Processes to Evaluate the Safety and Efficacy of Drugs for Rare Diseases or Conditions in the United States and the European Union

EURORDIS' contribution
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Disclaimer

I am a Member of the European Medicines Agency (EMA) Management Board representing Patient Organisations.

However, views expressed here are my owns and do not reflect those of the EMA or its Management Board.

Outline

1) Perspectives on the study statement of tasks
2) Lessons learned from the EMA PRIME scheme and its impact on the development of drugs for RD
3) Engagement of people with lived experience of RD throughout the EMA regulatory process: Committees, working parties, collaboration with Patient Organisations, early involvement with CHMP, Patient Experience Data
4) Current revision of the EU pharmaceutical legislation, including the Orphan regulation: EURORDIS Advocacy versus the legislative proposal and points to consider.

Perspectives on the study statement of tasks

- Thanks for inviting us to contribute to this study
- EURORDIS is a non-profit alliance of over 1000 rare disease patient organizations from 74 countries (https://www.eurordis.org/)
- We represent the voice of the 30 millions of People Living with Rare Disease in Europe
- We welcome this Consensus study and the ‘learn from each other’s experience’ approach. It is crucial as, especially in the context of RDs, most of the big pharma companies' developing medicines are operating at global level
- An interesting forum for international exchanges and leverage, the International Rare Diseases Research Consortium: https://irdirc.org/ and one of its output, the Orphan Drug Development Guidebook: https://orphandrugguide.org/

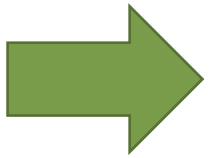
Lessons learned from the EMA PRIME scheme and its impact on the development of drugs for RD

- Europe has gained significant experience and success with the **EMA PRIME scheme**: rare diseases represent the half (**56%**) of the **products designated under PRIME** and more than two thirds (**89%**) of those **approved through PRIME**
- Accelerated approval is absolutely essential to bring innovation to patients as early as possible, when a medicine is transformative, or potentially curative, in areas of unmet needs, thus **it should be extended to all orphan medicinal products**
- A recent study revealed that in **non-oncological rare diseases** where a gene therapy had received orphan designation, only 15% had applied for PRIME designation. This is an interesting finding as 66% of these designations were targeting conditions with a prevalence of less than 1 in 10,000 (**The European landscape for gene therapies in orphan diseases: 6-year experience with the EMA Committee for Orphan Medicinal Products** https://www.cell.com/action/showPdf?pii=S1525-0016%2823%2900540-3)
- Hanaizi Z, Kweder S, Thor S, Ribeiro S, Marcal A. **Considering Global Development? Insights from Applications for FDA Breakthrough Therapy and EMA PRIME Designations**. Ther Innov Regul Sci. 2023 Mar;57(2):321-328. doi: 10.1007/s43441-022-00475-0. Epub 2022 Oct 28. PMID: 36307671; PMCID: PMC9905154.

Engagement of people with lived experience of RD throughout the EMA regulatory process (1)

EURORDIS contributes to the **engagement of patients** in different **EMA activities** by involving and supporting its members in:

- EMA Scientific Committee members (i.e., COMP, PDCO, CAT, PRAC)
- Protocol Assistance/Scientific Advice
- Scientific Advice Groups (SAGs)
- Surveys, consultations
- Product information/Safety issues
- EMA stakeholders dialogue



1. Patient Experience Evidence

2. Having a common regulatory framework and supportive processes

3. Opportunities in the upcoming pharmaceutical regulation

4. Strategic alignment EMA/HTA/Payers

EURORDIS supports the work of the rare disease patient representatives' members in the different EMA Scientific Committees which represents 300 days/year approx.

In addition, during 2021/2022 EURORDIS helped EMA identifying and involving 58 patients in Protocol Assistance (90% of the dossiers requiring patient input).

https://www.ema.europa.eu/en/documents/presentation/presentation-how-patient-engagement-can-contribute-development-approval-medicines-y-la-cam-eurordis_.pdf

Engagement of people with lived experience of RD throughout the EMA regulatory process (2)

- Since 1 January 2021, the EMA has been running a new pilot **procedure** from the **beginning of the evaluation of a marketing authorisation application submission**. (https://www.ema.europa.eu/en/documents/other/pilot-phase-chmp-early-contact-patient/consumer-organisations_en.pdf)
- For each product, EURORDIS is contacted to answer some important questions the CHMP rapporteurs have before they start analysing the benefit and risks of a medicine.
- These questions relate to the **impact** of the disease in the life of patients, treated or not; patients' **unmet needs**; the **relative effects** of patients' treatments; any aspect of the disease the CHMP does not understand well; groups of patients with **different manifestations** of the disease, or different responses to treatments; **expectations** from a new treatment; treatment **constraints** that are acceptable to patients; and the **experiences** of patients who took part in clinical trials.
- To answer these questions, EURORDIS explores the websites of relevant patient organisations that might have published information relevant to the questions, contacts its own members, and conducts **interviews** with two to six patients on average.
- EURORDIS published seven notes (for seven different products), representing 21 interviews with patients of one hour each. To interview 17 patients, it was necessary to contact 60 patients.

Engagement of people with lived experience of RD throughout the EMA regulatory process (3)

- Procedure for **Qualification of novel technologies** - https://www.ema.europa.eu/en/documents/other/letter-support-patient-data-platform-capturing-patient-reported-outcome-measures-dravet-syndrome_en.pdf

- The **use of Real World Data for regulatory purposes** in the rare diseases setting (https://www.frontiersin.org/research-topics/30222/the-use-of-real-world-data-for-regulatory-purposes-in-the-rare-diseases-setting#articles) - Editorial & 7 articles
  - Licensing of Orphan Medicinal Products—Use of Real-World Data and Other External Data on Efficacy Aspects in Marketing Authorization Applications Concluded at the European Medicines Agency Between 2019 and 2021 - Naumann-Winter F et al - DOI: 10.3389/fphar.2022.920336
  - Contribution of patient registries to regulatory decision making on rare diseases medicinal products in Europe - Jonker CJ - DOI: 10.3389/fphar.2022.924648

- Consultation on **Single-arm trials** as pivotal evidence for the authorisation of medicines in the EU (https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-establishing-efficacy-based-single-arm-trials-submitted-pivotal-evidence-marketing_en.pdf)

Current revision of the EU pharmaceutical legislation, including the Orphan regulation (1)

EURORDIS Proposals

01. Maintain the prevalence threshold to leave no disease behind, while including an incidence threshold
(incidence of less than 6 individuals per 100, 000 a year)

02. Encourage structured early dialogue in a multi-stakeholder format to address unmet needs at the right time point: a process rather than criteria

03. Introduce an "Orphan Drug Development Plan" to guide the development of new treatments with the continuous input of experts

04. A modulation of incentives, rewarding earliest dialogue and favouring areas with no therapeutic options

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https://download2.eurordis.org/omp/OMP_Proposal_On_Revision.pdf

EURORDIS RARE DISEASES EUROPE

Current revision of the EU pharmaceutical legislation, including the Orphan regulation (2)

EURORDIS Proposals

05. Maintain Market Exclusivity as an incentive, to ensure global competitiveness

06. Conditional significant benefit until the conversion into full Marketing Authorisation

07. Strengthen the responsibilities and functioning of the Committee for Orphan Medicinal Products (COMP), while reporting to CHMP

08. Include PRIME within the revision of the OMP Regulation or within the wider Pharmaceutical Package as it applies beyond rare diseases

https://download2.eurordis.org/omp/OMP_Proposal_On_Revision.pdf

Current revision of the EU pharmaceutical legislation, including the Orphan regulation (3)

Points to consider

- Reshuffling of the EMA Committees structure → disappearance of the Committee for Orphan Medicinal Products – Need to ensure that we retain expertise and keep an oversight of the field as such
- Patient Engagement – wording needs to be strengthened to retain the expertise gained since 23 years. E.g. 3 Patient experts are full Members of the COMP since 2000, Patients are contributing to Protocol Assistance procedures
- High Unmet Medical Needs / Unmet Medical Needs raises concerns in the Community: Modulation of incentives could be based on other grounds (https://od-expertgroup.eu/wp-content/uploads/2021/06/european-expert-group-on-orphan-drug-incentives-report.pdf) + a multi-stakeholder process is needed to define unmet medical needs
- PRIME is in the legislative proposal → need to ensure synergies with the access pathway

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Thanks!

https://www.rare2030.eu/

http://download2.eurordis.org/rare2030/Rare2030_recommendations.pdf

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