DEVELOPMENT IN THE EUROPEAN UNION AND ACCESS TO MEDICINES

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ABSTRACT

The problem of reduced access to medicines is being increasingly felt throughout Europe including Malta. A country’s National Medicines Policy (NMP) must consider accessibility together with other factors such as affordability, regulation and rational use of medicinal products, financing, and supply and distribution systems. These areas can all be presented within a framework as exemplified by the World Health Organisation (WHO) framework which is the most effective in incorporating NMP components and objectives.\(^1\) (World Health Organisation, 2001) The Descriptive Logic Model (DLM) was used as an essential tool to collectively represent relevant framework areas focusing on the entry of a medicinal product in the Maltese market.\(^2,3\) Pharmaceutical policy is one of the basic elements of an efficient health service and provides guidance as to the standard of health and pharmaceutical service to be delivered. Pharmaceutical policies may portray an array of aspects within a given health care system. Policies are by their nature dynamic as they consider the past; strategically address current patient needs and project future challenges. Thus strategy and pharmaceutical policy form a dynamic scientific tool which attempts to maximise resources and to provide appropriate pharmaceutical care whilst being able to evolve and adapt to any changes. Throughout the years Europe has increased its collaboration among various stakeholders in order to address health care demands such as an increased need for innovative treatments.

Keywords: Access; Regulation; Policy Framework; Innovation; Health care systems.

INTRODUCTION

Access to medicines has become increasingly debated and controversial throughout the years with several national policy documents drafted one of the first was of the World Health Organisation (WHO) in 1977 which included a list of essential medicinal products - this was updated over subsequent years.\(^4\) At the time, the concept of providing guidance to counties regarding the selection of essential medicinal products was evolving and such a document contributed to this. By 2001, WHO had issued a publication addressing the development of national drug policies.\(^1\) This was followed in 2002 and 2003 by a series of policy perspectives concerning the selection of essential medicines, the development and execution of a national drug policy, effective regulation, and equitable access.\(^5,6\) These texts were complemented by a 2004 publication regarding priority medicinal products and existing therapeutic gaps in an enlarged European Union (EU), WHO introduced the concept of “value for money” and pharmaceutical innovation.\(^9\) Malta participated in such initiatives and took cognisance of the importance of drafting a national drug policy as a first step. Following expert assistance from WHO the Pharmaceutical Services within the Ministry of Health produced a document which outlined a NMP.\(^3,10\)

In parallel to WHO publications, the European Commission (EC) also released a series of reports identifying related issues within the European Union.\(^11\) The European Commission also set up a High Level Group on Innovation and Provision of Medicines (G10 medicines). The G10 group evaluated concerns within the pharmaceutical arena and in May 2002, identified fourteen key points.\(^12\) In 2005, in response to such recommendations, the EC established the Pharmaceutical Forum that analysed three major aspects: Information to Patients, Relative Effectiveness and Pricing and Reimbursement through respective working groups. It formulated recommendations whilst enabling the industry to thrive and ensuring maintenance of national health care systems with the aim of bringing together the EC, EU Member States (Member States), EU Parliament Representatives, and stakeholders.\(^13\)

Early in 2004 the European Medicines Agencies (EMA) initiated an exercise to establish and formulate a discussion report entitled, “The European Medicines Agency Road Map to 2010: Preparing the Ground for the Future” made publicly available in March 2005. This was formulated in the context of two key issues, an enlarged European Union and the challenges posed by an intricate regulatory framework. The main objectives included speedy access to safe, efficacious medicinal products, delivery of adequate information to patients, promotion of innovation and research, consideration of health issues, and strengthening collaboration between EMA and
national competent authorities (NCAs). In 2006, the European network for HTA (EunetHTA) project was initiated and launched in November 2008. The EunetHTA took on board and started to execute sustainable collaboration for Health Technology Assessment (HTA) in Europe. The network linked together representation from the Member States, regional agencies and non-profit organisations to improve sharing of knowledge whilst enhancing HTA procedures. The EunetHTA was formulated after recommendations from a High Level Group on Health Services and Medical Care. It was supported by the Directorate General of the EC on Health and Consumer Protection (DG SANCO). This initiative also aimed at enhancing active participation thereby yielding effective decision making at a national level. In 2007, the Heads of Medicines Agencies (HMA) set up a Task Force (TF) on the availability of medicinal products and the lack of access particularly in context of states with small and medium sized markets. In tandem, the Directorate General for Enterprise and Industry of the EC funded a report on the diversity and commonalities in pricing and reimbursement systems within the EU. The HMA drafted its strategic document (2011-2015) identifying the difficulties that would be faced over that period. This report was drafted in parallel with, and complimented the EMA road map (2010-2015). Simultaneously in 2010, the Belgian Presidency Conference on innovation and solidarity was held against the backdrop of the promotion of EU partnership amongst Member States on current health matters such as chronic diseases, cancer, and medicinal products. In March 2011, a report commissioned by the Directorate General for Internal Policies analysed medicinal product pricing differences across different Member States. Within this background in 2008, the High Level Pharmaceutical Forum put forward and recommended that each patient should have “equitable access”. These problems were being experienced in Malta at the time, in part due to its small market size but also for other reasons.

**RESULTS AND DISCUSSION**

**Registration of Medicinal Products**

Upon Malta’s European Union accession, in 2004, the introduction of a new system for the registration of medicinal products raised a number of aspects within the Maltese scenario. The adoption of the European legislation enhanced and guaranteed the quality, safety and efficacy of medicinal products that were placed on the market. The legislation offered manufacturing companies the opportunity to come into line with EU standards. The new regulatory environment was attractive to the industry, offered them protection and opened a window of opportunity for a number of generic manufacturing companies to set up base locally. This increased the number of production facilities as shown in table 1. Malta also began acting as a reference member state receiving its first application in December in 2007. During 2010, Malta starting acting as a Reference Member State for 17 decentralised procedures out of which 2 were concluded by 2010. Notwithstanding this, it was being increasingly felt that Malta as a small Member State, like others of similar size, was being left out of European procedures such as Mutual Recognition Procedure and Decentralised Procedure.

**Access and Availability of Medicinal Products**

Medicinal products imported into Malta prior to 2001 were required to possess a valid Certificate of Pharmaceutical Product (CPP). On the derogation list there were 1823 different active ingredients available and 7020 medicinal products (that were not all locally marketed), of which 5162 products were also authorised in European Union. Following EU accession, in May 2004, products’ packaging had to be in line with EU legislative requirements and registration cost were introduced. These, coupled with the small dimensions of the local market were straining accessibility at that time. The number of products decreased as portrayed by an analysis of the market in May 2006 as shown in Table 2. This issue was addressed in 2007 through the use of article 126a Directive 2001/83/EC (as amended by Directive 2004/27/EC) which was a means of filling ‘gaps’ in access to medicinal products. This, together with a reduction in fees successfully addressed the issue of reduced availability as depicted in Table 2. The local registration fees were subsidised by the Government.

The level of access to medicinal products generally improved throughout the years of study and especially from 2007 till present, as evidenced by the number of medicinal products available on the local market in table two. Notwithstanding this, shortages of specific medicines was evident in the study and up to date this is still creating problems both in the private and more so in the public local sectors. Medicinal product shortages and estimated time to be back in stock could be made available to health care professionals to improve utilisation of available stocks within the given time frame. Currently, the Pharmacy of Your Choice scheme, which is the process of dispensing medicines on the National Health Services

**Table 1. Manufacturing Companies Licensed in Malta**

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Manufacturing Companies</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>1 company</td>
</tr>
<tr>
<td>2003</td>
<td>9 companies</td>
</tr>
<tr>
<td>2006</td>
<td>11 companies</td>
</tr>
<tr>
<td>2011</td>
<td>24 companies</td>
</tr>
</tbody>
</table>

Figures given by Medicines Authority, Malta.
Scheme through private community pharmacies, utilises a similar system, where health care professionals are informed via email when a medicinal product is back in stock.

Table 2. The number of medicinal products marketed from December 2005 – December 2012

<table>
<thead>
<tr>
<th>Year</th>
<th>126a authorizations per year (and cumulative authorisations 2006 - 2012)</th>
<th>National Marketing Authorisations/ Provisional Marketing Authorisation</th>
<th>Mutual Recognition Procedure/ Decentralised Procedure</th>
<th>Collective number of authorised Medicinal products (excluding Centralised Procedure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>Not Applicable</td>
<td>2228</td>
<td>57</td>
<td>2288</td>
</tr>
<tr>
<td>2006</td>
<td>2</td>
<td>2401</td>
<td>158</td>
<td>2800</td>
</tr>
<tr>
<td>2007</td>
<td>295</td>
<td>1856</td>
<td>341</td>
<td>2151</td>
</tr>
<tr>
<td>2008</td>
<td>453 (751)</td>
<td>1651</td>
<td>294</td>
<td>2442</td>
</tr>
<tr>
<td>2009</td>
<td>256 (1806)</td>
<td>1671</td>
<td>454</td>
<td>3135</td>
</tr>
<tr>
<td>2010</td>
<td>297 (1304)</td>
<td>2173</td>
<td>141</td>
<td>3597</td>
</tr>
<tr>
<td>2011</td>
<td>250 (1554)</td>
<td>2140</td>
<td>220</td>
<td>3947</td>
</tr>
<tr>
<td>2012</td>
<td>285 (1839)</td>
<td>2151</td>
<td>283</td>
<td>4273</td>
</tr>
</tbody>
</table>

Table figures were obtained through Medicines Authority Annual Reports 2005, 2006, 2007, 2008, 2009, 2010, 2011, and 2012. (Collective total number of medicinal products including national procedures for Malta)

In relation to access and availability to medicinal products the 2005-2010 EMA roadmap emphasised the need for scientific evaluation in manufacture of new chemical entities, well-timed access to efficacious, safe and innovative treatment through efficient centralised procedures, pharmacovigilance and monitoring importance, and access to information. EMA recommended collaboration among regulatory authorities and adoption of legal provisions enabling timely access, safety and innovation.\(^{14}\) In its second formulated road map (2010-2015). EMA outlined, amongst various areas of focus, the need for improvement in access to medication and the importance of increasing safety and rational use of medicinal products.\(^{35}\)

In 2007, the TF on the availability of medicinal products was set up by the HMA. The HMA TF emphasised the problem of reduced availability with special reference to small and medium-sized national markets. The report examined availability issues relating to marketing authorisation processes and legislation. The dimension of a market was linked to the refusal of a marketing authorisation holder (MAH) to market a product. Parallel import and export and price diversity were seen as availability barriers. The TF discussed the pharmaceutical industry and its crucial role in product availability and this role was pronounced in small markets. The HMA recommended sharing of procedural knowledge on addressing availability concerns, increasing debate on availability of products among stakeholders, avoiding parallel import procedures to circumvent Directive 2001/83/EC, removal of cumbersome labelling bureaucracy, acceptance of multi-lingual language sources, creation of warning systems regarding the unavailability of specific medicinal products, use of article 126a, article 15, article 24, and article 81 Directive 2001/83/EC, and increasing joint collaboration among Member States on pricing and reimbursement.\(^{17}\) A report funded by the DG Enterprise and Industry stated that restriction of public expenditure was common among Member states but priority setting and processes capping expenses varied. Emphasis was made on the need for collaboration and sharing of knowledge on cost containment. The report discussed common aspects shared by Member States such as cost capping, enabling adequate access whilst providing compensation for innovation and the maintenance of pharmaceutical manufacturing.\(^{18}\) A Ministerial Conference on solidarity and innovation (September, 2010) debated EU policy and its relation to valuable, innovative products whilst ensuring access, promoting research, and defining and allocating value to innovation.\(^{36,37}\)

In 2011, the Directorate General for Internal Policies recommended a permanent and sustainable collaboration for information and experience sharing.\(^{32}\)

**Procurement and Supply of Medicinal Products**

The local introduction of the Pharmacy of Your Choice (POYC) scheme was intended to cut down patient waiting times at the pharmacy and enables Maltese patients to obtain reimbursed medicinal products supplied through public health services from their chosen, privately owned pharmacies. The scheme commenced in 2007 as a pilot phase. Prior to such a scheme patients would be given their entitled medication from Government Community Pharmacies at designated Health Centres in Malta. The scheme continued to expand throughout all of Malta and Gozo whilst considering innovative procurement, storage and distribution methods.\(^{30}\)

**Medicinal Product Pricing**

Following Malta’s accession into the European Union, pricing of medicinal product was debated and became a matter of public concern where such prices were perceived to be on the increase and no control mechanism was being utilised to curtail this. Thus an agreement was reached between the Government and concerned stakeholders within the public sector on a voluntary mechanism in 2006.\(^{39}\)

During 2007 a pricing comparison exercise was started by a Working Committee on the Pricing of Medicinal Products under the Consumer and Competition Division. Prices were considered in relation to EU average prices.\(^{40}\) Further discussions were held during 2010 and in July 2010, the Office for Fair Trading published a list with reduced prices. Another list of price reductions was published in April 2011. The mechanism for price reductions in the private sector remains voluntary and without any legal basis, yet a number of prices were reduced, increasing the affordability and consequently the access to medication.\(^{41,42,43,44}\) It was also being suggested that a reduction in prices could be achieved through changes made to the importation of medicinal products as well as having the government import essential medicinal products that would be unavailable.\(^{45}\)

Presently Malta does not regulate the prices of medicinal products for the private sector. As a small Member State is often faced with reduced levels of access to medicinal products and furthermore it is often difficult to utilise and adapt all legislative systems and provisions to be able to counteract such lack of access.\(^{17}\)

**Reimbursement of Medicinal Products**

In 2007, Legal Notice 165/2007 was drafted to update Legal Notice 399 of 2003 from transposition of Transparency Directive 89/105/EC and later amended to
Legal Notice 58/2009 to increase transparency. These three Legal Notices related to the government health services’ availability of medicinal products. Over the years the patient entitlement to reimbursed medicinal products was improved through addition of the list of conditions in the Social Security Act’s fifth Schedule and inclusion of new medicinal products available for reimbursement. In 2008 there were 1309 medicines on the Government Formulary List, in 2011, this increased to 1332 items and in 2012 there were 1336 medicinal products (Figures were obtained through the Department for Pharmaceutical Affairs within the Ministry of Health) available on the formulary. In March 2012 the Social Security Act Cap 318 Article 23 and the Fifth Schedule of the same Act were changed, and resulted in an increase in the number of conditions that fall under this Act, from a previous 38 conditions to 79. The Act’s updated conditions include:

- Cerebrovascular and peripheral vascular disease
- Psychiatric disorders including those occurring in childhood
- Mood disorders that are chronic
- Down’s Syndrome
- Type I and Type II Diabetes Mellitus

To aid in access to medicinal products, the prescriber criteria within the health services were changed and doctors (both private and National Health Services) could alter medicinal product doses for items marked as ‘protocol regulated’, ‘medical practitioner’ and ‘consultant’ on the government formulary for specific conditions (Hypertension, Diabetes Mellitus, Chronic Heart Failure, Asthma, Chronic Obstructive Pulmonary Disease, Chronic Mood Disorders, Chronic Neuritic Disorders, and hypercholesterolaemia treatment according to Schedule V condition). According to the 2012 budgetary speech approximately 100,000 Maltese citizens now have access to medicinal products that are completely reimbursed by the Government.

One of the High Level Pharmaceutical Forum final recommendations included the consideration of access to orphan medication and access in small national markets. The working group on Pricing and Reimbursement recommended that access to orphan medicinal products and to medicinal products in small markets required a careful approach whereby it suggested that EU Member States should ensure availability and supply of medicinal products whilst considering recommendations made by the HMA TF report. The forum urged all involved stakeholders to adopt the working group for Pricing and Reimbursement recommendations. Recommendations included early discussions on research and development, the sharing of information on scientific assessment and pricing and reimbursement logistics coupled with enhanced orphan disease consciousness. It was suggested that access occurs in a timely manner and includes innovative treatment whilst targeting all patients and following the EU Transparency Directive 89/105/EC. Member States were counseled to define innovation whilst considering compensation. National pricing and reimbursement policies had to recognise and display this. Pricing and reimbursement policies had to enable appropriate use of price control measures, coherent supply and demand procedures whilst having price regulation that applies to reimbursed products. This excluded the non-reimbursed or privately sold medicinal products. WHO had been discussing this issue (throughout the years) as well as the diversities among the pricing and reimbursement in different countries and their dependence on countries’ perspectives. There were inconsistencies among EU Member States. Market failures were leading to therapeutic gaps, and lack of innovation within certain disease categories both at European and global levels prompting WHO to urge Europe to address this.

In 2004, the European Council considered HTA collaboration among EU countries as promoting the sharing of knowledge and capacities. The EunetHTA project was initiated in 2006. The HTA International Network of Agencies housed forty six members by 2008. Member States such as Estonia, Malta, Luxembourg, Portugal, Slovakia and Slovenia could not possess such an agency as national expertise and resources were scarce. The importance of having an ongoing collaboration on HTA across Europe was increasingly being felt in order to avoid replication of efforts, making the best use out of the limited resources, and enhance HTA use. In the present study an isocratic reversed phase-high performance liquid chromatography (RP-HPLC) method was developed for checking the Quantity based quality in the formulated Diclofenac Sodium tablets. The linearity was calculated 0.999, which significant at the level p=0.1% error. The limit of detection and limit of quantification were calculated 0.03 and 0.09 µg/mL. The inter-day and intra-day average percentage recovery at three concentration levels were calculated 100.69 % with the coefficient variation percentage 2.240 (<10) and 0.8351 (<1.0). Hence, applied method validation was significant. Therefore this method is acceptable for checking the quantity based quality from formulated tablets.

CONCLUSION

Policy and similar social systems are often complex and difficult to define. The Descriptive Logic Model aids the descriptive evaluation by graphically portraying the various aspects of the case as well as being a systematic approach to data collection. When vast amounts of data are obtained, the Descriptive Logic Model displays the collection of such data in a structured and concise manner for easier data handling. Since a snapshot of the chosen time (2001-2010) was desired the Descriptive Logic Model served as an adequate research tool allowing comparison of snapshots at chosen years through longitudinal analysis. The model allows a way of studying the impact of new policies. It is often useful to use a Descriptive Logic Model for particular cases since it aids in evidencing improvement for that case whilst presenting ways of obtaining results for a study and enhancing the data collection.

Healthcare provision is evolving at European Level and health requirements should be targeted through innovative medication and EU policy and collaboration among all involved stakeholders that work jointly for public protection. The major difficulties encountered in EU policy includes access to innovative therapy for specific patient needs, whilst maintaining quality and ensuring equity, solidarity and cost containment. The role of policy has now shifted to target areas that are not being covered by legislation.

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