ACCESS OF RARE DISEASE PATIENTS TO TREATMENT WITH ORPHAN DRUGS
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INTRODUCTION

Healthcare systems in Europe have increasingly been confronted with numerous challenges such as population ageing associated with the rise of chronic diseases and multi-morbidity, rapid spreading of new (high-cost) health technologies, increasing citizens’ and patients’ expectations and, at the same time, a tightening of health budgets.

Over, particularly the last decade, pharmaceutical expenditure per capita has been rising. During the global financial crisis, the growth in health and pharmaceutical expenditure has slowed down and was negative in several European countries with particularly negative impact in some like Greece, Spain and Portugal. As of 2013, however, OECD data are demonstrating a rise again reaching pre-crisis levels in several European countries, mainly as a result of demographic changes in the EU, the emerging of new high-cost medicines and an increasing use of ‘personalised’ or ‘stratified’ or ‘genomic’ medicines.

An increasing number of research projects and companies are focusing on developing differentiated and specialised medicines targeted at smaller patient groups.

All this is good news, as it holds the promise of more effective and tailored, to the individuals’ needs to the patients’ specific needs therapies. However, most, if not all, of these new treatments are often extremely expensive and patients cannot benefit unless these become accessible and affordable to them.

The below information underlines the situation more comprehensively.

TRENDS IN PHARMACEUTICAL EXPENDITURE IN THE CONTEXT OF NEW MEDICINES

Pharmaceutical expenditure has risen rapidly in recent years, growing on average more than 3.5% per year between 2000 and 2009 among OECD countries. Overall, among OECD countries it averaged 18-19% of total health care expenditure in 2009, with similar averages across Europe. More recently, 2009-2013 saw a fall in pharmaceutical expenditure in some European countries as a result of the global financial and economic crisis - for example, through specific policy interventions as in Greece, Iceland and Portugal but in several others its growth remained constant. In 2011 average pharmaceutical expenditure per capita in OECD countries was US$ 483, and as a share of GDP it accounted for an average of 1.5%.

In the two years following 2009 average growth rates for pharmaceutical expenditure among OECD countries fell by 0.9%, with the reduction steepest in those countries hardest hit by the financial and economic crisis - for example, in Greece pharmaceutical spending per capita decreased by 10% in both 2010 and 2011. Estonia (-7.2%), Portugal (-5.9%), Iceland (-4.7%) and Ireland (-4.4%) also saw reductions in pharmaceutical expenditure between 2009 and 2011, while in France (-0.6%) and Germany (-0.7%) the drop was less steep. It is clear, however, that the crisis has forced countries to revisit their pharmaceutical expenditure and, in some cases, to rethink how to improve efficiency as well as focus more on appropriate use of medicines.
Expenditure on pharmaceuticals per capita and as a share of GDP, 2012 (or nearest year)

Source: OECD (17)

Access to medicines is a major policy objective which needs to be balanced with other policy objectives. In the EU, Member States (MSs) are committed to balancing their policies in order to achieve the partially conflicting policy objectives of:

i. Timely and equitable access to pharmaceuticals for all patients in the EU
ii. Control of pharmaceutical expenditure for MSs and
iii. Reward for valuable innovation within a competitive and dynamic market that also encourages Research and Development.
WHAT ACTIONS HAVE THE EU AND THE WORLD HEALTH ORGANISATION (WHO) TAKEN

During the last 12 years, Europe has developed (as shown in the table below) many activities and actions - several in collaboration with other relevant international, European and national bodies e.g., WHO and EMA) - on the very important question of access of citizens/patients to high-quality, safe, innovative/new drugs.

Study on enhanced cross-country coordination in the area of pharmaceutical product pricing, Final Report (European Commission)

MSs of the EU have all committed to the 2030 UN Sustainable Development Agenda and goals, with goal number 3 stating: ‘Ensuring healthy lives and promote well-being for all at all ages’ and thus profiles health as a desirable outcome in its own right. Importantly, however, health contributes to the achievement of other sustainable development goals, and is a reliable indicator of how well sustainable development is progressing in general.

Universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all by 2030 is also what the high level UN goals define (see table below). In addition, article of the EU Treaty’s commitment to the principle of well-being and to the fundamental European values of equity, solidarity and good quality in healthcare as well as the very Charter of Fundamental Rights and Charter of Patients’ Rights and Council Conclusions on common values and principles in EU health systems are contrary to sadly existing great in many cases inequities in access to essential quality treatments and medicines.
WHO Submission to the UN SG High Level Panel on Access to Medicines

☐ The High-Level Panel may wish to highlight the importance of the WHO Model List of Essential Medicines as a tool to advocate for access to priority medicines in all countries.

☐ The High-Level Panel may wish to consider calling for transparency of the patent status of all essential medicines worldwide, as this information is not presently easy to obtain. This would allow countries to assess whether they can procure generic copies, or produce them locally.

☐ The High-Level Panel may wish to consider calling for further expansion of the mandate of the Medicines Patent Pool to all disease areas, and for all patented essential medicines on the WHO Essential Medicines List to be licensed into the Pool.

Median availability of essential generic medicines in developing countries

<table>
<thead>
<tr>
<th>Public sector</th>
<th>Private sector</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-income countries</td>
<td>37.7 %</td>
</tr>
<tr>
<td>Middle-income countries</td>
<td>46 %</td>
</tr>
</tbody>
</table>

- The High-Level Panel may wish to call for more work to be done to assess which models provide an appropriate balance between affordability and maintaining incentives for investment, including into R&D.

The conclusion is that to achieve such goals for better health, safe and effective access to medicines for all is a prerequisite and sadly current pricing models today, as described below, DO NOT SUPPORT EQUITABLE ACCESS.
PRICING MODELS

**External Reference Pricing (ERP)** - A model practiced by most, if not most MS, which, although generating savings and room for shifting cost, it bears significant disadvantages for patient access particularly in poorer Member countries.

*Study on enhanced cross-country coordination in the area of pharmaceutical product pricing, Final Report (European Commission)*
Figure 4: Role of EPR in the price setting process

- **EPR is the sole trade criterion**
- **EPR is a supportive criterion**
- **Not applicable**

**DE**: EPR is provided for in law but not used in practice.

**DK**: EPR is used to set the price cap for new medicines in the hospital sector; in the out-patient sector the manufacturer can freely set the prices.

**IE**: EPR is used as a supportive policy to set prices for new single source on-patient medicines, and as a main criterion for realignment of existing prices. It is applied as a supportive policy for medicines with extraordinary higher prices, and for medicines with lower prices agreed between the manufacturer and the purchaser/payer.

**SE and UK (and in DK in the out-patient sector)**: other pricing policies are in place.

Source: GO FP, based on bi-annual surveys with competent authorities represented in the PPRI network and a survey as of spring 2015

*Study on enhanced cross-country coordination in the area of pharmaceutical product pricing. Final Report (European Commission)*
Study on enhanced cross-country coordination in the area of pharmaceutical product pricing, Final Report (European Commission)

Differential Pricing - alternative strategy by pharmaceutical industry and other stakeholders and is based on the price setting according to different economic situations between countries. Until today, it has been used by companies to optimise market access but as a political strategy driven by collaboration between MSs, has been less explored. A major barrier is clearly the existence of parallel trade which may lead to shortages and consequently reduced access.

More recently, attention has shifted towards the concept of value-based pricing i.e. price linked to health benefit. However, this raises the need to measure health outcomes and generally motivated by the desire to improve the quality of care and public health and foster greater transparency and accountability health systems. It is also proposed that value-based pricing may balance the short-term cost-effectiveness with long-term incentives for industry for develop added-value products. On the other hand, ‘value’ and ‘cost effectiveness’ are defined quite differently in the different countries and different factors are applied in their definition.

The combination of linking the (added) value of a drug for a patient while involving at the same time some degree of differentiation between countries may be a better further approach towards pricing and reimbursement and thus access to patients.
In this context, the HTA model grew and adopted by many countries.

Health Technology Assessment (HTA) is used to assess the relative effectiveness of a new medicine compared to existing ones, supporting decisions on pricing and reimbursement that are meant to be fair for patients and for society. In its broad form, HTA is meant to be “a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner, its aim is to inform the formulation of safe, effective, health policies that are patient focused and seek to achieve best value.

However, HTA as currently practiced tends to be a much less broad exercise, aiming to reach a decision quickly and prioritizing cost-effectiveness over other factors, such as the value itself, ethical and societal benefits. Moreover, different member states weight these factors differently.

The importance of incorporating the patient perspective in HTA is increasingly recognised, and the integration of quality of life factors in HTA is considered necessary in order to arrive at an accurate assessment of a medicine’s added value. But in practice, patient involvement in HTA is still very limited, and so far there is no agreement on the best method of involving patients.

Transparency of prices constitutes an issue which is of concern:

1. The actual cost of research and development is not known and hence there is lack of transparency on the pricing of medicines
2. There is no effective sharing of information on prices of and expenditure on medicinal products including innovative ones and the database including list prices (EURIPID EU-funded project) which although constitutes a great advancement, it does not include the actual prices – which are achieved as a result of negotiations with companies, which remain confidential.

If real prices could be shared, then MSs could drive prices down. Views however, on full transparency vary both on behalf of the pharmaceutical industry as well as between MSs.
NEW IDEAS AND CONCEPTS (under discussions)

Added Therapeutic Value (ATV) refers to the therapeutic advantage offered by a new medicine compared to existing ones. However, there is not yet a universally agreed definition of the concept and the current definition of the therapeutic value is related to patient-relevant endpoints, effectiveness, efficacy and safety of the medicine. The patient’s perspective is essential in the assessment of the therapeutic value to demonstrate its advantage. The patients’ view of what therapeutic benefit is almost certainly related to different priorities and different levels of acceptance of potential risks than those of medical professionals.

Another issue that may add concerns and difficulties in accessing therapeutic benefit is that enough data to support its added value may not be available at the time of marketing authorisations and only over time and through the collection of real-world data may be possible.

Adaptive pathways and early dialogue constitute new concepts that are being explored between MS, European Commission (through the setting up of an expert group in safe and timely access to Medicines for Patients-STAMP), EMA, the industry, the patients and other stakeholders.

As science advances, advanced therapies will require new ways of evaluation, as they target specific populations who require quick access to them.

ADAPT-SMART is a project exploring the scientific, practical, ethical and legal aspects of adaptive pathways while early dialogue can build on already existing examples of SEED and Mechanism of Co-ordinated Access to Orphan Medicinal Products (MoCa) initiatives.

Other existing activities to be further explored and integrated into a model

It is important to support and promote the development of the Medicines Adaptive Pathways to Patients (MAPPs) approach, in particular at the EMA (Scientific Advice and Adaptive Licensing), at the HTA level (Early Dialogue, adapted core value dossier and European common assessment report), but also with payers. “Only patients can legitimately determine how much risk or harm they are willing to accept for a given benefit.

Patients know better than anyone which trade-offs between the benefits and the risks/uncertainty are acceptable”. This is why the risk/benefit assessment at the CHMP needs to take into account the patients’ position in a context of higher uncertainties. This will help payers to take well-informed decisions.

Price negotiation and post marketing evidence

A mechanism based on the MoCA process should be developed while taking into account the recent trend towards Medicine Adaptive Pathways to Patients. In this context, the link between the Table for price negotiation and post-marketing evidence generation has to be underlined: negotiations between payers and industry to determine the price, with the participation of experts and patients, based on the value assessment tools of medicines (such as the EPARs, HTA reports, European transparent Value Framework), together with a certain degree of transparency on costs, and an estimation of the volume of patients to be treated in Europe, has to be linked to the generation of post-marketing evidence. Price and post-marketing evidence generation should be closely linked so that prices will fluctuate based on re-assessments at key time-points over the life cycle of the medicine. This approach calls for close collaboration with EMA and HTA European collaborative work, in order to align post-marketing requirements.
WEAPONS AND TOOLS TO FACILITATE DECISIONS

1. **Systematic collection of real-model evidence** is a tool which refers to the collection of post-market data on ADTs. These will help changes to be made to the benefit-risk balance and to accessing better, health outcomes. The necessary infrastructure can be built through well designed interoperable registries to capture those treatment outcomes including the case of use of ‘off-label’ drugs. The system should be in line with companies’ compliance with regards to their data-collection obligations. Such data should be made as quickly as possible available to regulators, industry, medical professionals and patients.

2. **Managed entry agreements (MEA)** refers to tools used to support better understanding of the risks associated with uncertainties regarding the value of new medicines compared to the high prices. These could be:
   (i) Rebates and discounts linked to price-volume agreements and capping schemes to share risk models.
   (ii) More outcome focused approach when the company is obliged to provide additional data on real-life performance of a medicine.

CALL ON PAYERS TO GET THINGS DONE

EPF (European Patients Forum) and Eurordis (European Organisation for Rare Diseases) worked jointly to drive attention to the need for establishing new mechanisms that would improve access to medical products for patients in Europe, while addressing the existing challenges in terms of sustainability of the health care systems.

Already, the joint efforts of the Pharmaceutical Forum with the Working Group ‘Improving Access to Orphan Medicinal Products’ and of the EU High Level Group on corporate responsibility in the field of Pharmaceuticals, specifically within the Working Group on a ‘Mechanism of Co-ordinated Access to Orphan Medicinal Products (MoCa)’ process, has helped cultivating and establishing in recent years a new culture of dialogue.

Eurordis and EPF made two proposals:

1. To establish a ‘table for price negotiations’ with a group of voluntary MSs involving patients, industry, payments, national health authorities and HTA bodies. The model will need to address specific challenges in small populations which is the case with OMPs.

   Netherlands, Belgium and Luxembourg agreed to joint negotiations. Similar discussions started between Romania and Bulgaria other elements to be explored in different EU platform and need to be integrated into a model.

2. To Fostering Early Dialogue between payers and industry:
   i. Through the implementation of the MoCA pilots:
      It is more than five years now that the Working Group (WG) on a Mechanism of Coordinated Access to OMPs, established within the Process of Corporate Responsibility in the field of Pharmaceuticals and launched under the Belgian Presidency of the EU Council in 2010, has gathered the most relevant stakeholders, including for the first time HTA bodies and payers. The WG has been meeting on a regular basis to reflect and develop proposals on a way to create voluntary collaboration at EU level in order to improve access to OMPs for rare disease patients. Two years ago, in April 2013, the final Report from the MoCA Working Group was published concluding that enhanced collaboration and coordination would lead to improved access to OMPs for patients. The Report also identified that defining the (added) value of a new OMP represents an important aspect for improved access.

      In order to achieve this goal, the MoCA group proposed a European Transparent Value Framework as the basis for collaboration between different Member States and other stakeholders towards a common assessment of the value of orphan medicinal products, bearing in mind that this value may evolve over time, depending on the evidence generated all along the life-cycle of a medicine.
From the beginning, the MoCA process has been conceived as an “Early Dialogue” process, on the basis of voluntary collaboration, increased mutual trust and understanding, within the existing legislative framework, and with no binding commitment for parties involved. This early dialogue and enhanced cooperation would help responding to the challenges linked to bringing treatments to small populations, in areas of high unmet medical needs, high uncertainties and high prices.

It is currently felt by all the stakeholders who participated to the MoCA process that now is the time for a new series of pilots to be thoroughly implemented in a more structured and better supported way in order to generate concrete results and learn from these experiences. Today, some maturity and agreement on the main concepts around the MoCA has been reached: the process needs to be further supported and substantiated with concrete pilots.

We are therefore calling on National Competent Authorities to support more broadly the MoCA Pilots which has to be pursued within the MEDEV (Medicines Evaluation Group) as originally envisaged, in an open and flexible way.

ii. Through the participation of representative of payers to EMA & HTA Parallel Scientific Advice as well as to the Scientific European Early Dialogue of the EUnetHTA:

The pilots of EMA & HTA Parallel Scientific Advice started in 2010 and are now a routine practice with approximatively 55 pilots to date. They have become mainstream (9) with a large support from EMA, Commission, all HTA agencies, industry at large, overcoming the initial scepticism, resistance and causiousness. A next step, will be to have EMA-EUnetHTA Parallel Scientific Advice, hence between to the European institutions.

The HAS (Haute Autorité de Santé, France) on behalf of the EUnetHTA is conducting since 2014 the project on Scientific European Early Dialogue (SEED) with over 20 pilots in one year. Few additional pilots are directly conducted by the EUnetHTA. The next EUnetHTA Joint Action, starting in 2016, does plan to have an intensive number of SEED (11) every month with product developers.

One of the limit and missed opportunity is the absence of payers so far in this two innovative and successful early dialogue processes with product developers.

We are therefore calling on National Competent Authorities to engage into these EMA - HTA Parallel Scientific Advice and EUnetHTA Scientific European Early Dialogue. The representation of payers could be through the MEDEV or through the core group forming the table of negotiation.

The Eurordis Call on Payers

The starting point

• The Joint “Call to Payers” was originally issued in May 2015 by EURORDIS and the European Patients’ Forum (EPF).

• It was widely disseminated to national competent authorities for pricing and reimbursement, European Institutions, the EMA, pharmaceutical trade associations as well as all EURORDIS members.

• It received substantial attention in the press and in social.

Why did we issue the ‘Call to Payers’?

• The debate on improving patient access to medicines -particularly orphan drugs.

• At a time when the different stakeholders increasingly tend to antagonise themselves -and often at the detriment of the patient ultimately! we feel is fully the role and mission of patients themselves through their national NGOs.
What was the vision behind the ‘Call to Payers’?

- The EU Orphan Drug Regulation has been very successful in accelerating translation of science into therapies, and has the potential to deliver even more approved treatments by 2020…but only if the right ecosystem is in place.

- The one single burning issue remains patient access!
  - It is unacceptable that 1/3 of patients living with a rare disease still have no access to the orphan medicine they need.
  
  - It is not less unacceptable that another 1/3 have access only after years of waiting, as an OMP may be introduced first in major markets and only much later after MA in others (despite EU Market Exclusivity!).

  - More recently still, it is problematic that some orphan medicines of major importance are not being made available, or that their reimbursement is reversed, because of cost considerations.

- The main challenge to overcome is the lack of trust between HTA/payers and companies on the value of orphan drugs.
  - A more appeased and more constructive dialogue can help by identifying ways in which the uncertainties associated with orphan drugs can be reduced, and their budget.

- Now is the time to flesh out a “new deal” between all parties for a more structured model of patient access, which will guarantee better value for money and stronger sustainability for all.

- Access and sustainability rather than access vs sustainability.

Towards a ‘new deal’?
All stakeholders – regulators, health authorities, industry… – need to rethink radically how new treatments reach patients faster and more affordably.

A more structured patient access/market access, guaranteeing better value for money of medicines, requires to tackle two main “drivers”:

Science

- Pre-requisite for OMPs: recognise that evidence generation has to be all along the lifecycle of medicines
- Assessment of safety, efficacy / effectiveness for small populations requires post-MA research activities agreed and aligned at European level between companies, EMA, HTA and payers
- Current system is siloed and no longer suited to today’s scientific reality

Economy

- Current value demonstration models generally avoid the “elephant in the room” and only result in a disconnect between supposed value and final price
- Industry and payers together must agree upfront on how to approach value (e.g. in situations of small populations and limited knowledge), how to ensure more robust value assessment over time, and how to better link value and price

MAPPs and seamless EMA-HTA-payers dialogue at the European level

“The EURORDIS Call on Payers to Get Things Done”, Yann Le Cam, Chief Executive Officer, EURORDIS, Edinburgh, 28 May 2016
What were we asking for in the ‘Call to Payers’?

• The “scaling-up”, or more extensive implementation, of existing pilots for Early Dialogue between payers and companies.

• The establishment of a “table for price negotiation” with a group of volunteering Member States.

More expensive use of Early Dialogues

• Case-in-point example: MoCA (Mechanism of Coordinated Access to OMPs).

• Who? - A panel of selected EU Member States’ competent authorities, patients (EURORDIS) and industry representatives.

• What? - MoCA pilots have been implemented since 2014 by MEDEV9 pilots initiated since mid-2015.

• A (typical) example of a current pilot:
  - Early dialogue on a targeted gene therapy for a very small population (~ 10,000 patients in Europe).
  - Very complex therapy (80 days min for all treatment steps + 6 months of active follow-up) => crucial need to build an early understanding common to payers and the company of which endpoints matter and can serve as foundations to determine the value of the product.
  - Almost impossible to set up a Europe-wide network to serve all Member States => treatment will be limited to a few selected “Centers of Excellence” across Europe (similarity with ERNs).
  - If all European patients are to have access to treatment, huge implications in terms of:
    o enabling genuine cross-border patient mobility,
    o obtaining administrative pre-authorisations for treatment,
    o securing national payers’ acceptance of need for, + price of, treatment etc…
Towards a new ‘table for price negotiation’

- Our belief:
  - For decisions on products for small patient populations (as is the case with orphan drugs, medicines for paediatric use or precision medicine), in a context of high uncertainty, the national “silo” can no longer be the appropriate level at which to make the decision.
  - What is needed is a collaborative approach between several EU Member States.
  - Only such an approach can enable a more informed and integrated decision-making on aspects related to the assessment of the value of a therapy, the volume of patients that should receive it, or still the process for the generation of real-world evidence post-marketing authorisation.

- That “table for price negotiation” would also be the right place where new models can be explored and start being implemented, e.g.:
  - Common Principles for Value Assessment and common criteria to frame dialogue
  - Joint purchasing
  - Transactional price + differential pricing + control over parallel trade?
  - Price based on Value + Volume + a certain degree of information on costs
  - Price facing and Discount for Uncertainties
  - Price final price linked to additional generated evidence and re-assessment
  - Payment based on outcomes
  - Managed entry or risk-sharing agreements

Fast forward – One year later, where are we?

Cooperation between European countries has stepped up

“The EURORDIS Call on Payers to Get Things Done”, Yann Le Cam, Chief Executive Officer, EURORDIS, Edinburgh, 28 May 2016
• EURORDIS and EPF issued a new letter to public authorities in Belgium and the Netherlands.

- In it, we warn them against the temptation to use such multi-country collaborations only with a narrow economic, cost-driven approach, i.e. solely to obtain lower prices from the industry.

- Instead, we encourage them to use such collaborations to move towards a more structured and coordinated mechanism for patient access, that addresses today’s nationally fragmented and often disjointed HTA and payer decisions.

- We also inform them of the latest state of play of our contacts with other EU Member States:
  - Austria, Italy, Portugal or Estonia are confirmed as willing to associate themselves with Belgium, Luxembourg and the Netherlands.
  - Others like Romania, Malta, Cyprus and Slovakia are willing.

We have all the pieces...

...Let’s build a better future!

“The EURORDIS Call on Payersto Get Things Done”, Yann Le CamChief Executive Officer, EURORDIS, Edinburgh, 28 May 2016
Where we are today?

**Overview for orphan medicinal product designation procedure since 2000**

<table>
<thead>
<tr>
<th>Year</th>
<th>Applications submitted</th>
<th>Applications discussed in reporting year</th>
<th>Positive COMP opinions</th>
<th>Applications withdrawn</th>
<th>Final negative COMP opinions</th>
<th>EC designations</th>
<th>Orphan medicinal products authorised</th>
<th>Orphan designations included in authorised therapeutic indication</th>
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<td>2015</td>
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<td>177 (65%)</td>
<td>94 (35%)</td>
<td>1 (1%)</td>
<td>100</td>
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<td>259</td>
<td>196 (76%)</td>
<td>62 (24%)</td>
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<td>187</td>
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<td>2013</td>
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<td>197</td>
<td>136 (69%)</td>
<td>60 (30%)</td>
<td>1 (1%)</td>
<td>136</td>
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<td>148</td>
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<td>96</td>
<td>54 (56%)</td>
<td>37 (40%)</td>
<td>1 (1%)</td>
<td>55</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>2002</td>
<td>80</td>
<td>75</td>
<td>43 (57%)</td>
<td>32 (42%)</td>
<td>2 (2%)</td>
<td>49</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>2001</td>
<td>83</td>
<td>90</td>
<td>62 (70%)</td>
<td>26 (29%)</td>
<td>1 (1%)</td>
<td>64</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>2000</td>
<td>72</td>
<td>32</td>
<td>26 (81%)</td>
<td>3 (10%)</td>
<td>0 (0%)</td>
<td>14</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>2713</td>
<td>2531</td>
<td>1827 (72%)</td>
<td>681 (27%)</td>
<td>23 (1%)</td>
<td>1805</td>
<td>126</td>
<td>140</td>
</tr>
</tbody>
</table>

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Committee for Orphan Medicinal Products (COMP) meeting report on the review of applications for orphan designation EMA/COMP/747832/2016

Overall, all parties will gain from an early dialogue between payers and product developers. In itself, this participation enables payers to perform a horizon scanning of products under development. Payers will acquire a better knowledge on the disease or condition, on the product, on the therapeutic indication pursued, on the strategy of the company particularly with regards to its clinical development plan and regulatory approach. Payers will be able to express their questions, concerns, expectations early on e.g. acceptable level of uncertainties, need for a registry, study on living with the disease, estimation of hospital costs saved, etc. Product developers will acquire an earlier uptake on what to do to address payers concerns and build solutions within the clinical research so to streamline the development and optimise the allocation of resources.

This approach is a must when bringing to market innovative products at the end of phase 2 with convincing but limited data and high uncertainties, when conditional approval is envisaged, when authorising a gene or cell therapy which may require a high tech hospital environment limited to few countries, hence requiring an anticipation of the economic model and route of access for patients.
A PUBLIC HEALTH INITIATIVE (AN EXAMPLE OF COLLABORATION)

An important advancement in the protection of EU public health - Joint procurement agreement.

The purpose of this document is to outline the scope of the Joint Procurement Agreement on medical countermeasures. In particular, the document describes what should be understood under “medical countermeasures” and “serious cross-border threat to health”, and it provides examples of medical countermeasures that could be procured in common under the Joint Procurement Agreement.

The document goes back to the first request by Ministers of Health to “develop a mechanism for the joint procurement of vaccines and anti-virals” and details how this has been implemented through Decision 1082/2013/EU on serious cross-border threats to health. It will be for Member States participating in the Joint Procurement Agreement to decide, on a voluntary basis, and as deemed appropriate by each of them, for which medical countermeasures they would like the Commission to analyse the feasibility of a specific procurement procedure.

The minimum number of the Contracting Parties to launch a specific procurement procedure has been set by the Joint Procurement Agreement at 5, including the Commission (Article 13(1)), which means that any specific procurement procedure could be launched once 4 Member States agree to do so.

REDUCING WASTE - ADDITIONAL ACTIONS FOR IMPROVING ACCESS TO DRUGS

Certainly policy makers need to promote and focus on other areas to reduce waste in health system allowing them to address quality of care and better patient outcomes such as:
- Overtreatment
- Use of inappropriate therapies or serious under treatment
- Fluctuations on prevention strategies
- Patient non adherence to effective medication/treatment
- Corruption

PATIENT INVOLVEMENT IN ACTION/ACTIVITIES

Involvement of patients by legislation:
PDUFA, FDA, EMA, Paediatric/Pharmacovigilance

Partnering with Patients

Box 4. Examples of overarching patient organizations and involvement

- The European Patients Forum (EPF), the European Organisation for Rare Diseases (EURORDIS) and the European AIDS Treatment Group (EATG) have been active in promoting a patient-centred philosophy and agenda within EU institutions and TIF Internationally. In the US, the National Organization for Rare Disorders (NORD) is also driving greater patient involvement.
- The US National Health Council (NHC) brings together all segments of the health community to provide a united voice for the more than 133 million people with chronic diseases and disabilities and their family caregivers (NHC).

Partnering With Patients in the Development and Lifecycle of Medicines, Review Article, Therapeutic Innovation & Regulatory Science

Projects on educating the patients for meaningful involvement

1. Eupati
2. Clinical Trials Transformation Initiative
3. Patient-Centered Outcomes Research Institute (PCORI)
4. Regulators Inviting Patient Input
5. Prescription Drug User Fee Act (PDUFA)
6. FDA, EMA, HTA Bodies
7. Payment Organisations
THE SITUATION IN CYPRUS

The positions of the Pancyprian Federation of Patients Associations and Friends on patients’ access to drugs

General Information
In the absence of a National Health Insurance System, the drug’s sector in Cyprus is torn between the Private and State (Government) sectors, making equal access to both sectors particularly problematic.

There are two formularies i.e., official lists of available drugs. The National Formulary which includes all drugs that are available in the Cyprus market and the State (Public Hospital’s) Formulary which lists drugs available in public hospitals and prescribed by public sector doctors as well as a limited number of specialist doctors in the private sector treating serious diseases (ex. multiple sclerosis, Parkinson’s disease, rheumatoid disease, all types of cancer).

Access of Rare Disease Patients to Treatment with Orphan Drugs
The Drugs Council is the Drug Regulatory Authority in Cyprus. Its tasks, like all authorizing bodies includes: licensing, variations, withdrawals, pharmacovigillance, record keeping, issuing of manufacturing licenses etc. Therefore, it is the responsible body for all drugs circulating in the Cyprus market and listed in the National Formulary.

In contrast, the inclusion of new drugs in the State (Public Hospitals) Formulary falls within the responsibilities of the Minister of Health, following consultation with the Drugs Committee. Access to State (Public Hospitals) Formulary drugs is granted to beneficiaries based on financial criteria, including income. The employees of the public sector at large, as well as the patients with chronic diseases are also beneficiaries of the State (Public Hospital’s) Formulary drugs.

The State (Public Hospital’s) Formulary lists both branded and generic drugs, which are according to the needs of Public Hospitals. The State Formulary also includes innovative drugs for the treatment of serious or rare diseases, (orphan drugs). Drugs included in the State Formulary are purchased through tender procedures and distributed to public hospitals according to their requirements.

Protocols are specifically developed to limit access of innovative and expensive drugs to those who will benefit most from these treatments. To this end, the Drugs Committee establishes ad hoc committees or subcommittees which have the key role to advise the Drugs Committee and support the implementation of its decisions. The subcommittees and ad-hoc committees ensure that only patients fulfilling the specific protocol requirements receive a certain treatment.

A Committee for Nominated Requests has also been established to examine individual requests that are not covered by specific protocols, or, for the provision of drugs that have are not licensed for a certain indication, addressing a specific health condition of the patient. In addition, and for the first time, a Vetting Council has been set up enabling Individuals to submit their appeals to the Vetting Council challenging any decisions of the Drugs Committee or of the Committee for Nominated Requests which, they may consider unjust or unfair. Patient representatives participate as observers in the ad hoc committees recommended by the Drugs Committee to develop protocols for granting access to innovative, expensive drugs. Note that legislation has been voted, which requires and controls that all government departments consult with POSPF prior to taking any decisions influencing patient-related issues.

Considering the above, the associations of patients with Rare Disorders invites all health stakeholders and policy makers to abide by the following Fundamental Principles:

1. The State should invest in Quality, Safe and Effective drugs.

2. Drugs are not like any other consumable good. Patients’ timely access to drugs is a provided health service, which the State has the obligation to offer timely and consistently.
3. Treatment must be decided upon and result from collaboration between the treating physician and the pa-
tient. That is, the patients will be able to co-decide with their treating physician about the best treatment 
option available to them.

4. All processes should be fully transparent and the patients should have easy access to the entire range of 
information concerning the different therapeutic interventions available for their specific medical condition.

5. Patients’ treatment should abide by the principles of equality and equal treatment and be implemented with 
utmost respect and dignity.

6. The patients should be allowed to choose the doctor and pharmacy of their preference. Subsequently, and in 
the context of the anticipated changes in the area of Health, the two sectors, Public and Private, need to be 
merged.

The Cyprus Alliance for Rare Disorders invites all health stakeholders and policy makers to promote the following 
procedures that will facilitate the implementation of the above-mentioned principles:

1. Ensure that all the indicated, safe and high-quality treatments are made available and offered to patients on 
the sole criterion of providing therapeutic benefit, clear of all financial or other constraints, and in accordance 
with their particular needs.

2. Ensure that the majority of patients receive the medication they need within less than three weeks from the 
prescription issuance date.

3. Ensure that, in particularly complex cases, no patient is left on the waiting list looking to secure medication 
for more than six weeks from the prescription issuance date.

4. Ensure that patients are allowed access to off-label drugs for conditions other than those for which the drugs 
have been officially approved. It is necessary to set criteria based on transparency, equity, and objectivity, 
and existing scientific documentation. In rare, exceptionally serious cases, there are special conditions that 
should be taken into account. For instance, in cases where there is a chance of prolonging the patient’s life 
(usually over 3 months) or in cases where the life or vital organs of the patients are at risk, these conditions 
must be weighed against existing scientific evidence. The appropriate medication should be immediately 
given according to the cooperation between patients and attending physician.

5. Ensure that existing laws and legislations are adhered to and that new ones are promoted. Very importantly, 
state control as well as information and education of both healthcare professionals and patients/citizens 
must also be enhanced to ensure that falsified/counterfeit drugs are not used.

6. Ensure that the implementation of the European legislation on Pharmacovigilance is well-monitored and that 
adverse reactions and/or occurrences due or possibly due to the drug are unescapably reported by all of the 
healthcare professionals and patients (following patients’ education and information through educational 

7. Create records of various conditions to clearly represent patient population numbers and to monitor the 
safety and efficacy of drugs.

8. Ensure that the evaluation and introduction of drugs into the State Formulary is carried out in full transpar-
ency throughout the process, maintaining that the therapeutic benefit for the patients is the primary consid-
eration.
9. Ensure that the introduction of new drugs at the State Formulary is carried out based on pharmacoeconomic criteria and by applying proven analytical tools (e.g. CMA, CBA, CEA, CUA analysis) used by other EU countries for this same purpose. Subsequently, any evaluation should take into consideration the three principal pillars of equity, effectiveness and efficiency.

10. Review and regularly update the State (Public Hospitals) Formulary within a maximum timeframe of one year.

11. Review and regularly update the treatment protocols within a maximum timeframe of one year with the focus to facilitate patients’ needs and including the patients’ perspective.

12. Develop and implement the concept of Health Technology Assessment (Health Technology Assessment) in Cyprus, with the participation of patient representatives.

13. Introduce and implement the new modern Risk-Sharing Agreements (RSAs) immediately in order to secure new innovative drugs at affordable prices. Examples of this type of agreements between the buyer and the companies can take different forms, such as special price agreements, which remains confidential, agreements that are based on either drug performance or the presentation of new evidence, as well as agreements in which the price varies depending on the amount of available drugs. RSAs are being successfully applied in a large number of European Cards.

14. Consult with all partners in the area of drugs to ensure that drug prices are and remain reasonable, drugs are sufficiently available in Cyprus, promote and adopt joint agreements between member states, especially those of small and homogeneous populations such as Cyprus, to increase their negotiating power and with the ultimate aim to lower the price of drugs.

15. Make all the necessary arrangements to establish an Independent Drug Agency with similar characteristics to those of other European Countries.

16. Make all the necessary arrangements to allow the patients’ full participation in all procedures and processes taking place in relation to drugs at all decision-making centres.

17. Ensure that in the new Legislation for the National Health Scheme, which is at the moment at the hands of the politicians, the drugs will be included in a way to serve first and above all the benefit to the patients including the right of the patient and the doctor to choose timely the right drugs for the right condition for the right patient. All drugs for a condition should be included in the same list with an average price so that co-payment can be accessible to all and most in those in need and financial constraints and there should be exceptions, for some expensive drugs to be fully reimbursed, based on the seriousness of the condition and the benefit the patient most likely will have in the absence of any other drug alternative.

- Investment in health is a POLITICAL CHOICE -

- Ensuring universal access to new, innovative medicines for all is a POLITICAL CHOICE

- Health budgets should not be regarded as fixed and immutable but instead take a positive action to make health a POLITICAL PRIORITY