is required to safeguard current distribution[45].

3.3.9.3 Licensing and registration of Medicines

[45] British Broadcasting Corporation BBC Drug exports restricted 'to protect NHS patients'. 2019; [cited 2021 Mar 26] Available from: URL:https://www.bbc.com/news/health-49907056.

The guidelines and procedures around the registration and licensing of pharmaceutical goods are quite complex and there is a set of rules which apply across all EU countries which are difficult or at least have different effects on different countries depending on so many factors one being the size of a country, and this affects Malta because Malta is a very small country. Ideally all drugs should get a Marketing authorization (MA) which is a very long and lengthy and vigorous process, it involves a lot of fees and expenses. MA application is a lengthy process which given the size of the island and the size of the market does not encourage the big companies to invest because of profitability issues for example Roche withdrew a lot of their MA because of profitability issues at a certain point. Importers must register their products in Malta or else they would have to convince the parent company to get a MA in Malta which is not easy.

If the medicine had an MA in the UK before Brexit the MA is no longer valid in Malta because the UK is no longer an EU country. They would have to reapply. For example, if Scotland goes out of the EU and reapply as a dividual nation, they will need to go through the process again even though they were a member of the EU as part of the UK for so many years. And it would involve not only the upfront expenses but also issues such as pharmacovigilance and so many other expenses for the company which they would have to set up locally the process cost tens of thousands of euros. Given the size of Malta that would create an obstacle.

The European Medicines Agency (EMA) is accountable for the systematic assessment of centralized marketing authorisation applications (MAA). As soon as it is approved by the European Commission, the centralised marketing authorisation is acceptable in all European Union (EU) Member States, Iceland, Norway, and Liechtenstein. Drugs should

get registered quickly so that they are available in the pharmacy and eventually to the patients[46].

Marketing authorizations approved by the integrated process permits the marketing-authorization holder to trade the medication and make it accessible to patients and health care specialists all over the EU centred on one marketing authorization. For importers to register with EMA they must do the central marketing authorization with the EMA. The EMA would prefer big British pharmaceutical companies to register all their drugs in the EU through the MMA mechanism, but it is a very long process usually taking up to two to three years. And it entails having all the dossier translated in all the official languages of the EU. This involves time, expertise, and expense.

A lot of products do not have an MAA because most companies would prefer to register their products in individual countries rather than just get MAA that would make it available to all the EU countries, because it is a very time consuming and complex process in most cases for example the COVID-19 vaccine was authorized by the EMA in spite of all the pressures it still took them a whole month and this was a special conditional authorization.

[46] Politico.The policy headaches the EU-UK Brexit deal didn't solve. 2021 [cited 2020 Jun 26] Available from: URL: https://www.politico.eu/article/outstanding-uk-eu-brexit-headaches-trade-customs-health-care-travel/

3.3.9.4 Lack of cooperation in the regulation of medicines between the EU and the UK post Brexit

The absence of collaboration in the control of medications between the EU and the UK after Brexit is a very big problem. This has resulted in the disruption in trade, inaccessibility to medicines (Fahy et at, 2017). Now that the UK has withdrawn from the EU and most of Malta's medicines are registered and comes from the UK. The absence of partnership in the control of medications amongst the EU will be difficult to address because it requires co-operation between other countries. Brexit agreement incorporates a treaty on reciprocal acknowledgement of excellent production routine reviews. The UK has independently decided to receive batch assessment of medications completed in the EU, but the EU has not reciprocated in the same manner. In the UK Medicines and Healthcare products Regulatory Agency (MHRA) is currently in control of medications authorisations, but it is uncertain what association, if any, the MHRA will impact on the European Medicines Agency.

3.3.9.5 Drug shortages

In the private practice, sometimes the agents in Malta have shortages because they do not have enough medicine and they run out of stock due to worldwide shortages. This happened some time ago with budesonide Turbohaler® there was a worldwide shortage and Malta was among the first country to be hit. Sometimes because some drugs are not popular or used as much as possible the agents and the pharmacy end up not stocking enough supply.

Another problem is that patients that are transferred from Mater Dei Hospital (MDH) to Karin Grech and they have medications which Karin Grech do not have available and no means to get urgent supply. In the past they used to phone the ward to ask them to send

an amount over with the patient. Now with the new system at MDH, where they have a robotic system, the ward does not physically have the stock, so the ward does not have any medication coming with the patient. There was a problem with MDH not sending the patients with medicines. This problem with access can be very difficult to resolve, and the patient may end up missing some doses of the medication because stocks are gotten from CPSU directly not through MDH. Karin Grech is billed by CPSU. Example a patient had a prescription of demeclocycline that was not in stock. A pharmacist on shift in MDH supplied the medication.

A countries budget would affect shortages. Cost containment is the main emphasis of a lot of strategy initiators, and the ability to profit possibly will always be superior to the incomes accessible. Nevertheless, patients ought to have certain independence in choosing what they consider will improve their wellbeing, or what their needs that are not met are, particularly regarding accessibility to medicines (Asadi-Lari, et al, 2003). Producers might have short term problems either by their plants being down or not getting the raw materials to make the medicines. Cross-border problems like drugs being stuck in customs or duties or if there are any short-term problems like batches of medicines suddenly becoming contaminated.

3.3.9.6 Falsified medicines

Falsified medicines have become a very big problem that threatens health and reduce access to medicine. They are counterfeit medications that are described as authentic, approved medications. Counterfeit medications could comprise of components of minimal value or in the incorrect amounts; be intentionally and falsely labelled in regard to their uniqueness or supplier; have got forged container, the incorrect components, or small amounts of the effective items. Misrepresented medications do not go through with

the normal assessment of value, security, and effectiveness, which is mandatory for the European Union (EU) authorisation processes and for the reason of this they can be a risk to the public wellbeing (Rebiere et al, 2017).

To optimize access to medicine politicians, patient groups, pharmaceutical agents, EMA MHRA in the UK and the EU must come together and reduce all the bureaucracy to achieve the same goal for something as important as health otherwise both Malta and the UK would have problems.

3.3.9.7 Problems with drugs in GFL

There is a problem with first line drugs not being approved on the GFL due to the process of how drugs are approved. Clinical pathways are first set out by the clinicians for a specific disease for example inflammatory bowel disease (IBD) then there is recommendation for clinical pathways to go to the GFLAC (Government Formulary List Advisory Committee) which has pharmacist to review the evidence and make sure that they are signed. Typically, valid, and then the GFLAC makes a recommendation to the Advisory Health Care Benefits Committee (AHCBC) within the ministry of health according to priority and available funds. For example, with IBD even if there are other biologics approved and procured for the condition, vedolizumab is being approved through the exceptional medicine treatment policy.

Drugs are considered in the GFL according to priority. For instance, Oncology is a huge priority; Hepatitis C is priority there was one occasion where either because the government dealt with the drug company itself, but procurement was quite efficient and rapid. Otherwise, the whole process is quite a lengthy one and it involves so many stake holders. There is the obstacle of funding especially when dealing with these newer expensive medicines. Cost is the major determinant since on the one hand to drive down

cost there must be competition, but a level field competition is difficult to create when you have all these regulatory restrictions which are meant to safeguard patient safety. There is a bit of conflict in the sense that the more secure your patient safety features are the higher the cost tends to go. The more regulation you have the higher the cost. Any government and certainly the Maltese government is very much into keeping those cost down because the demand for medicines is ever expanding. There is quite a very difficult balance playing out between ensuring patient safety and high-quality of medicines and making sure that high quality drugs are available at a cheap accessible price both on the private market and the GFL.

3.3.9.8 Patients' perspective

Patients think that generics are better than branded products. Or if they get used to a specific generic and the trademark of the new drug is not the same, they think that it is not working for them. For those patients it is better to get authorisation for the type of drug to which the patient feels comfortable with. Some patients are established and well controlled on certain medications. Sometimes shortages can be false in the sense that the system in Malta still allows many medicines to get to the patient resulting in a lot of false shortages. Patients come with a lot of drugs which they have had at home in large quantities and these drugs may have been out of stock. The system does not have a good idea of the stocks that patients have at home, hence the system needs an improvement. Patients are under the false impression that if they do not take their monthly due medicines, they will be taken off them. Take asthma for example a lot of patients say if they do not collect their salbutamol, that they hardly use they will not give them when they need it.

3.4 Review of results from interview

To optimise medicines after Brexit early notification of medicines withdrawal would be helpful. Introduction of a law that enables supplies disruptions or pending withdrawals to be reported because pending withdrawals are showing as active because of none reporting in the system. Alternative products should be used to replace medicines that are in shortage example Shortages of ranitidine due to worldwide shortages because of recall for safety reasons was replaced with famotidine. Products should be sourced from other European countries that are registered in their data base. International companies and manufacturers/suppliers were contacted to see if they can supply the Maltese local market and the information retrieved was forwarded to the local suppliers. The pharmaceutical companies have been encouraged to register products in Malta or to make Malta a concerned member state in products that have already been registered. Example the 126A authorisation used in public health emergencies to increase accessibility for instance the COVID vaccine. Enalapril has a pending 126A application that hopefully would be on the market soon. Because there was no intelligence received before enalapril went out of stock plans were not made to mitigate the problem but as soon as it was known MMA sourced for agents that were willing to supply the product and three (3) local suppliers have been found that would get it from Ireland using the FMD and also from Cyprus and Greece and the wholesaler has to relabel the pack to either English or Maltese and attach a patient information leaflet (PIL) as a requirement for registration. New applications for registration to replace drugs from the UK are on the rise and this is helping the private market to counteract shortages due to Brexit.

CPSU together with MMA and other stakeholders such as the EU, collaborated and started shifting supplies of medicines from the UK to other European countries because of the dependency of Malta to purchase medicines from the UK reduced from

approximately 85% to about 60% to 65%. Effects to reduce dependency on the UK has been difficult and has been escalated to the EU through the Malta representatives in the EC and trying to get a balance by using waivers until Malta is able to reduce its dependence on the UK to a reasonable level. Setting up relabelling, local registration and trying to source from other non-English language speaking countries and then change the pack and translations however it is time consuming. The legislation to limit packaging to English language should be changed to accept other packs as with other sectors like food using Italian language because most Maltese understand Italian language and therefore there would not be a relabelling issue. Products that are registered in other EU country does not need to go through the whole registration process in Malta. There should be comprehensive legislation for the use of article 126A.

The fact that Malta is a small country few companies are willing to invest in registration, time, and money when they can make better profit in bigger countries. Therefore, if a product is registered in another EU country there should be free trading across the EU to enable small countries like Malta to benefit from such products. It should not be registered in Malta again. The current legal framework is not effective therefore there should be modifications to include sourcing from the UK where there are accessibility problems still going on without getting alternative treatments to avoid patients being left without treatment. This is an ongoing negotiating process putting patients first as patients cannot remain without treatment.

Chapter 4: Discussion

4.1 Suggestion to enhance access to medicine after Brexit

The solution to Brexit and the UK bans on export of medicines is to explore other alternatives such as generics and combination of 2 strengths to make up the required dose and importing from other EU countries. The scales from table 3.1 from the government formulary list (GFL) approved for use within the local NHS were used as a basis for analogy for illustration purpose as tools to test this methodology. Other Pathways can be found after Brexit for example through a third pathway. Wholesaler who can sell medicines to third countries and then send to Malta. Maltese authorities such as the CPSU can have private contracts with other nations that are not in the EU for instance America and Japan. Alternative to British medicines within the EU that can replace what was provided from the UK. Importers must seek medicines which are either registered in other EU countries so that they can utilize mutual recognition procedures.

There are regulations for example there is article 20 where if there is an emergency for example the COVID-19 pandemic all the article 126A can be waivered. if there is an exception where there is a public health need but very often, they are unclear, and it is up to the individual countries to interpret them and there can be objections from the European medicine's authority.

There are considerable number of drugs produced in the EU excluding the UK, but many local drug importers do not feel comfortable although many drugs come from Italy, Germany, Spain and even Portugal. Some effort can be made to source alternatives from EU countries even though the same medicines may not have the same combination of the same medicine. It would be better to get drugs that patients perceive that is working for them into the formulary. Then once they in the formulary having a consistent supply of the same medicine to which the patient has become used to. Medicine for patients that are

established and well controlled on certain medications should be put under a named patient basis in exceptional circumstances.

Education in terms of patient's perspective. The system needs an improvement in monitoring the stocks that patients have at home. To avoid shortages and save money patients should bring back the empty inhaler and the empty cannisters of inhalers should be collected and replaced with another one. This can be done in a hygienic way as in the case of alcohol bottles.

When patients are admitted to hospital relatives should be advised to bring their medications especially high-cost medication like erythropoietin. The politicians in the UK and EU should limit bureaucracy and team up with patient groups, pharmaceutical agents and EMA. They all must come together and decrease bureaucracy.

Malta should team up with the Irish more since this can overcome the language barrier. Improve or at least facilitate the procurement of medicines, the agents, and importers should come together and source for alternative sources for medicines at cheaper prices across the EU. It was easier for the agents because they were more familiar with the UK suppliers, but they should start working with other EU countries now that the UK is no longer in the EU.

The measures used to get medicines from non-EU countries like India could be used for the UK as well. The wholesalers should consider having centres or hubs both within the UK and EU countries to enhance drug supply. There is a lot of stock piling. Agents in Malta have stocked up enough medicines but once it starts to expire there would be challenges. Therefore, careful planning is necessary to mitigate the problem.

Conditional marketing authorization (CMA) in the European Union (EU) is an initial entry route for medications that exhibit efficient beneficial outcomes, but for which

thorough information are not presented. EMA needs to strike a balance among suitable accessibility to innovative and essential medications and a request for broad information on the advantages and threats of these medicine (Eichler et al, 2008).

The Falsified Medicine Directive (FMD) is the regulation agreed by the European Union Parliament, the goals are to intensify the safety of the trading and distribution of medications all over Europe it safeguards patients and avoids counterfeit Medications from going into the authorised distribution chain and getting to patients. FMD presents standardised security and improves monitoring procedures all over the EU by utilising latest protection methods. These measures are categorised into four major foundations:

a. Serialisation FMD entails that all components of trade boxes of prescription medications should have a security element containing a Datrix Matrix code and person legible information and must not obstruct the views to prove that they are genuine.
b. Intensifies conditions for the assessment of the inspection of manufacturers of active products and tougher rules on import of active pharmaceutical ingredients.
c. The responsibility for producers and suppliers to inform of any concern a counterfeit medication.
d. A compulsory badge that must be put on the internet site of legitimately functioning internet pharmacies with a connection to central EU repository. Source: Adapted from Rebiere H et al, 2017.

The non-existence collaboration in the control and licencing of medications between the EU and the UK after Brexit has proven to be more difficult to address because it requires co-operation between other countries. However, Partnership, consultation, collaboration

between the health system and pharmaceutical industry is important to avoid and control medicines accessibility challenges.

The disruption on the current distribution chains triggered by deviations to the UK monitoring agenda because of Brexit, shall have a very substantial undesirable effect on access to medicine (Song, 2016). However, there are ways to reduce this impact by stockpiling up to six months and change in registration, as well as sourcing medicines from other European countries which is already ongoing following action by the CPSU inside the Ministry for Health in cooperative care model with the businesses in Malta, the reliance on UK procurement of pharmaceutical supplies was dropped from 85% to about 65%[1].The EU medications monitoring network intentions is to minimize the effect of medication scarcities on sick persons by; collaborating with pharmaceutical businesses to unravel production and supply problems; allocating data with global associates about substitute means of distribution; looking for involvement from patients and healthcare experts on the effect of medication scarcities, to assist in making of decisions; taking actions to permit substitute medications or dealers to be used (Ahmadiani et al, 2016). Companies wanting to supply drugs in EU countries would have to relocate to the EU from the UK and this would benefit EU countries as this will bring in more companies and businesses and subsequently increase supply and improve access to medicine in Malta.

4.2 Strengths and limitations of the research

Bradshaw (1972) has proved how various perceptions on need can be conveyed. Each view provides valuable data to the treatment administrator or strategy creator which contributes to the extent and scope of knowledge of need, but no awareness of need is adequate alone and therefore the structure can be a valuable instrument for setting up

suitable facilities. Felt need illustrates what individuals say they need and is crucial since it is about listening to the opinions of people themselves (Heine et al, 1999). On the other hand, establishing treatment or financing outcomes on felt needs by itself is vague because people could be creating suggestions from a restricted understanding on the basis that whenever they have a slight point of view on health (Epstein, 2004). People could convey needs in phrases of potential outcomes; they may think that the probable outcomes are constrained to the facilities that are currently obtainable (Doyal and Gough 1991). Expressed need is the want conveyed by people's usage of facilities, for instance the period of stay for accessible facilities. Expressed needs merely take into consideration the current facilities and does not permit people to convey the desire for potential initial facility or strategy modifications. Normative need is the desire defined by specialists centred on exploration and expert views (Talbot and Verrinder 2005). The restrictions of simply employing normative need as a foundation for developing is the patriarchal position that specialists are continuously accurate, and they understand everything that ultimate for the patient's medicine needs. This standpoint overlooks to take justification of the various desires of certain consumer categories, the individual beliefs of the specialists, and the advancing ways of health care facilities. Comparative need is the desire measured by evaluating the existing facilities amongst various sites. Comparative need can be important to put forward a reason for supplementary supplies; nevertheless, the belief is that the service needs amongst regions are the similar (Talbot et al, 2008). While the concept of need as described by Bradshaw may be outdated, it has been found helpful to use the four steps described as fundamental basis to apply in the context of meeting patient medicines needs (Muscat, 2020).

This research applies hypothetical notions to actual practice by considering several real patients with access problems where knowledge was employed as a best practice to

propose interventions to enhance access to medicines. The research was conducted within a theoretical method that recognises attributes of health especially access to medicine.

In addition to other investigative and explorative areas of meeting the requirements of quality, safety and efficacy which are the pillars of any accessibility situation. An analysis of the findings of this research point to the need of applying a scientific methodology to the justification of the procedures applied in meeting the medicines needs of patients especially in situations like Brexit and COVID 19 that were unexpected.

A limitation of this research was that the focus group was suitably chosen and included a team of four experts. Inclusion of a larger number of experts may have resulted in more robust discussions and recommendations to enhance access to medicine. The Findings of this research were not generalised since the selection process was not well-designed and the models were not the characteristics of the study populace. The data were relatively difficult to analyse they do not fit neatly in standard categories. Surveys targeted at consumers and healthcare professionals to detect and measure the opinion of people in accessing medicines and healthcare services were not explored because of the lack of adequate information since it is a new topic. Data collection was time consuming because the study did not measure the quantitative analysis of access problems since it is a grey area data where limited.

The research developed an innovative scientific framework to proactively address access issues. This research provides relevance in adapting regulation in a patient-oriented manner while keeping within the legislation requirements. This has been exemplified through the patient's personal experiences which were resolved with the best practical methods keeping the patient at the centre of all activities. Considering that the three pillars for regulatory sciences are quality, safety and efficacy, these pillars can only be optimally

met if the patient is kept in the centre of all processes. This research endeavoured to put the patient in the centre of a regulatory body considering the accessibility to medicines as a principal purpose of the mission of the Malta medicine authority.

As various modifications and circumstances impacts the pharmaceutical and medical sectors, access continues to be a complex, multidimensional challenge which may lead to adverse consequences on the patient health outcomes after Brexit. While disruption can negatively affect access to medicines such as the contamination of active pharmaceutical ingredients with genotoxic impurities, and the coronavirus pandemic. Partnership, consultation, collaboration between the health system, pharmaceutical industry, Patient groups, the UK and EU is important to avoid and control medicines accessibility challenges through informed decision-making and develop opportunities to safeguard patient medicines needs and wellbeing after Brexit. It should be noted that while major events can have widespread risk, notwithstanding the level of risk are deemed significant to proceed with interventions in a personalised-patient approach to guarantee that the ‘correct patient obtains the correct medicine at the correct time, in the correct dose and through the correct route (Grissinger, 2010; Macdonald, 2010; Muscat, 2020). The innovative scientific framework was formulated in such a way to proceed in line with the policy of the Malta Medicines Authority in the ration for establishing as a fundamental principle to move from regulatory affairs to regulatory sciences (Muscat, 2020).

4.3 Recommendations

Further research should focus on to carry out additional studies to quantitatively measure the enhanced patient access to medicines and quality of life because of the implementation of the risk-based approach to evaluate accessibility to medicines issues and the effect of unprecedented occurrences like Brexit and the novel corona virus (COVID 19) contagion. It is recommended to implement the medicines risk-based approach as a best practice across other pharmaceutical services including the CPSU and MMA quality management system to assess and take timely actions to resolve access issues for the benefit of patients. Once the innovative scientific framework is implemented, it is proposed to perform a comparative study to investigate the timeliness in which access issues were resolved.

As a result of the research, it is recommended to conduct surveys targeted at consumers and healthcare professionals to detect and measure the opinion of people in accessing medicines and healthcare services. It is suggested to arrange collaborative seminars directed to individuals, health care clients and health care experts to raise awareness on the patient-centred functions in addressing access issues and assisting in patient detail added value medicines interventions. It is proposed to extend the application of accessibility issues to innovative aspects of the regulatory sciences including medical devices, cannabis for medicinal use and veterinary medicines.

It is recommended to devise a framework to enhance access to medicines by explorative analysis of alternative routes using Micromedex® and international regulatory authorities.

4.4 Conclusions

This research recognised the significance of a proactive personalised-patient approach to bridge the gap between patients, the regulatory and healthcare systems to enhance access to medicines. Access to medicines has gotten more relevance internationally as a result of the continuing interruptions. Medications protects human beings and enhance health outcomes for as long as they are obtainable, inexpensive, accessible, adequate, acceptable, accurate, of assured safety, efficacy, quality and are used rationally.

An inventive method to identify, tackle and alleviate challenges to accessibility to medicines centred on explorative analysis of alternative routes involving international regulatory authorities would be recommended. A rational proactive strategy to enhance accessibility of medicines should be developed to meet patient needs. This provides a vital foundation for dynamic emergency planning so healthcare systems are prepared for circumstances that may affect access to health, from patient experience of need to benefiting from the use of medicines. Caution should be taken when devising structured accessibility frameworks to allow sufficient room for interventions related to personalised care.

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Appendix 1

The University of Malta Medicine and Surgery Faculty Research Ethics Committee ethical approval

L-Università ta' Malta

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Ref No: FRECMDS_2021_098

10 May 2021

Ms Doubara Jessica Zuofa
32 A
Triq Santa Venera
L-Imsida
MSD03
Malta

Dear Ms Zuofa,

With reference to your application submitted to the Faculty Research Ethics Committee in connection with your research entitled:

The Effect of Brexit On Accessibility to Medicine

The Faculty Research Ethics Committee is granting ethical approval for the above-mentioned application reviewed on 27 April 2021.

Yours sincerely,

Professor Pierre Mallia
Chairman
Faculty Research Ethics Committee

Appendix 2

Overall Research Question, Focus group questions and Interview questions

Overall Research Question

a. How can medicines be accessed safely after Brexit?

b. What are issues that affect access to medicines?

c. What legal framework can promote effective access to medicines after Brexit?

d. What alternative ways could be used to improve accessibility to medicines in terms of safety, efficacy, availability, affordability, accessibility, acceptability, and high quality?

Focus group questions

a. How can medicines be accessed safely after Brexit?

b. What are the obstacles to access medicines encountered in your practice?

c. What alternative ways could be used to improve accessibility to medicines?

d. What measures do you recommend optimizing access to medicines post Brexit?

e. What legal framework can promote effective access to medicines after Brexit?

f. What is responsible for shortage of medicines and what are the ways to combat these shortages?

g. On a scale of 1 to 10 what would be the next best option outside the GFL 1 being the closest alternative option with an example and 10 being the last resort again with an example?

h. From the given list presented how do you rank the possible alternative brands or generics per active ingredient?

Interview questions

a. What are the obstacles to access medicines encountered in your practice?

b. What therapeutic classes have drug shortages in your organisation due to Brexit?

c. What measures do you recommend optimizing access to medicines post Brexit?

d. What legal framework can promote effective access to medicines after Brexit?