Revision of the EU legislation on medicines for rare diseases and for children

Key points from the perspective of people living with PKU

Background

EU rules to incentivise the development of medicines for people with rare diseases (Orphan Medicinal Products (OMPs) Regulation) and for children (Paediatrics Regulation) have been in place for nearly 20 years. These Regulations aim to improve treatment options for the 30 million European citizens affected by one of the over 6000 rare diseases, including PKU, as well as the more than 100 million children in the EU.

Prior to the existence of these Regulations, limited or no medicinal products were available for both groups, mainly due to the lack of basic science because of the small patient populations affected by rare diseases and the complexity of the research and development process.

Both Regulations have introduced obligations, incentives and rewards for companies to develop therapies for rare diseases and children. These include fee waivers for the regulatory process, administrative and procedural assistance, and a 10-year market exclusivity.

A recent evaluation has shown that the two Regulations have indeed stimulated research and development of medicines in these areas: before the introduction of the OMP Regulation, for example, only 8 rare diseases therapies were approved in the EU; now there are over 200 – 2 of which specifically developed to treat PKU.

The evaluation also found that there are areas that could be improved, and the European Commission is currently undertaking a review of both Regulations, including seeking stakeholders' input.

Key points to consider in any legislative revision:

The current prevalence threshold for a rare disease needs to be maintained

In the EU, a rare disease is currently defined as a disease with a prevalence of less than 5 patients in 10,000 people. This definition is highly relevant as it determines whether a particular rare disease is eligible for support under the OMP Regulation. Based on this threshold, PKU is considered a rare disease, and research and development for therapies for PKU therefore fall under the Regulation.

The Commission's suggestion to group similar rare diseases together when assessing prevalence – PKU could be grouped with Hyperphenylalaninaemia (HPA), for instance[1] - could

[1] [1]Other related diseases are Maple Syrup Urea Disease (MSUD), Glutaraciduria (GA) Type 1, Isovalerianaciduria (IVA) and Tyrosinaemia (TYR)

lead to some combinations of rare diseases passing the current prevalence threshold and therefore no longer individually being considered as a rare disease.

Consequently, therapies for these diseases would not be able to benefit from the incentives and rewards provided by the OMP Regulation. Without these incentives, such diseases risk not being viewed as economically interesting for companies, given the small patient populations. This could lead to patients suffering from these rare diseases not benefiting from future innovation.

The Commission is also consulting about reducing the prevalence threshold to less than 5 patients in 10,000 people. Any reduction of this prevalence threshold is also not advisable, for the reasons outlined above.

In order not to exclude any rare disease patients from future therapeutic innovation, it is crucial that the current prevalence threshold defining a rare disease is maintained.

A legally binding definition of 'unmet medical need' is neither necessary nor helpful

The Commission seems to be considering limiting the incentives provided by the OMP Regulation only to those therapies that address an 'unmet medical need'. In this context, the Commission is proposing a legally binding definition of the concept of 'unmet medical need'. However, this concept is highly complex; many factors play a role in determining unmet need, such as the severity of a disease, the burden of illness, the ease of treatment, the quality of life of persons living with PKU and their families.

It will be impossible to agree on a definition that takes all these factors into account. For example, what would qualify as treatment? In the case of PKU, dietary treatment does exist and can be quite effective - but it is difficult to adhere to, creating a burden for patients and families. Would that mean that the 'medical need' for those living with PKU is sufficiently met and that PKU related pharmaceutical treatment would be excluded from the incentives and rewards provided by the OMP Regulation?

It is also important to note that, as is the case for PKU, treatment for certain subpopulations of people living with a certain rare disease may exist, which may be mistakenly viewed as meeting the needs of the entire population affected by that particular disease.

As also stated by other organisations active in the field of rare diseases[2], a legally binding definition could cause more problems than it would solve, potentially leading to lengthy discussions to the detriment of the populations intended to be served. We fear that one of the consequences could be that diseases for which treatments currently exist for a subpopulation would no longer be interesting for companies to invest in due to the small patient population, as these treatments would not be deemed to address an unmet need and would therefore not benefit from the incentives and rewards provided by the OMP Regulation.

In order not to exclude any rare disease patients from future therapeutic innovation, it is crucial that an unnecessary and unhelpful legal definition of unmet medical need is not introduced.

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[2] Feedback from: EURORDIS Rare Diseases Europe (europa.eu)

Conclusions

It will be crucial to avoid unintended negative consequences during the revision of the OMP Regulation as this legislation must provide equally and support better access to the best treatment for all people with rare diseases.

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