EUROPEAN COMMISSION
HEALTH AND FOOD SAFETY DIRECTORATE-GENERAL

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

Pharm 823

PHARMACEUTICAL COMMITTEE
28 May 2021

Subject: Future proofing of the legislation and incentives for innovation that reaches the patient

Agenda items 3 and 4

---

1. FUTURE PROOFING: ADAPTING THE LEGISLATIVE FRAMEWORK FOR MEDICINAL PRODUCTS TO SUPPORT PATIENT CENTRED AND NEED-DRIVEN INNOVATION AND SCIENTIFIC DEVELOPMENTS

a) Regulatory readiness

Fast developments in digital technologies enable novel approaches to research and development of medicinal products. Examples include the use of complex algorithms and AI to support patient recruitment for clinical trials or to determine the composition of the product per patient. Such development also affect regulatory decision-making. This can be in analysis of evidence from real world settings such as electronic health care records to support scientific advice, marketing authorisation decisions and pharmacovigilance.

These developments provide new methods of evidence generation and assessment supporting the development, authorisation and use of medicines. New possibilities also include advances in the areas of personalised medicine and digital as well as the interplay of medicines and medical devices. It is therefore timely to clarify if there is a need to adapt the current pharmaceutical framework in view of developments in digital technologies (e.g. AI, machine learning, cloud computing) and new sources of evidence, namely from real word settings (Real World Data).

The Commission will propose to revise the pharmaceutical legislation to consider how to make best use of this transformation. The discussion is an opportunity to collect the stakeholders' views on whether the current regulatory environment is suitable to address scientific/technological developments and whether changes to the regulatory system are needed.

Question: What are the changes to make to the regulatory framework so that it is better adapted to support scientific developments and need driven innovation?

b) Regulatory tools

Certain products already benefit from regulatory tools to support their development.
Under the pharmaceutical framework and practice, important existing (regulatory) tools are:

- **Priority Medicines** (PRIME) scheme - promotes accelerated assessment including through an early dialogue between the various stakeholders, additional advice and support.[1] It builds on existing regulatory tools such as scientific advice and accelerated assessment.
- **Accelerated assessment**[2] - reduces the timeframe for review by the European Medicines Agency of an application for marketing authorisation for medicines of major public health interest and in particular from the viewpoint of therapeutic innovation;
- **Conditional marketing authorisation -** granting a marketing authorisation although without comprehensive clinical data referring to the safety and efficacy of the medicinal product, but the risk-benefit balance of the medicinal product is positive.

Question: At which stage of the development are regulatory interventions necessary to support innovative product development? Which tools/instruments are necessary? (e.g. CMA, PRIME, Accelerated Assessment, Scientific Advice, rolling review, others?)

[1] The PRIME scheme has not been codified in the EU pharmaceutical legislation.
[2] https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/accelerated-assessment.

2. PROVIDING INCENTIVES FOR INNOVATION THAT REACHES THE PATIENT

One of the aims of the strategy is to stimulate innovation and breakthrough therapies,[3] especially in areas of unmet medical needs (UMN). Defining UMN in the context of the pharmaceutical legislation relates to creating regulatory tools and incentives and to foster innovation and facilitate approval of medicines for UMN, as well as their availability and access.

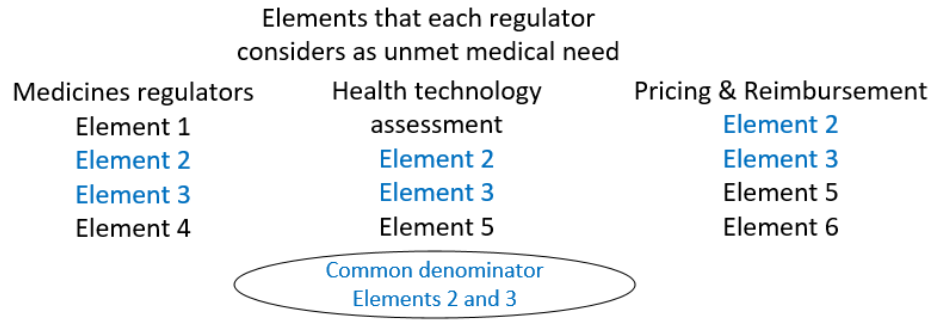
Factors *beyond* the legislative framework and/or the remit of the EU, such as pricing and reimbursement decisions, also influence accessibility and affordability of medicinal products and may impede the competitive functioning of the markets. However, the discussion foreseen in the extended Pharmaceutical Committee will focus on the EU legislation. In particular, it aims to shed more clarity on how the legislation could perform better in terms of incentivising unmet medical needs that also reach patients, in line with the objectives of the strategy. Ideas for improvement may be proposed and discussed, taking the impact of these factors beyond the legislative framework into account.

a) Unmet needs in the context of the general pharmaceutical acts

Need for criteria

An overarching *definition* of UMN would be hard to reach given the intricacies of the different policy angles linked to the stages of medicine development (development and clinical trials; authorisation; HTA and pricing and reimbursement (P&R) decisions).

Instead, a *principles-based approach* may be used. In such case, a common denominator may be established of what constitutes an UMN in each stage of the medicine lifecycle, including agreement that when a medicinal product fulfils the criteria set then it can be considered for a privileged regulatory pathway and incentives.



The following elements will be important to be taken into account when discussing unmet medical needs:

- Individual unmet needs are often bigger than societal unmet needs.
- Not all innovation is necessarily coupled with addressing an medical needs:
    - There can be non-innovative treatments still addressing UMN;

[3] In the US, qualifying criteria for a breakthrough therapy is a medicinal product: 1. That is intended alone or in combination with one or more other drugs to treat a serious or life threatening disease or condition AND 2. Preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. See also: https://www.fda.gov/regulatory-information/food-and-drug-administration-safety-and-innovation-act-fdasia/fact-sheet-breakthrough-therapies

- Repurposing of existing medicines may also to be taken into account, and finding ways to support repurposing may facilitate the identification of other pathways for true innovation in UMN.
- There is often a graduation in UMN.
- Innovation often progresses stepwise in a sense that rarely breakthrough therapies are suddenly developed.
- Patients and academics should have a say in the identification of UMN.

Current definition

Only one definition currently exists for UMN in the EU pharmaceutical legislation (namely, in Article 14-a of Regulation (EC) No 726/2004 regarding the conditional marketing authorisation):

'1. In duly justified cases, to meet unmet medical needs of patients, a marketing authorisation may, for medicinal products intended for the treatment, prevention or medical diagnosis of seriously debilitating or life-threatening diseases, be granted prior to the submission of comprehensive clinical data provided that the benefit of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. In emergency situations, a marketing authorisation for such medicinal products may be granted also where comprehensive pre-clinical or pharmaceutical data have not been supplied.

2. For the purposes of this Article 'unmet medical needs' means a condition for which there exists no satisfactory method of diagnosis, prevention or treatment authorised in the Union or, even if such a method exists, in relation to which the medicinal product concerned will be of major therapeutic advantage to those affected. [...]'

Question: - Would it be possible to set in the legislation criteria to identify products addressing unmet medical needs? What criteria can be considered?

- *Should the following criteria be considered?*
  (1) seriousness of disease; AND
  (2) the absence of satisfactory method of diagnosis, prevention or treatment authorised in the Union; OR
  (3) major therapeutic advantage over existing treatments.

b) Incentives to support the development of products addressing unmet medical needs

Regulatory incentives

The current system of regulatory incentives[4] enshrined in the basic acts[5] concern data exclusivity (8 years of data protection of pre-clinical tests and clinical trials) and market protection (10 years of market protection for medicinal products).[6]

[4] This is without prejudice to the system of protection of intellectual property and possible patent extensions in the form of a supplementary protection certificate and specific incentives and rewards relating to orphan and paediatric medicines.

[5] Article 10 (Directive 2001/83/EC) and Article 14 (Regulation (EC) 726/2004).

[6] This period is extendable by 1 year under conditions ('new indication with significant benefit').

A possible revision of the system of regulatory data protection may include options that would better attract and promote innovation, especially in areas of highest unmet medical need.

Question: How can the system of regulatory incentives (data and market protection; possible novel incentives) better address unmet needs? Are changes to the existing system needed and what would these be?

- *Think about which other elements of the current regulatory framework should be adapted to support products addressing UMN.*

c) A regulatory framework which better supports access to medicines for all patients

Innovative and promising therapies do not always reach the patient and, across the EU, there are still different levels of access to medicines. This constitutes a particular challenge to the underlying principle of the centralised authorisation procedure. This procedure allows marketing authorisation holders to market medicinal products and make them available to patients and healthcare professionals throughout the EU based on a single marketing authorisation[7].

- ***Question: - How can the regulatory framework better support a wider access to medicines?***
  - *For example, if novel incentives would be provided to products addressing UMN (or to innovative products) should they be coupled with obligations and/or conditions in order to ensure their availability and access?*

[7] https://ec.europa.eu/health/human-use/strategy/market-launch_centrally-authorised-medicinal-products_en