

**Process on Corporate Social Responsibility
in the Field of Pharmaceuticals
Platform on Access to Medicines in Europe
Working Group on Mechanism of Coordinated Access to Orphan Medicinal
Products (MoCA-OMP)**

FINAL REPORT – 17th April 2013¹

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¹ The present document is without prejudice to any existing or future EU/ national and international legislation.

1. Background

In September 2010 the European Commission launched the Process on Corporate Responsibility in the Field of Pharmaceuticals² focusing on, amongst others areas, non-regulatory conditions for a better access to medicines following their marketing authorisation.

Under its Platform "Access to Medicines in Europe", EU Member States, countries of the European Economic Area and relevant stakeholders were invited to participate in a project group to develop the concept of a coordinated access to orphan medicinal products based on the set up of programmes between companies and groups of competent authorities, and on a mechanism for the assessment of clinical added value of orphan medicinal products. The results of the project were intended to be a potential mechanism for approaching this on a collaborative, voluntary basis. The initial idea was to set up a pilot project in a second stage.

Following this call – which was stimulated by the initiative of the Belgian EU Presidency in 2010 “Unmet medical need and solidarity in Europe: a mechanism for coordinated access to orphan medicinal products (OMP)” – a number of Member States, experts, patient organisations, industry representatives and other relevant stakeholders volunteered to participate in the so-called “MoCA” (Mechanism of Coordinated Access to Orphan Medicinal Products) Working Group.

The purpose of the MoCA Working Group was to develop proposals as to how to create a future voluntary European collaboration, as well as a pilot project on voluntary basis, to improve access to orphan medicinal product in Europe.

This paper represents the collaborative outcomes from discussions of the MoCA working group that was formed by volunteers from Austria, Belgium, Estonia, Finland, France, Hungary, Italy, Malta, Netherlands, Portugal, Spain, European Patient Forum (EPF represented by the European Organisation for Rare Diseases, EURORDIS), Standing Committee of European Doctors (CPME), European Social Insurance Platform (ESIP), Association Internationale de la Mutualité (AIM), European Federation of Pharmaceutical Industries and Associations (EFPIA), European Association for Bio-industries (EuropaBio), and European Confederation of Pharmaceutical Entrepreneurs (EUCOPE), and the European Commission, with support from the EC-funded project Eminent.

The conclusions and recommendations on which consensus has been found within the group are also compiled in a separate paper. This full report however covers all aspects of access to orphan medicinal products for patients as thoroughly discussed in different workpackages. Where there were different points of view, it is as such reflected in the text.

²<http://europa.eu/rapid/pressReleasesAction.do?reference=MEMO/10/442&format=HTML&aged=1&language=en&guiLanguage=en>

2. Introduction

Decisions on Pricing and Reimbursement are the exclusive competence of the Member States of the European Union. Nevertheless, Member States foster the same undisputed principles of equity and solidarity, face common challenges when providing indispensable medicines for their patients and suffer similar burdens when organizing this access. All of these issues become even more explicit when limited numbers of patients are concerned and possible answers to meet the Unmet Needs of these patients are scarce and expensive, as is the case with Rare Diseases and Orphan Medicinal Products.

Despite the existing EU regulation on orphan medicinal products (Regulation (EC) No 141/2000) and the overall EU policy framework (for instance the European Commission Communication on Rare diseases: Europe's challenges and Council Recommendation on an Action in the field of rare diseases), delays and disparities in accessing therapies for rare disease patients are still being reported.³ The current scientific committees and instruments such as COMP, EUCERD or Orphanet cannot address the issue of lack of access to OMPs which is beyond the remit of their responsibilities. Indeed, it is today the prerogative of each Member State to ensure access to orphan medicinal products for patients in their territory. Each Member State shall determine the organisation of care, conditions of care and healthcare financing.

By contributing to this initiative, Member States and other participating stakeholders have expressed their common interest in improving access to orphan medicinal products (OMPs) in a coordinated manner.

The European Commission, Member States, patient organisations, the pharmaceutical industry and other stakeholders have recognized the importance to join forces. A number of projects have therefore been initiated by Member States and the Commission to coordinate investments in evaluation and assessment of new medicines and in exchange of information and knowledge.

As decisions on pricing and reimbursement are the exclusive competence of the Member States, it is clear that participation, engagement and/or involvement in a coordinated system on a European level can only be on a voluntary basis. Participation in the project is on a voluntary basis. Decisions taken are non-prejudicial for Member States or other processes and are non-binding up to and until a formal agreement is signed by all parties interested. The "opt-out"-option exists during preliminary negotiations and all prior processes.

The scope of this project, led by the Belgian National Institute for Health and Disability Insurance (RIZIV/INAMI) and the EC Directorate General Enterprise and Industry, is to identify possible options for the creation of a mechanism of coordinated access to orphan medicinal products, based on a voluntary, non-legislative, non-regulatory and non-binding collaboration among stakeholders who are willing to work together.

Legal framework

- Orphan Medicinal Products Regulation (1999): through this Regulation, Member States have committed to lay down a procedure for the designation of OMPs and to provide incentives for the research, development and "*placing on the market/availability*" of designated OMPs. Further, Article 9 identifies possible future activities by Member States to "*support research into, and the development and availability of, orphan medicinal products*".
- Commission Communication on rare diseases: Europe's challenge (2008): in the part on "*Operational actions to develop European cooperation and improve access to high quality healthcare for rare diseases*"⁴, Chapter 3 addresses the issue of access to OMPs and specifically mentions the bottlenecks linked to the decision-making process for pricing and reimbursement. The way forward has been identified to be an increased collaboration at the European level for the scientific assessment of the therapeutic added value of

³ http://img.eurordis.org/newsletter/pdf/mar-2011/ERTC_13122010_YLeCam_Final.pdf and

http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/access_orphans_initialinvest_052011_en.pdf

⁴ http://ec.europa.eu/health/ph_threats/non_com/docs/rare_com_en.pdf

OMPs and the exchange of knowledge between Member States on the one hand, and between Member States and European authorities on the other hand, in order to facilitate national pricing and reimbursement decisions. The cooperation between the EMA and the HTA bodies to assess (relative) effectiveness has also been underlined as a way forward to improve access to OMPs.

- Council Recommendation on an Action in the field of rare diseases (2009): within “*Chapter V. Gathering the expertise on Rare Diseases at European level*”, the sharing of relevant knowledge between MS in order to minimise delays in access to OMPs is also mentioned. Point 17 (e) recommends to support “*the sharing of Member States assessment reports on the therapeutic or clinical added value of orphan medicinal products at Community level where the relevant knowledge and expertise is gathered, in order to minimise delays in access to orphan medicinal products for rare disease patients*”.
- The EU Committee of Experts on Rare Diseases (EUCERD) Recommendation on Clinical Added Value of Orphan Medicinal Products (CAVOMP) Information Flow (2012): this mechanism is aimed at improving access to orphan medicinal products for Rare Disease Patients based on the exchange of knowledge between Member States and the European authorities to facilitate Member States’ informed decisions on post marketing evidence generation.
- The Cross-Border Healthcare Directive (2011) is aimed at facilitating the access to safe and high-quality cross border healthcare and promoting cooperation on healthcare between Member States, including prescription, dispensation and provision of medicinal products. Through article 12, in Chapter IV on Cooperation in Healthcare, special focus is being placed on European Reference Networks to be developed, in particular in the area of rare diseases, as a key element of the strategy to facilitate access to rare diseases therapies for patients in the real-life setting.

Initial key objectives agreed upon were

- to provide real access to orphan medicinal products for patients in real life setting (irrespective of their nationality and their cultural, economical, social or health status) with real unmet medical needs, for whom these medicines may be out of reach - in an affordable and sustainable way within a context of coordination and cooperation.
- to develop an operational mechanism optimising the return on human and financial investments of Member States and the quality of the healthcare through the sharing of knowledge and administrative/financial/logistical burden, as well as through proposals for coordinated actions.

This implies facilitating the process of

- Assessing orphan medicinal products, which can include horizon scanning, early dialogue, the assessment of the prevalence of the therapeutic indications (target population), coordination and sharing of the results of early access programmes (where possible) and the initial assessment of the OMP based on the initial evaluation at the time of marketing authorisation (**Work Package 1 “Assessment/Evaluation” coordinated by Italy and EFPIA**),
- Managing resources (structural access), taking into account a common European Transparent Value Framework (TVF) (**Work Package 2 “Structural Access” coordinated by Spain and ESIP**) and
- Coordination of individual access (**Work Package 3 “Individual Access” coordinated by Belgium and Eurordis**).

This reflection was conducted within the existing legal framework. Any MoCA proposals are based on existing national systems and do not seek to impose any change to the current decision-making process on budget and financing at Member State level. On the other hand, the MoCA identifies elements where cooperation – if legally possible and desired – could support more uniform and equitable access to orphan medicinal products.

It was made clear, that any participation in MoCA is, was and will be on a voluntary basis and will not commit organisations in future actions/ initiatives outside the project. To conclude the project, and based on the experience gained, members of the project were invited to propose recommendations.

Not all of these original objectives were met in the duration of the project. Those areas where agreement was reached and a way forward identified are set out in the key conclusions and recommendations.

The project on a Mechanism of Coordinated Access to Orphan Medicinal Products (MoCA) has been structured around three Work Packages (WPs):

- WP 1 Identifying and Assessing a relevant Orphan Medicine (Assessment/Evaluation)
- WP 2 Selection of the Target Population and Mechanisms for Funding (Structural Access)
- WP 3 Treatment (Individual Access)

Within the three WPs different pathways and operational steps were studied, assessed and proposed to realise the key objective of this project: bringing a promising Orphan Medicinal Product within reach of patients with unmet medical needs in an affordable and sustainable way.

These three WPs drew up a 'roadmap' with different options for realistic scenarios which are either already feasible or in the relative short or midterm. Taking into account and building on existing mechanisms and structures and, as much as possible, on earlier investments made in knowledge and know-how building, was a major concept underlying MoCA.

This report is based on the following papers (write-ups) that were developed in the course of the process and addresses, consensus statements as well as discussion points where no agreement could be obtained as they need further debate:

- MoCA Key messages for the Steering Group
- Summary Version of WP1 for Final Report
- WP 2 Transparent Value Framework
- WP 2 Draft write-up
- WP 3 Draft write-up
- Draft paper on logistics

3. Work Package 1 “Assessment/Evaluation”

Identifying and assessing relevant, potential orphan medicinal products (OMP) in development will be the first step in any mechanism of coordinated access to OMP. The earliest stages will be:

- The identification of the rare disease / condition in question;
- An understanding of what range of other therapies / treatments might be in development and the understanding of the contribution that a new OMP could make to treating a rare disease; and
- The positioning of an individual OMP within the therapeutic strategy for a disease or condition within the national healthcare systems.

These steps have, as their framework, the existing EU regulatory system for designation and approval of orphan medicinal products. Activities proposed build on and around those key steps and time points, as well as the existing interactions between stakeholders within this process.

The inputs of this step within the MoCA process will be:

- Information on the existing context;
- The disease/condition in question; and
- The therapy under consideration, other therapies or therapeutic options either available or in development.

The outputs will be:

- an OMP with an EU Marketing Authorisation;
- a collection of the information available at the time of Marketing Authorisation;
- a framework for building further understanding of the value of the OMP, based on a collaborative structured work done with all stakeholders.

In the following sections potential steps for such a voluntary collaboration are outlined.

3.1. Step 1: Rare Disease classification

Rare disease classification is a key element of the identification of the disease or condition in question as indeed being the subject of a potential orphan medicinal product. EU legislation requires the condition in question to be both rare AND serious (“*life-threatening, seriously debilitating or serious and chronic*”⁵).

In order to ensure that all parties “speak the same language”, it is important to be able to identify a distinct rare disease, that might be eligible for the development of an OMP – as defined in EU Regulation 141/2000 and related guidance – to treat it. The COMP scrutinises whether rare disease therapies are eligible for orphan designation within the terms of the regulation and published guidance⁶. The classification and scientific understanding of diseases continues to evolve, but the COMP’s scrutiny during the process already ensures that medicinal products are not given orphan designation if they are designed for “invalid sub-sets” of common diseases⁷.

⁵ REGULATION (EC) No 141/2000 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 1999 on orphan medicinal products

⁶ Recommendation on elements required to support the medical plausibility and the assumption of significant benefit for an orphan designation EMA/COMP/15893/2009 including “*To define a suitable condition for designation, the COMP must look at the rationale for development of the medicinal product in the proposed orphan indication. This is imperative to prevent the slicing of common conditions into invalid sub-sets (e.g., different stages of a condition such as “metastatic cancer”; subgroups of frequent diseases where the product would have interest in the rest of the disease; conditions defined based on the therapeutic use of the product such as “treatment in patients not responding to X”*).

⁷ Insert reference to the official guidelines as soon as available

Many rare diseases are not yet effectively determined and classified in the international disease classification systems and codes, such as the International Classification of Diseases (ICD). A coordinated approach to understand and classify the disease in question will be the first starting point in order to acknowledge that it is, indeed, a correct subject for the project (a potential orphan medicinal product) and to facilitate the starting of a voluntary dialogue.

Sources of information can be the European Public Assessment Reports (EPARs), the Orphanet database⁸. Data from a centralised compilation by the WHO could also be used. ICD 11, currently under development, could also provide useful data sources. Another alternative could be to use the combination of Orphacode, developed by Orphanet to assign an orphan code number for each disease⁹, together with ICD 10, which is a pragmatic approach already being used. This approach would also support international level collaboration.

3.2. Step 2: Coordinated Horizon Scanning

Once the “orphan disease” has been classified and defined as such, it will be important to recognize:

- What the existing treatment options are;
- The medical practices in different countries; and
- The potential availability of other therapies at a future stage.

It might occur that more than one treatment and/or technology is under development for a certain rare disease, although there is no guarantee that any of these projects will succeed and will be approved as a new medicine. Some Member States are already proactively looking at such situations.

Many organisations – e.g., national governments, clinical expert groups and Orphanet – conduct various horizon-scanning exercises for orphan medicinal products. However these are not yet coordinated: in view of avoiding potential duplication of investments a better coordination could be a benefit. Since an OMP must be assessed in terms of its ability to offer a “significant benefit” at the time of orphan designation, a coordinated approach between the Member States and other stakeholders will facilitate this ahead of such review and decision.

Data sources will continue to be those used currently (publications, epidemiology, natural history, etc.) by the individual sponsor of the potential orphan medicinal product in development, the work done by the Member States and the existing and constantly updated Community Register of orphan medicinal product designations¹⁰, as well as the Centres of Expertise and European Reference Networks. Data sources could be assembled on a collaborative approach in one place.

The outputs would be: (1) identification of those *diseases / conditions with a high, unmet medical need* – which might, in turn, be used to inform research programmes such as the EU’s Framework Programmes or joint international research initiatives such as the International Rare Diseases Research Consortium (IRDIRC)¹¹; and (2) identification of diseases where there are “clusters” of research and development efforts.

The highest added value could be created by having a coordinated approach between countries in horizon-scanning, rather than having each individual country taking responsibility for or investing in doing so, particularly where individual Member States are already conducting horizon-scanning. The involvement of the sponsors / Marketing Authorisation Holders will be important so that companies can also “signal” their development programmes into the coordinated approach.

⁸ <http://www.orpha.net/consor/cgi-bin/index.php>

⁹ <http://www.orpha.net/consor/cgi-bin/Disease.php?lng=EN>

¹⁰ http://ec.europa.eu/health/documents/community-register/html/index_en.htm

¹¹ http://ec.europa.eu/research/health/medical-research/rare-diseases/irdirc_en.html and <http://www.irdirc.org/>

3.3. Step 3: Early dialogue

The existing EU regulatory framework for review and approval of OMP foresees many opportunities for early and on-going dialogue between stakeholders on a voluntary and non-binding basis. This starts as early as at the time of orphan designation. This orphan designation can occur at any time in the development of a medicinal product, on the sponsors' request, as early as proof of concept with medical plausibility.

The recommendations for the Clinical Added Value of Orphan Medicinal Products Information Flow (CAVOMP-IF, previously known as CAVOD)¹², adopted by the EU Committee of Experts on Rare Diseases (EUCERD) describes – in Time-Point 1 – the basis on how such early dialogue / interactions could be articulated in the future.

The highest added value would be achieved by having the opportunity for coordinated input from both regulators and HTA agencies at the same time. This “coordinated parallel” scientific advice will allow the sponsor to fine-tune the relevancy of a programme for the clinical development phase.

These early dialogue initiatives are an opportunity to develop needed flexible value assessment approaches for new emerging rare disease treatments that incorporate scientific and technological innovation based upon unmet medical need and patient outcomes. *This value could be enhanced by having such input from different EU Member States' competent authorities in the same forum. Ideally, payers' representatives might also be invited to sit at the same table, to be aware of the information on a research project as early as possible, on an informal basis and where this is possible within national healthcare systems.* It is understood that this might not be possible in all Member States, but as the process is voluntary, it should not impact those countries where such an engagement is indeed possible. This also needs to be considered in the existing legal framework that separates the role of the Centralised Procedure / EMA in assessing quality, safety and efficacy from evaluating “economic and other considerations”.¹³ Nevertheless, the value of facilitating such early information exchanges will be high, even if it is necessarily on an informal basis.

3.4. Step 4: Advice incorporated into Clinical Development plans

The opportunity to receive input from different Member States' organisations in a coordinated way will give the sponsor the opportunity to incorporate the obtained advice (e.g., on population, potential endpoint(s), comparator and duration of treatment) and to design and fine-tune the relevance of a clinical development programme, with the objective of responding to as many requests as possible, within their capabilities and resources. Each individual Member State will retain however the ability to express specific, individual questions. At the same time, for patients it is important to know which clinical trials are ongoing for which disease or condition. Therefore transparency about clinical development plans is wanted.

If challenges are encountered in the execution of the proposed clinical trial programme, the sponsor should immediately signal this to the parties that participated in the early dialogue to find a more appropriate and realistic way forward, based on continued and on-going dialogue. This step requires a new way of collaboration: it does not require the creation of any new mechanism or system to implement, merely a dialogue linking the different steps.

3.5. Step 5: Early Access programmes

Effective, structured early access programmes already exist in certain Member States (e.g., France [ATU / RTU], Italy [Law 648 /1996] and Spain [Use of medicines in special situations: Royal Decree 1015/2009 and Medicines

¹² Published on 10 October 2012: <http://www.eucerd.eu/?p=1699>

¹³ REGULATION (EC) No 726/2004 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal product for human and veterinary use and establishing a European Medicines Agency

Law 1990]) for more than 15 years. These have demonstrated a positive public health impact and have also shown how policy incentives could successfully reconcile patient's early access to innovative treatments and rewards for innovation. They are not intended to replace clinical trials, but to improve patients' access, where the country may decide that the balance between knowledge and patients' need means that it is ethical to do so.¹⁴

Where such schemes exist, they can provide valuable early access to patients, with – in some cases – conditional pricing agreements (e.g. Italy – PBR agreement for brentuximab). Sometimes they can also provide the ability to gather data to build up knowledge of the orphan medicinal product, which might otherwise be lost.

These schemes, where they exist, differ from country to country. The proposal is not to harmonise the systems, which are tailored to each country's situation. However, where possible, facilitating more coordination and sharing of the information and data developed as a result of these early access programmes could support more information that would, support decision-making in each individual country. Sharing of information on these "cohort"-based early access programmes should therefore be encouraged, because they are promising potential platforms for better-structured, early collection of data. A failure to do so means that a lot of information and knowledge is not captured or even wasted.

An added value could therefore be created by increased sharing of information on the early access programmes for an orphan medicinal product, particularly where access is managed using pre-determined protocols. Communication between Member States granting early access and with the Sponsor / Marketing Authorisation Applicant / Marketing Authorisation Holder (MAH) could also identify the target patient group(s) for which the early access programmes are intended. Data coming out of the early access programmes could be fed into common databases or registries which would contribute to the on-going shared knowledge building about an orphan medicinal product.

In a future stage, coordinated Early Access programmes could be foreseen, which would allow the sponsor / MAA / MAH to talk with a group of volunteering Member States and to also agree on data to be captured during such Early Access programmes. This would likely come at a later stage.

3.6. Step 6: Therapeutic Scientific Compilation Reports

At the time of Marketing Authorisation, an orphan medicinal product has been reviewed by at least 3 Scientific Committees (CHMP, COMP and PDCO, possibly CAT and PRAC) comprising different representatives from the EU 27 Member States, meeting at the EMA under the framework of the existing EU regulatory processes.

During this time, the Committees of experts will review different elements of the data package or, in the case of the COMP, an increasingly comprehensive data package, developing between the time of initial designation and the time of CHMP positive opinion. The different reviews at different points in time during the process will contribute to building the knowledge about a product as it moves towards Marketing Authorisation.

This set of scientific reviews and assessments could be compiled into one therapeutic, scientific compilation report that could be made available to the Member States' HTA and Pricing & Reimbursement authorities at the time of Marketing Authorisation. (This is described in the CAVOMP process as Time-Point 2).

The new EPAR format and content could form the basis for this Therapeutic Scientific Compilation Report. These reports could be an additional resource for the Member States. The timing could be the same as the review of the designation criteria by the COMP at the time of Marketing Authorisation to confirm if the conditions on which the orphan medicinal product was granted designation are still fulfilled.

¹⁴ Finland endorses the statement that patients suffering from orphan diseases should get effective treatment as early as possible, but is not willing to engage in early access programs and rather supports clinical trials. There is a limited number of patients that can be recruited to trials, therefore, if the source (of patients) is exhausted in early access, it might become impossible to get real proof of efficacy, since not enough patients are left.

At the time of Marketing Authorisation, it is also suggested that the COMP be mandated to request information from the company about the prevalence of the approved therapeutic indication of the new treatment. This will update the assumed prevalence figures submitted by the company at the time of orphan designation.

The Therapeutic Scientific Compilation Report might also form the correct repository for any eventual information, depending on the agreements reached, gained not only during the normal clinical development programme; but also complemented by the Early Access Programmes as highlighted in Step 5, above. It will be important, however, that the potential inclusion of any Early Access data does not interfere with or delay the standard regulatory processes, which are subject to strict timelines. The report could, therefore, be updated on a rolling basis, in order to avoid any potential delays and/or interference.

The Therapeutic Scientific Compilation Reports could be sent to the Member States together with the request for reimbursement / inclusion in the formularies¹⁵.

Finally, these reports will provide several key sets of information with which to start populating the Transparent Value Framework as outlined in WP-2.

These steps would not replace the national assessment by Health Technology Assessment bodies. The objective is to seek a way to exchange information to support well-informed national decisions by the Member States.

¹⁵ National positive lists, hospital formularies

4. Work Package 2 “Structural Access”

This WP explored options, opportunities and possibilities for modalities and conditions for the organisation of structural access¹⁶ and discussed the framework needed for a potential future voluntary and non-binding pilot of coordinated access to an OMP. It deals with issues on purchasing and potential coverage of such products and the modalities of reimbursement and other forms of support (including non-financial, e.g. organisational) for the appropriate utilisation of OMPs. It focuses on one or two realistic possible common pathways. A number of other options were discussed by the group but eliminated because their implementation did not seem possible within the next five years. Several of the ideas raised by the working group are tentative and not fully specified and tested. Pilots involving a new orphan medicinal product would therefore be needed to refine and clarify details and feasibility of the proposals. To commence such a pilot, an interested company with a suitable OMP in the pipeline as well as a number of volunteering Member States would be necessary.

As decisions on pricing and reimbursement are the exclusive competence of the Member States, it is clear that participation, engagement and/or involvement in a coordinated system on a European level can only be on a voluntary basis. Participation in the project is on a voluntary basis. Decisions taken are non-prejudicial for Member States or other processes and are non-binding up to and until a formal agreement is signed by all parties interested. The “opt-out”-option exists during preliminary negotiations and all prior processes.

A core issue underpinning disputes and sensitivities on market access to OMPs is particularly trust – or the lack of trust – concerning price determination: Is the pricing decision-making process suitable for the specificities of treatments of patients with rare diseases? Industry demands a price which reflects actual financial reward for real innovation and for return on investment and risks. Payers question whether the value of what they are paying is fair, based on the clinical added value and post-marketing evidence generation for optimal medical practice and optimal resource allocation. Trust is not a one-way street or a unilateral issue. Building trust among patients, HTA agencies, payers and industry is a potential key deliverable of the MoCA process.

Common pathway leading to a structured scheme for patient selection and coverage

The objective and the output of this WP is a proposal for one or more common pathways leading to a structured scheme for patient selection and coverage.

The following aspects are addressed:

- A mechanism for selection and definition of the patients and patient groups.
This involves determining conditions (e.g. required expertise of healthcare provider) for providing the Orphan Medicinal Product. This requires interaction with delegated medical experts and where deemed necessary could also involve, representatives of financing/funding authorities (i.e. payers) and patient organisations¹⁷ for starting, monitoring and completion of therapies.
- Based on the above, agreeing on the core elements of value offered by the OMP e.g. via the TVF (Transparent Value Framework).
- Cost determination including pricing of the Orphan Medicinal Product
- Sharing information, processes and methods to assess the budget impact of the orphan medicinal product
- Finding through international cooperation solutions for reimbursing the orphan medicine on a national level/within the social healthcare system.

¹⁶ Note: In the context of this project, the term ‘structural access’ refers to the framework that healthcare providers (physicians, hospitals,..) and patients can use – or turn towards – when applying for financial support to cover the cost of the actual treatment.

¹⁷ Note: France expressed a concern on a possible conflict of interest in this matter

These elements interact, and are linked with information and most probably ‘activities’ on value assessment (WP 1) and actual treatment and follow up of the patients (WP 3).

Within this chapter all operational steps for the establishment of structural access are covered. Different levels of commitment in this process should be taken into account and distinction between full participation or participation on an observational basis should be made possible. Some Member States e.g. France, expressed reservations on WP 2 and, will have a position of observer on pricing, financing and budgeting issues.

Operational Steps and implementing activities

4.1. Operational step 1 – Determining the Number of Patients

Determining the number of patients to be treated by the approved therapeutic indication of a medicinal product is based on the assessment described in chapter 3 and does not require the development of new mechanisms or structures. Eventually, the number of eligible patients for whom coverage can be provided will depend on this basic number of patients (based on indication), and if necessary, adjusted depending on the following steps, e.g. value assessment (cf.5) or budget impact.

Alternative therapeutic options – either other OMPs licensed for the disease or other interventions such as surgical procedures will also limit the number of patients likely to receive the OMP in question.

4.2. Operational step 2 – Agreeing on elements of value

The process described herein will be based on the value of the medicinal orphan product itself (as established in the WP 1), on the value of its use/administration in clinical practice, (that is taking into account availability and magnitude of experience and expertise) and on priorities, capacities and resources. Roughly, the value of the product itself and its use determine the value of the product for the individual patient; the other elements compose its value from a societal perspective. The value could be determined for the patient group specified in Step 1 with the help of a so-called Transparent Value Framework (cf. separate paper on the Transparent Value Framework). The TVF should help to coordinate access pathways for OMPs in Member States by providing a simple and consistent terminology and methodology. Indeed, as the value of the orphan medicinal product expresses the medical/intrinsic value of the product, combined with its value from an individual patient perspective (in an unmet medical need situation) and from a societal perspective (including national priorities, preferences, available resources to allocate,...), this value might largely differ for different patients or patient subgroups (for instance according to age) even within the authorised indication.

4.3. Operational step 3 – Pricing

Information on the price of the product is necessary for the further steps of budget impact assessment and finding a solution for paying. Information on prices can be provided by the MAH and can be checked by public payers. Group members are aware that list prices not necessarily reflect the actual cost occurring for the third party payer due to a variety of reasons (co-payments by patients, rebates, managed entry schemes, etc.). To avoid confusion about this situation and to obtain a valid overview, further analyses of pricing mechanisms and systems for OMPs in Europe would be helpful. If updated on a regular basis, one single joint or coordinated analysis can serve as a reference.

Price and cost differentiation between Member States (reflecting the basic principles of solidarity) could be (more) acceptable for the different stakeholders if done by the way of a coordinated discussion. In the case of such differential pricing agreements, differences in purchasing power and (health) financial resources, indicated by differences in Gross Domestic Product and national healthcare budgets could be taken into account.

Currently, the individual price of OMPs can be very high¹⁸ which seems to be one of the major barriers for access; although the overall budget impact currently remains limited to between 2 % - 5 % of drug spending.. As mentioned above, trust is a basic issue with regard to the mean price per patient across all orphan medicinal products on the range. Payers and patients stressed that access to transparent and verifiable information about the level of industrial investment per OMP would facilitate building trust. The industry expressed their concern that trust entails acknowledging the value of the newly developed medicinal product. There was considerable discussion about what information would be needed to show that a price was “fair” and based on a proper and consistent assessment of value. One tool for this type of appraisal is provided in the accompanying paper on the Transparent Value Framework.

4.4. Operational step 4 – Determining the Cost of Treatment

Although the cost (and budget) assessment will be an individual exercise for each indication and OMP, one should reflect on potential added value in structural knowledge building in this very specific area. Health Economic principles, techniques and parameters might for instance not be adequate in very rare conditions (independent academic consortiums with pharmacoeconomic expertise could be asked to take up a role in this case). Experience gained from the first pilot shall be evaluated and the lessons learned shall be taken into account in future decisions, including national decisions.

For the actual assessment of the cost of treatment, added value can be found in a coordinated approach. The decision which cost of treatment (OMP and additional treatment costs vs. other options to be specified) to consider in a given case should involve all concerned parties in the discussions. This is specifically the case for healthcare providers (Centres of Expertise), industry, payers and possibly the patients. As needs (patients), resources and expertise most likely are spread unequally over the participating Member States, a coordinated approach would create added value by gathering information and knowledge (stratifying differentiation) that might be out of reach if Member States continue to work separately. An assessment of a possible effect of the economy of scale could be studied. Any coordinated approach, with involvement of relevant stakeholders, will have to be facilitated (and will then benefit the most from it) by some form of coordinating structure or mechanism such as a Task Force or a Consortium.

At the same time, medical/scientific information, experience, expertise and evidence obviously evolves. "Conditional Reimbursement" techniques can therefore be useful instruments to deal with the "dynamics" of knowledge-building. Another instrument could be managed entry agreements based on common terms agreed to by several payer organisations, which could be adapted to the local specificities as needed¹⁹.

4.5. Operational step 5 – Budget Impact Assessment and Budget Fixation

Basically, two elements determine the budget to be allocated to or set aside for the financial coverage of any treatment cost: the number of patients and the cost of treatment per patient. Where the number of patients is assessed earlier in the process, this particular assessment will result in forecast expenditures for all aspects/components of the treatment (scanning/detection, diagnosis, transport, non medicinal product costs of the treatment, medicinal product costs, add-on therapies, etc.). If for each of these aspects, financial resources (budget) are sufficiently available; this operational step could be irrelevant.

If, however, resources (financial – budget) are not sufficient or not at all available for one or more (or the whole) of the different components, solutions have to be found through allocation of financial means and/or

¹⁸ Estimating the budget impact of orphan medicines in Europe: 2010 – 2020, Orphanet Journal of Rare Diseases 2011, 6:62 doi:10.1186/1750-1172-6-62, Carina Schey (carina@gmasoln.com), Tsveta Milanova (tmilanova@celgene.com), Adam Hutchings (adam@gmasoln.com), The Terms of reference specified that recommendations on legal changes (including the regulation on OMP) were outside the scope of the project, so no proposals regarding improving access by limiting market exclusivity of OMP's were discussed.

¹⁹ Please consider the final report of the Working Group on Managed Entry Agreements under the Platform of Access to Medicines in Europe for more information.

reallocation of budgets and/or negotiating costs and prices and/or clustering of patients. By clustering patients an effect of economy of scale could be achieved, however further studies on this subject are required. Finally, budget impact assessment may also depend on the possibility of reduced expenditure that might result from the introduction of a new medicine. Depending on how health and social systems currently treat or support patients with the disease and their families/carers, there might be a wide range of costs that a new medicine might off-set: the costs of non-treatment can be substantial.

Neither a joint nor a coordinated budgeting approach seems feasible or even to have a legal basis at this stage. The allocation of a budget is the prerogative of individual Member States and experience points to the fact that budgeting at a national level seems to be more efficient than budgeting for OMPs at the individual hospital level. This is because hospitals find themselves in a very challenging financial situation due to their involvement in rare diseases: hospitals are encouraged to create Centres of Expertise to enhance their competence on rare diseases, hence attracting more patients and creating a critical mass, better practices and more rational healthcare organisation. If, at the same time, budgets for OMPs are taken from the hospital's overall pharmacy budget, these hospitals are penalised by their involvement in rare disease healthcare. Hospitals are trapped in the following situation: the more they build up their competence in diagnosing and treating rare disease patients – namely the more they do what they are expected to achieve by rare disease policies at EU and national levels – the more the expenditures for OMPs are weighting negatively on their pharmacy budget.

4.6. Operational step 6 – Finding a solution for paying

At this point in time, *price negotiations* of medicines and in some/most cases on cost of treatment are already possible in the individual Member States. A coordinated approach, whereby projects can cover countries or therapeutic areas where access is currently severely limited, enables a forecast of larger numbers of patients – and thus turnover – and might consequently enhance economic predictability and negotiation room for the pharmaceutical company (on prices and costs for the medicinal products) and/or the healthcare provider (on prices and costs for the healthcare package).

Another option to be looked into in the long run could be to expand current pricing, reimbursement and purchasing procedures to *comprehensive care packages*. Such packages could include not only the cost of medicine, but also initial diagnosis, as well as monitoring and medical devices, etc. Indeed, in an 'all in one approach', 'comprehensive treatment packages' could be defined, for all aspects and elements of patient care (transport, diagnosis, medical interventions, nursing, accommodation, non- medicinal product treatment, follow-up,...), including or excluding the actual OMP. Cost and budgets for these packages (including personal costs for patients) could be established, discussed and/or negotiated with different (consortia of) healthcare providers, Centres of Expertise or future ERN (European Reference Networks). Still these options were not discussed in detail and would need further exploration.

4.7. Acquisition

The acquisition phase formalises the process which will provide the structural access to the Orphan Medicinal Product. In this phase, criteria for patient (groups) selection and eligibility, (sub) indications and diagnostic prerequisites, healthcare provider selection and/or qualification, treatment specifications (dose schemes, stopping rules, time limits, etc.), price and cost of care agreements are consolidated.

Positive lists for reimbursement of pharmaceuticals and/or medical acts and reimbursement procedures already exist in some Member States and could immediately be 'used' or applied. 'Local' or 'national' procedures for pricing and reimbursement would here benefit to a maximum from joint assessments and coordinated negotiations done before and during the ongoing project.

Currently, a joint or centralised European pricing and reimbursement procedure is not feasible or even conceivable, mostly for legal and political reasons. Still, coordinated pricing and reimbursement contracting is a viable option in the sense that local or national market entry agreements could converge or be standardised. Like the alignment or coordination of local and national 'classical' pricing and reimbursement procedures, these

agreements could benefit from the investments in voluntary joint assessments and negotiations on cost and pricing.

Enhanced coordination of purchasing an OMP could be possible as a mid-term option. If legal obstacles can be overcome, and if applied in clearly defined situations and with clear terms of reference, this could be politically acceptable. Moves in this direction will need to build on an experience base and demonstration of the added value of such collaborative approach.

Such coordinated purchasing schemes could co-exist together with conventional local or national reimbursement schemes, provided that they do not conflict with national laws. They would need to provide clear and formal protocols on financing, as well as on the distribution of the Orphan Medicinal Product. However, due to the voluntary nature of the whole project, they would not conflict with the subsidiarity principle.

5. A Transparent Value Framework (TVF)

The proposed Transparent Value Framework (TVF)²⁰ should help to coordinate access pathways by providing a simple and consistent terminology and methodology.

²⁰ For more details, see the separate paper on the Transparent Value Framework.

6. WP 3 – Individual Access

Member States have expressed their commitment to improve and accelerate access to rare disease therapies, including OMPs, through a variety of legislative actions and policy documents adopted in recent years, which all share the overarching goal of working together towards establishing a “mechanism of coordinated access to OMPs”.

As mentioned in the introduction, the MoCA is integrated within the existing European and national frameworks.

In order to establish a functioning system that would help access to rare disease therapies for patients in a meaningful way, it would be necessary that Member States do actually implement all the elements they have committed to and that are included in e.g. the national plans for rare diseases. These should be in place by 2013 and provide the ideal place for incorporating and anchoring the elements of cooperation foreseen in the MoCA project.

The outcomes of work packages 1 and 2 of the MoCA require willingness from Member States to make the overall system geared at delivering “real life access” to patients. This means that the system must be ready and willing to deliver diagnosis, treatments, and healthcare to rare disease patients in a comprehensive manner and able to deliver this in an affordable and sustainable way.

Important challenges in ensuring patients’ access to OMPs are the growing cost involved with treatment of rare diseases. Recent restrictions in healthcare budgets caused by the financial crisis already affect the coverage of OMPs in some Member States. The proposals for structural access (WP 2) aim at overcoming this situation.

The adoption in September 2012 by the EUCERD of the Recommendation on the Clinical Added Value of Orphan Medicinal Products (CAVOMP) Information Flow proposes a mechanism for increased collaboration between Member States and the EMA so to produce better evidence and the ability to identify the real place of a product in the treatment strategy. The overall work of the MoCA group proposes a possible way forward in a win-win approach for all parties involved. This way forward is based on a coordinated method, based on the Transparent Value Framework (cf.5). A high level of collaboration should be achieved through early and continuous dialogue between all stakeholders along the product development chain and beyond, including Member States, pharmaceutical companies, payers, treating physicians and patients’ representatives.

Still, outcomes of a MoCA in terms of identification of unmet medical needs, assessment of the relevant OMPs and organisation of the general structural access, will not make much difference for patients access in real life if the Centres of Expertise are not being established and working properly, if the European Reference Networks are not developed and well-organised, and if the provisions of the Cross-Border Healthcare Directive are not implemented in a way to allow for rare disease patients’ mobility, as well as for mobility of data, patient databases, registries and expertise.

Individual access to OMPs for rare disease patients will be enhanced if the process is integrated at national level within a well-functioning comprehensive structure and the strategies implemented at national level address the pricing and reimbursement steps with the aim of making OMPs available to patients through the avenues and tools that have been described in the documents adopted by Member States in the recent years and consider the proposed MoCA.

It is only through a comprehensive implementation of the existing instruments – including effective, joined-up and integrated National Plans / Strategies for Rare Diseases – that Member States will be able to ensure that rare diseases patients are diagnosed and treated optimally, in the national centres of expertise being set up, or by recognised experts, or within a European Reference Network.

7. Logistics

To operationalize the concept of a Mechanism of Coordinated Access, options for logistic and administrative mechanisms and structures were examined. The proposed solution, is based on the premise that the process is voluntary and non-prejudicial.

The Working Group agreed on the necessity of a continued collaboration. A group of voluntary stakeholders will focus on:

- The continuation of the discussions on the items identified in this report
- The checking on a regular basis for which activities initiatives have been taken or are envisaged regarding the identified pathways
- The organisation of pilot projects

To that purpose, activities could be managed by an ad hoc taskforce. The taskforce would be composed of all volunteering stakeholders (industry, patients, payers, regulators, healthcare providers, healthcare authorities, Member States...) and its main activities would be the abovementioned.

MEDEV (Medicines Evaluation Group, the informal group of experts from competent authorities on reimbursement hosted by ESIP) has offered to take the project forward and work toward a pilot.

A patient organisation, a healthcare provider (or consortium), a pharmaceutical company, a Member State (such as a payer, healthcare authority...) or another EU stakeholder could initiate a specific MoCA project. Whoever initiates a (pilot) project for a given orphan medicinal product or an identified unmet need, pathways will have to be chosen, agreements will have to be found and commitments will have to be made.

A specific pilot group, composed of all volunteering stakeholders and led by the initiator could act as a steering committee for the management of the following operational steps:

- Preparatory steps such as early involvement in the development of clinical development plans and patient registry;
- Evaluating the unmet medical needs through (partly already ongoing) early dialogue notably involving EMA, European HTA Institutions and companies;
- Application of the TVF
- Operationalizing the agreements decided upon (real life access)

The cost of the taskforce would include the costs for organising regular meetings (secretariat, rooms...)

In a first phase, especially to design the process and necessary steps in detail, one or two annual face-to-face meetings (with approx. 30 stakeholders) seem to be necessary.

For the approach described some organisational framework is preferable, such as a secretariat. Individual initiators, would then turn towards this single point of contact and would not have to carry all administrative and logistic burden.²¹

Stakeholders expressed their interest in facilitating such a framework. Prior to the founding of such a new body it should be explored whether boards of already existing or planned EU-wide initiatives such as MEDEV could take up a role in order to avoid duplication and overburdening bureaucracy or generate more costs. Moreover, this would facilitate quick recommendations, respectively decisions.

²¹ A preliminary estimation of resources necessary yielded an investment of:

- one halftime coordinator
- one half time secretary
- the organisation of 1 (or 2) annual face to face meetings (approx. 30 stakeholders)rooms, catering, etc.)

Where necessary or desired, external (independent) expertise or know-how (for instance for economical assessments) could be solicited and hired.

The benefit of this approach (“ad-hoc task-force”) would be its flexibility and its relative simplicity in terms of setting up and managing a project.

8. Possible pathway for implementation

Based on the described proposals for pathways and implementing activities in the different Work Packages, consensus could be found on a scenario which is already doable today, based on existing measures, structures and schemes. If coordinated, it could form the basis for a better coordination and dialogue.

This scenario would need to include:

- **The use of all available databases** (e.g. Orphanet) and the EU Community Register of Orphan Medicinal Products²² to conduct the horizon-scanning of other therapeutic options / potential therapies in development, particularly where the horizon-scanning is already happening. The **co-ordination of horizon-scanning** would already be an added benefit, because it would avoid duplication and improve efficiency in planning for the Member States' healthcare systems on a collaborative basis;
- **The involvement of HTA and payers bodies in early dialogue** as early as at the time of orphan designation, depending on when in the process this regulatory step happens, and throughout the process – allowing the EMA / regulators to step out of the process when they need to from a legal basis;
- Upon agreement of the sponsor, to invite **HTA and payer authorities to participate in parallel Protocol Assistance / Scientific Advice** for orphan medicinal products, to allow key questions identification to be built into the clinical development programmes – this is already possible in some cases;
- An **additional question to the MAH** at the time of confirmation of continuation of orphan designation, requesting information on the prevalence of the approved therapeutic indication [updating the prevalence of the condition, which is what is contained in the original orphan designation]. This will be subject to approval by the European Commission;
- The use of the **Therapeutic Scientific Compilation Reports** in addition to the European Public Assessment Reports (EPARs) – if these are adopted – as a tool to capture and report all information known about an orphan medicinal product at the time of Marketing Authorisation, based on the development programme. Where possible, the information based on **early access programmes** (prior to Marketing Authorisation) can also be captured and reported. This Therapeutic Scientific Compilation Report capturing a collection of all information available at the time of Marketing Authorisation could be shared with the Member States' pricing and reimbursement authorities in addition to the EPAR;
- The use of EU research funds, including the **International Rare Diseases Research Consortium (IRDiRC)**, to expand or establish pan-European registries for disease areas where current data collection is weak but where horizon scanning indicates that the potential for new product development exists.
- Transparency/communication about clinical development plans for patients.
- The determination of the **number of patients** based on COMP information, product value, patients' needs and society's priorities. This would be specified by means of reimbursement criteria and modalities. This specification could be done by an ad hoc task force.
- Discussions with the company about the elements of **value that the OMP offers** and with healthcare providers about **cost of care**. Once agreed, these elements would be used as input to the **Transparent Value Framework** (cf. 5).

The output of this scenario would be a "MoCA report" on the number of patients and the value of the medicinal product (regarding responders, effectiveness, societal value, etc.) assessed through a Transparent Value Framework.

²² http://ec.europa.eu/health/documents/community-register/html/index_en.htm

Other scenario(s) to be studied²³

In addition to the proposed consensus scenario, the MoCA group suggests - through continued discussion - the study of the feasibility (within a reasonable time frame) of a scenario that would include the following:

- Joint cost and budget impact assessment by the taskforce, based on an overview of prices as described in Operational Step 4.3 on Pricing and on the cost of care.
- Discussions with the company (on medicinal product price/cost) in order to provide a price/cost framework which could be included in the "MoCA report".
This framework would need to be completed by local data on cost of care and prices for the concerned Member States..

The following steps and options for scenarios were explored without any consensus or agreement. The MoCA group, however, agrees that further examination and discussion is relevant and thus needed:

- Joint discussions of the taskforce (with the MAH) on the price/cost framework of the OMP.
If an agreement is reached, the results of these negotiations could be formalised at the national level.
- Formal commitment of all stakeholders on post marketing and evidence generation plans
- Joint procurement of the OMP or a 'comprehensive treatment package' by a group of volunteering MS

In all these cases, if such agreements are reached, the formal pricing and reimbursement procedures at national level could be done in a shorter period of time.

²³ Some member states, e.g. France expressed reservations on the conclusions of the WP2 and, will have a position of observer on pricing, financing and budgeting issues.

9. Conclusions

- The MoCA group concluded that enhancing collaboration and coordination could lead to an added value in the process of improving access to OMPs for patients.
- Cooperation should be possible within the current legislative framework. Since the provision of healthcare is the responsibility of the individual Member States, no changes to the national law are proposed.
- Decisions on pricing and reimbursement are the exclusive competence of the Member States. The participation in and commitment to any future actions concerning the mechanism of coordinated access on a European level are expressed on a strictly voluntary basis by all stakeholders, including Member States and the Marketing Authorisation Holder (MAH). Decisions taken are non-prejudicial for Member States or other processes and are non-binding up to and until a formal agreement is signed by all parties interested. The “opt-out”-option exists during preliminary negotiations and all prior processes.
- Existing expert groups such as the EMA (COMP) and EUCERD, networks such as EUNetHTA and on-going and proposed initiatives for creation of knowledge and exchange of information such as CAVOMP-IF, Orphanet, ERNs, as well as on-going developments on Database and Registries Platforms, should be taken into consideration.
- Enhancing mutual understanding and trust at the EU level between all the stakeholders when exchanging relevant information to support well-informed decision-making at national level, where the decisions remain, is crucial.
- An important aspect for access (in addition to others, such as the organisation of diagnosis and care, as well as affordability and budget impact) is defining/identifying the (added) value of a new orphan medicinal product. The group is aware that this value may change over time, depending on evidence generated (i.e., value determination is a dynamic process). Coordination and/or collaboration in that perspective – e.g., using a Transparent Value Framework, or in follow-up studies – is expected to have added value for individual Member States and stakeholders.
- The Transparent Value Framework (TVF) should help to coordinate access pathways for orphan medicinal products in EU Member States by providing a simple and consistent terminology and methodology.
- It is important that the processes and elements proposed in the MoCA project take account of and are linked with existing, on-going projects. In particular, there should be a coordinated approach for post-marketing authorisation research activities and further evidence generation. In the proposed MoCA elements, the proposals for evidence generation, such as those exemplified by the CAVOMP and for early dialogue, to be continued throughout the development of an orphan medicinal product, will be a vital element of ensuring that projects in the field of orphan medicinal products are consolidated and “joined up”. The Centres of Expertise, according to the Recommendations adopted by the EUCERD²⁴, which will be gathered into European Reference Networks (ERNs) as laid down in the EU Cross-Border Healthcare Directive, will play a vital role²⁵.
- When it comes to individual access the MoCA group concluded that, based on the current existing legislative and political environment, MoCA should complement the following activities:
 - The strategy on Centres of Expertise and European Reference Networks for Rare Diseases;
 - The establishment of patient data bases and registries; and
 - The elaboration of standards of diagnosis and care.
 - The implementation of National Plans for Rare Diseases, as promoted by EUROPLAN.

²⁴ http://www.eucerd.eu/?post_type=document&p=1224

²⁵ http://www.eucerd.eu/?page_id=163#CEERN

- It is only through the enactment of a comprehensive strategy that the voluntary collaborative efforts of the MoCA will deliver equitable access and benefit to patients in a real-life setting in an affordable and sustainable way.
- The Working Group agreed on the necessity of a continued voluntary collaboration between stakeholders focusing on:
 - The continuation of the discussions on the items identified in this report
 - The checking on a regular basis for which activities initiatives have been taken or are envisaged regarding the identified pathways
 - The organisation of pilot projects.
MEDEV (Medicines Evaluation Group, the informal group of experts from competent authorities on reimbursement hosted by ESIP) has offered to take the project forward and work toward a pilot.

To that purpose, activities could be managed by an ad hoc taskforce. The taskforce would be composed of all volunteering stakeholders (industry, patients, payers, regulators, healthcare providers, healthcare authorities, Member States...) and its main activities would be the abovementioned.

ANNEX: List of abbreviations

AIM: Association Internationale de la Mutualité

ATU: Autorisation Temporaire d'Utilisation

CAT: Committee for Advanced Therapies

CAVOD: Clinical Added Value of Orphan Drugs

CAVOMP: Clinical Added Value of Orphan Medicinal Products

CAVOMP-IF: Clinical Added Value of Orphan Medicinal Products Information Flow

CHMP: Committee for Medicinal Products for Human Use

COMP: Committee for Orphan Medicinal Products

CPME: Comité Permanent des Médecins Européens (Standing Committee of European Doctors)

EFPIA: European Federation of Pharmaceutical Industries and Associations

EMA: European Medicines Agency

EPAR: European Public Assessment Report

EPF: European Patient Forum

ERN: European Reference Network

ESIP: European Social Insurance Platform

EUCERD: European Union Committee of Experts on Rare Diseases

EUCOPE: European Confederation of Pharmaceutical Entrepreneurs

EUNetHTA: European Network for Health Technology Assessment

EuropaBio: European Association for Bio-industries

HTA: Health technology Assessment

ICD: International Classification of Diseases

ICER: Incremental Cost/Effectiveness Ratio

IRDiRC: the International Rare Diseases Research Consortium

MAA /MAH: Marketing Authorisation Applicant / Marketing Authorisation Holder

MEDEV: Medicine Evaluation Committee

MoCA: Mechanism of Coordinated Access

MoCA - OMP: Mechanism of Coordinated Access to Orphan Medicinal Products

MS: Member State

NIHDI/RIZIV/INAMI: Belgian National Institute for Health and Disability Insurance/Rijksinstituut voor Ziekte en Invaliditeitsverzekering/ Institut National d'Assurance Maladie-Invalidité

OMP: orphan medicinal product

PDCO: Paediatric Committee

PRAC: Pharmacovigilance Risk Assessment Committee

RTU: Recommandations Temporaires d'Utilisation

TVF: Transparent Value Framework

WHO: World Health Organization

WP: Work Package