ESIP-MEDEV position on the Revision of the EU legislation on orphan medicinal products

European Social Insurance Platform (ESIP)
Medicine Evaluation Committee (MEDEV)

12-12-2022

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About the European Social Insurance Platform (ESIP)

The European Social Insurance Platform (ESIP) represents 45 national statutory social insurance organisations in 17 EU Member States and Switzerland, active in the field of health insurance, pensions, occupational disease and accident insurance, disability and rehabilitation, family benefits and unemployment insurance. The aims of ESIP and its members are to preserve high profile social security for Europe, to reinforce solidarity-based social insurance systems and to maintain European social protection quality. ESIP builds strategic alliances for developing common positions to influence the European debate and is a consultation forum for the European institutions and other multinational bodies active in the field of social security.

Statement regarding positions submitted by ESIP: ESIP members support this position in so far as the subject matter lies within their field of competence.

About the Medicine Evaluation Committee (MEDEV)

The Medicine Evaluation Committee (MEDEV) is a network of 22 national authorities from 18 Member States and Norway bringing together all the relevant institutions responsible for the assessment, pricing and reimbursement of medicines in Europe. MEDEV members include national HTA agencies and social health insurers (payers). The Committee meets six times a year, usually at the premises of ESIP in Brussels. The overarching mission of MEDEV is to further the sustainable provision of medicines to patients who are publicly insured. The European Social Insurance Platform (ESIP) in Brussels was commissioned with the role of coordinating the activities of the Committee.

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Executive summary

ESIP & MEDEV welcome the initiative from the European Commission to evaluate and revise the legal framework concerning orphan medicinal products (OMPs) and its interactions with the Regulation on paediatric medicines as well as the EU general pharmaceuticals legislation.

While the existing legal framework contributed to the development of new treatment addressing rare diseases, it also brought about unintended consequences in terms of market distortions, such as concentration of R&D in specific disease areas (of higher profit) and artificial segmentation of conditions into smaller subgroups. In parallel, OMPs have come to the market with often unjustified high price demands, leading to excessive profit and hampering the financial sustainability of healthcare systems in the long run.

ESIP & MEDEV strongly advocate to rebalance the incentives system to steer and support research and development (R&D) for new OMPs in areas of unmet needs and truly rare conditions. To ensure that the revised legislation is fit for purpose we recommend to:

- **Adjust the prevalence criterion for orphan designation** in order to focus incentives on the development of therapies for truly rare diseases: lower the threshold for single indications (to 1:10,000), introduce a threshold for all authorised indications combined (of 5:10,000);
- **Revise and clarify the definition of 'significant benefit'** laid down in Regulation (EC) 847/2000: 'major contribution to patient care' should be deleted, since it cannot be easily defined;
- **Maintain the profitability criterion for the re-evaluation of market exclusivity** (ME), by setting a threshold for the volume of sales (to 1 billion EUR per year) for all combined indications;
- **Clarify and strengthen criteria for maintaining ME**: combining profitability, prevalence, proof of a clinically meaningful benefit, submission of pricing and reimbursement (P&R) applications in all EU Member States within 2 years after marketing authorisation (MA);
- **Anticipate the review of ME criteria** at the end of the second year after MA and henceforth annually;
- **Entrust the EMA with these regular reviews**, followed by the termination of ME if the criteria above are no longer met.

Introduction

The Regulation (EC) No 141/2000 has undoubtedly made important contributions to the overall development of new OMPs resulting in increased R&D and eventually availability of medicines for the treatment of patients with rare diseases.

As payers, ESIP & MEDEV nevertheless observe a number of unintended consequences as well as market distortions. We believe that several changes are needed to make the legislation fit for purpose and up to date.

The original goal of the OMP Regulation was to ensure that patients suffering from rare conditions benefit from the same quality of treatment as any other patient in the EU. The Regulation therefore aims to incentivise companies to develop medicinal products for the diagnosis, prevention and treatment of rare conditions (including those for children) which occur so infrequently that the costs of developing and bringing them to the market would not be recovered by the expected sales of the medicinal product.[1] This goal must be brought back into focus in order to re-balance the pharmaceutical system in the EU.[2]

As the rules are currently enacted, many pharmaceutical companies merely focus their efforts on licensing drugs for specific disease areas, foremost oncology. Also, only approximately a quarter of newly marketed OMPs address conditions for which no alternative treatment options exists.[3] Stricter measures are therefore needed to prevent exploitation of monopoly positions. This is especially crucial for those products that no longer meet the criteria for ME.

Unjustified high price demands for OMPs hinder timely patient access to treatment while allowing manufactures to generate excessive profits. Even though the impact of OMPs on the total pharmaceutical expenditure might currently seem minor,[4] the OMP drug sales growth continues to be much higher than the overall pharmaceutical market. It is estimated that by 2026 orphans will make up a fifth of all prescription drug sales and almost a third of the global drug pipeline's value.[5]

In order to enable equitable and timely patient access, a system is needed which stimulates R&D and at the same time facilitates competition rather than maintaining exclusivity where the necessary conditions are no longer met. Today's regulatory framework leads to monopolisation of markets and Member States are forced into situations where it is almost impossible to refuse coverage for expensive products although they do not bear adequate proof of benefit. Furthermore, high price demands could also jeopardise regular reimbursement. Eventually, this exacerbates further access inequalities and contradicts the initial goal of the OMP legal framework.

[1] Regulation (EC) 141/2000, Recital 1
[2] Council conclusions on strengthening the balance in the pharmaceutical systems in the European Union and its Member States (2016/C 269/06)
[3] Technopolis Group. Study to support the evaluation of the EU Orphan Regulation. 2019
[4] IQVIA. Understanding Net Pharmaceutical Expenditure Dynamics in Europe. 2022
[5] Senior M. and Hadjivasiliou A. Orphan Drug Report. April 2022

ESIP & MEDEV proposes amending Regulation (EC) 141/2000 and Regulation (EC) 847/2000 as follows:

- **To focus incentives on the development of effective therapies for truly rare diseases, the orphan designation (OD) criteria should be adjusted** as follows:
    - the prevalence threshold for an orphan designation should be reduced to 1:10,000 persons AND an overall prevalence threshold of 5:10,000 persons for all authorised indications should apply
    - "major contribution to patient care" should be deleted from the current definition of "significant benefit" as laid down in Regulation (EC) 847/2000.

According to Article 3(1)(a) of the Regulation, the current prevalence threshold for an OMP designation is 5:10,000, meaning 5,000 persons in a population of 10 million. Only within the EU, about 220,000 patients can be affected by such a condition. With increasing prices for OMPs, this population size is sufficiently large to be an attractive target for a conventional market authorisation and could hence allow to cover the cost of R&D. By reducing the prevalence to 1:10,000, OMP incentives will be re-focused to truly rare or ultra-rare conditions, a criterion that just over 50% of all OMPs licensed between 2000-2017 would have fulfilled.[6] Reducing the prevalence criterion will allow to meet the main goal of the Regulation as mentioned above.

Additionally, to maintain ME, the prevalence of all indications that a medicinal product is licensed for, including orphan and non-orphan, should be combined and should not exceed the limit of 5:10,000. The introduction of such criterion would efficiently prevent a misuse of OMPs incentives by companies seeking subsequent extensions of ME by splitting conditions into subgroups, or by first obtaining an orphan designation for a product and then extending MA to more common therapeutic areas.

Eventually, "major contribution to patient care" should be removed from the current definition of "significant benefit" as laid down in Regulation (EC) 847/2000. Ease of self-administration or improved adherence are not sharply delineated concepts and might vary within different healthcare settings or according to the natural history of the disease. It should also be emphasised that products that do not address a defined real unmet need or only have a very weak potential (of added clinical benefit) to treat a rare condition should not be granted incentives under the OMP legislation.

- **Article 8 on market exclusivity (ME) (Regulation (EC) 141/2000) should be amended**:
    - In order to allow earlier competition for often very costly OMPs, the duration of ME can be reduced, if the ME criteria are no longer met.

[6] Technopolis Group. Study to support the evaluation of the EU Orphan Regulation. 2019

- The EMA (and not the Member States) should be responsible for regularly reviewing the ME criteria. These reviews should take place at the end of the second year from marketing authorisation and henceforth annually.

The current duration of ME of 10 years for one indication should be reduced if the EMA establishes within the regular reviews that the criteria for maintaining ME are no longer met. First and foremost, it should be EMA's responsibility and not only upon request by Member States' to regularly review whether the basis for ME is still valid. A review should be performed at the end of the second year from marketing authorisation and henceforth annually, followed by the termination of ME if the criteria in article 8 are no longer met. In any case, a review should be automatically initiated if an applicant extends the therapeutic indication, especially the application concerns a new (non-orphan) indication.

- **New criteria for maintaining ME should be introduced**:
  - the prevalence threshold (per indication) should not exceed 1:10,000 persons AND the overall prevalence threshold (for all authorised indications) should not exceed 5:10,000 persons AND
  - the drug should not exceed a set threshold for its volume of sales, defined as above 1 billion EUR per year AND
  - it has demonstrated a clinically meaningful benefit AND
  - the OMP has been marketed and a P&R application has been submitted, if applicable, in all EU Member States within two years after authorisation.

Maintaining ME should also be tied to the fulfillment of specific additional criteria lightly different from those for orphan designation. Besides the initial prevalence criterion, the benefits granted to developers should be based on an economic threshold indicating sufficient profitability and therefore strengthening the economic criterion already existing in the Regulation. ME should only be maintained if the total product revenue has not exceeded volume of sales above 1 billion EUR, a threshold commonly used to mark blockbuster drugs.[7]

As with the prevalence criterion, all indications regardless of their orphan designation status should be considered when determining the revenue generated. Furthermore, since incentives for developing OMPs are intended for products addressing diseases which are seriously debilitating or life-threatening and where there is no satisfactory treatment authorised in the Union, a pricing and reimbursement application has to be submitted, if applicable, in all EU-Member States within two years. At the same time, in order to maintain ME for the maximum period of 10 years, all of the above criteria have to be met. The overall goal should be to prevent that incentives are not artificially maintained for products that do no longer need protection.

[7] As stipulated in Regulation (EC) No 726/2004, Art. 23a, the competent authority, particularly in the context of pharmacovigilance, the marketing authorisation holder shall provide the competent authority with all data relating to the volume of sales of the medicinal product.

Conclusion

Ultimately, this Regulation must bring patient needs back into focus and steer R&D efforts to truly rare diseases where an UMN exists. As payer/HTA organisations with an assignment to provide the best possible treatment for all patients, we need a proper balance between supporting R&D for new drugs addressing both rare and more common diseases threatening public health on the one hand, and financial sustainability of our healthcare systems on the other. Consequently, it is of utmost importance that support and incentives for OMPs tackle areas where additional measures are really needed. The ongoing review of this legislation gives ample opportunities to formulate improvements.

Fact box: Regulation (EC) No 141/2000 (the OMP Regulation) was adopted in 1999 and came into force in January 2000 as well as Regulation (EC) No 847/2000 which entered into force in April 2000. The main objective of the orphan legislation was to ensure that patients suffering from rare diseases have the same quality of and access to treatment as any other patient in the EU. This Regulation eventually aimed at incentivising companies to develop and market medicinal products for the diagnosis, prevention and treatment of rare conditions (including those for children), for which the expected return would not cover the necessary upfront investment costs. This was not prioritised at the time since it was seen that there would not be sufficient return for investments.
Since 2000, over 2,552 orphan designations have been issued by the European Commission, resulting in 207 authorised OMPs.[8]

[8] https://www.ema.europa.eu/en/documents/report/annual-report-use-special-contribution-orphan-medicinal-products-2021_en.pdf