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HEALTH AND FOOD SAFETY DIRECTORATE-GENERAL

Health systems, medical products and innovation
Medicines: policy, authorisation and monitoring

Pharm 820

PHARMACEUTICAL COMMITTEE
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Subject: Revision of the orphan and paediatric medicines legislation

Agenda item 2

1. INTRODUCTION

One of the main problems identified in the evaluation[1] of the orphan and paediatric legislation is insufficient development in areas of greatest unmet medical needs for patients. Furthermore, the development of medicines in the realm of rare diseases and children has not covered all major therapeutic areas.

In the area of medicines for rare diseases, it was found that 95% of rare diseases still have no treatment option. Concerning medicines for children, developments have not sufficiently addressed the highest unmet needs of children (areas like mental and behavioural disorders and neonatology, for instance). Furthermore, both Regulations have been built around "one-size-fits all" incentives and rewards, which do not always provide an adequate tool to stimulate developments in areas of unmet needs.

As indicated in the inception impact assessment published in November 2020, one of the objectives of the future revision of the two Regulations is to foster the development and the authorisation of medicines for rare diseases and for children in areas of unmet need and in better alignment with patient needs. In the inception impact assessment, possible options to address the shortcomings identified in the evaluation of the two legislation were described. We are now starting the impact assessment phase where the impact of these proposed options will be assessed.

In order to provide input to the impact assessment exercise we have discussed during a previous Pharmaceutical Committee meeting and then at a dedicated STAMP meeting the possible *criteria* to identify unmet medical needs in rare diseases and children. Such criteria will serve as a basis for the discussion related to specific rewards and incentives for products addressing these unmet medical needs.

No detailed discussion on possible incentives has taken place during these meetings.

[1] https://ec.europa.eu/health/human-use/paediatric-medicines/evaluation_en

2. OBJECTIVES OF THE MEETING

We would like to present the discussions which have taken place during the STAMP meeting and have an exchange of views with the Committee about them. The aim is to feed the reflections collected into the impact assessment on the revision of the two legislations.

3. CRITERIA UNMET MEDICAL NEEDS AND INCENTIVES FOR THE IA STUDY

Criteria to determine unmet needs for children and rare disease patients and a system to identify products developed to address such needs may be enshrined in the legislation. Products identified by such a system could be eligible to one or more of the following incentives:

- Non-clinical research support (dedicated research funding for academia and SMEs to support developments in the areas of unmet needs).
- Increased scientific support by EMA and priority assessment (a system similar to the existing PRIME scheme[2] could be put in place).
- Post-authorisation incentives such as the market exclusivity, an extended Supplementary Protection Certificate ('SPC')[3], extended regulatory protection periods (data protection, market protection); ; possible *novel* incentives.

A 'grading system' of current and novel incentives will be tested during the impact assessment study. The graduation would depend on the type of product and the extent of unmet medical need the product would address. Prolongation of the incentives could also linked to the availability of the product in all/most Member States.

[2] https://www.ema.europa.eu/en/human-regulatory/research-development/prime-priority-medicines

[3] https://ec.europa.eu/growth/industry/policy/intellectual-property/patents/supplementary-protection-certificates_en

ANNEX:

Reflection paper for discussion[4]

Criteria for unmet medical need in rare diseases

Seriousness of the disease[5]

- Life-threatening
- And/or seriously debilitating
- And/or chronically and progressively leading to a seriously debilitating status

Designation stage[6]

a) No treatment available

No authorised treatment for the disease is available (therefore a clear need for any treatment for a disease) or no commonly used method not subject to marketing authorisation requirements available (e.g. surgery).

b) Treatments available

Treatments are already available, but the corresponding therapeutic efficacy and/or the safety could be significantly ameliorated;

OR

Treatments impose an elevated treatment burden for the patients;

OR

Available treatments are not addressing unmet medical need in all subpopulations (ex. adapted doses and/or formulations/route of administrations specific for some populations).

Marketing authorisation stage[7]

The developments/products addressing the above needs will need to be able to justify the potential to address to a significant extent the existing unmet medical need.

[4] The views presented in this paper do not necessarily represent the views of the Commission and of the Member States participating in the Pharmaceutical Committee meeting.

[5] For children, we are referring to conditions which are life threatening, serious chronically or progressively debilitating in this population.

[6] A development addressing such diseases would be entitled to "non-clinical" support.

[7] A product which has been entitled to non-clinical support and which would fulfil this requirement would be entitled to post-marketing incentives.

Paediatric medicinal products

Concerning medicines for children, the intention is not to limit the paediatric Regulation to cover only areas of high unmet needs for children. The current obligation to agree and conduct a PIP (which includes measures to adapt the formulation of the medicinal product for different subsets of the paediatric population) where the intention is to apply for a marketing authorisation, will remain unchanged.

We have discussed during the STAMP meeting two possible parallel ways to boost the development of medicines for children where no or limited development has taken place since the application of the paediatric Regulation

1. Better taking into account the potential for the mechanism of action of an adult product to address a different disease/condition in children. Currently if the adult disease or condition for which the adult product was developed does not exist in children, the obligation to agree and conduct a PIP can be waived.
   With the revision of the paediatric Regulation it could be envisaged to make compulsory the agreement and the conduct of a PIP when the mechanism of action of an (adult) product could be effective in treating a different disease or condition in the same therapeutic area in children[8].
   Waivers in such system would still be possible, for example in case of toxicity issues, feasibility of the studies in the paediatric population, no substantial differences with products already available (precise list of waivers to be further determined).
   In order to guide applicants, open and "evolving" inventories of molecular targets per therapeutic area could be set up (these lists are not intended to be considered as exhaustive):

   (1) Molecular targets which are involved in paediatric diseases;
   (2) Molecular targets which are not involved in paediatric diseases (so deserving a waiver from the obligation to conduct clinical studies in children).

   Two possible scenarios could be considered when setting up such a system (the respective impact will be assessed):
   - A progressive system, starting with the area of oncology where experience has already been collected following the introduction in the US by the Race for Children Act (RACE)[9]. Areas other than oncology could become subject to the same obligation progressively. In the meantime, the conduct of PIPs based on the mechanism of action of the product in other therapeutic areas would remain voluntary. A "name and shame" system could be considered, when a voluntary PIP would not be agreed.
   - The obligation would cover all areas.

2. The criteria described under the first section of this non-paper could also be used to identify paediatric only developments which could be supported with the incentives

[8] It has been suggested that the same reasoning could also apply for a development in a specific class of age with a product whose mechanism of action could treat a different pathology specific to another class of age.

[9] https://www.fda.gov/media/122696/download

mentioned in the initial part of this document. The potential effectiveness of this strategy to foster novel developments will be assessed in the impact assessment.