Update on PRIME and CHMP Guidelines for early access tools

4th STAMP meeting, 10 March 2016

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Launch of PRIME and updated guidelines

The European Medicines Agency (EMA) is committed to enabling early patient access to new medicines, particularly those that target an unmet medical need or are of major public health interest. The Agency seeks to support the medicine development process from an early stage and to offer regulatory mechanisms to help promising new medicines reach patients as early as possible. Companies developing such medicines can apply to EMA for their products to make full use of these regulatory opportunities.

The European Union (EU) pharmaceutical legislation includes several provisions to foster patients' early access to new medicines that address public health needs and are eligible for the centralised procedure such as:

- accelerated assessment: reduces the timeframe for review 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: grants marketing authorisation before complete data are available;
- compassionate use: allows the use of an unauthorised medicine for patients with an unmet medical need. The Committee for Medicinal Products for Human Use (CHMP) issues an opinion on criteria and conditions, which national patient access programmes can consider when making such medicines available.

Medicines approved since 2006 using early access tools


1 Update on PRIME and CHMP Guidelines for early access tools
PRIME

After discussions at all STAMP 2015 meetings

- Draft reflection paper adopted by CHMP
- Public consultation
- Review of comments and revision of the document
- Finalisation and adoption of the document

Scheme launched on 7 March

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Public consultation on PRIME

- 36 contributions from 42 stakeholders
- Wide range of stakeholders
- > 300 comments
- All comments published on EMA website, together with summary and responses
PRIME - Main changes after public consultation (1)

Eligibility criteria - Clarifications and refinement of wording

3. PRIME-Eligibility-criteria

The PRIME scheme is limited to products under development which are innovative and yet to be placed on the EU market. There should be an intention to apply for its initial marketing authorisation through the centralised procedure.

The scheme aims to support medicinal products of major public health interest and in particular from the viewpoint of therapeutic innovation (i.e., those which fulfill the accelerated assessment criteria).

As such, medicines eligible for PRIME support shall target conditions where there is an unmet medical need, i.e., for which there exists no satisfactory method of diagnosis, prevention or treatment in the Community or, even if such a method exists, in relation to which the medicinal product concerned will be of major therapeutic advantage to those affected.

In these conditions, a product eligible for PRIME support should demonstrate the potential to address to a significant extent the unmet medical need for maintaining and improving the health of the Community, for example, by introducing new methods of therapy or improving existing ones.

Data available to support a request for eligibility in a given indication should support the claim that the product has the potential to bring a major therapeutic advantage to patients, through a clinically meaningful improvement of efficacy, such as having an impact on the prevention, onset or duration of the condition, or improving the morbidity or mortality of the disease.

The appropriateness for access to the PRIME scheme depends on both the magnitude of the treatment effect, which could include duration of the effect, and the relevance of the observed clinical outcome. Relevant clinical outcomes generally refer to an endpoint that predicts an effect on associated morbidity, mortality or progression of the underlying disease.

Consequently, entry to the scheme for the majority of products is expected to be supported by evidence of clinical response in patients (i.e., generated in exploratory clinical studies) substantiating the product’s potential to significantly address the unmet medical need by providing a clinically relevant advantage for patients.

As the data submitted will vary depending on the product, stage of development and therapeutic area, each request will be considered on a case by case basis.

Detailed guidance on the justification to be submitted by applicants to be part of the scheme is provided in Annex 1.

Annex 1 - Justification for eligibility to PRIME

The request should be submitted with justification that the eligibility criteria are met in a given indication and should be presented as a short but comprehensive document (not more than 30 pages in length). The following aspects could be considered, as appropriate, in the justification:

Unmet medical need

- In general, the justification will be more convincing if based as much as possible on epidemiological data about the disease (e.g., life expectancy, symptoms and duration, health-related quality of life). The claims could be substantiated e.g., from published literature or registries or healthcare databases.
- Where relevant, the unmet medical need should be described separately for different indications or subpopulations.
- A description of the available diagnostic, prevention or treatment options/standard of care (SOC), including all relevant treatment modalities, e.g., medicinal products used in clinical practice (whether approved or not), devices, surgery, radiotherapy should be included. The effect of available methods should also be described together with a description of how the medical need is not fulfilled by the available methods.

Potential to significantly address the unmet medical need

- The extent to which the medicinal product is expected to address the unmet medical need (described in the above bullet point) is essential to its eligibility for PRIME support. The justification should include a description of the medicinal product's observed and predicted effects, their clinical relevance, the added value of the medicinal product and its impact on medical practice. It is noted that a new mechanism of action or a technical innovation per se may not necessarily represent a valid argument for justifying major interest from the point of view of public health.
- In case authorised treatments or established methods exist, the expected improvements should be discussed through a critical review comparing authorised or clinically established treatments and the proposed product.
Increased transparency

Publication of name of active substance/INN of eligible products

An overview of the number of recommendations adopted will be published in the CHMP Monthly report. The EMA will also publish information on products for which eligibility to the scheme has been granted, including the name of the active substance/INN, the type of product (chemical, biological or advanced therapy), the intended indication, the type of data supporting the eligibility request and the type of applicant (SMEs, applicants from the academic sector or others). For products that have been denied eligibility, similar information will be published, with the exception of the name of the active substance/INN, to avoid unintended negative connotations on the merit of the product at the early stage of its development. In case of a subsequent centralised marketing authorisation, reference to eligibility to the PRIME scheme and relevant information will be mentioned in the European Public Assessment Report.
Focus on SME and Academia

Clear acknowledgement of hurdles faced by SME and academia

Progressing to proof of concept stage is often a difficult step for smaller actors with limited experience in regulatory aspects and medicine development. This may hinder the development of promising products. Therefore, there is value in opening the scheme to SMEs and applicants from the academic sector at an earlier stage. This additional support is expected to be exceptional and limited to situations where earlier proof of principle/proof of mechanism stage (prior to, or during, early exploratory clinical studies) is supported by compelling data that can be presented to justify a product’s potential public health impact.

Additional benefits of PRIME

Early regulatory support
Potential to help capital investment
Fee reductions

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## PRIME - Main changes after public consultation (4)

### Innovation offices
Role in raising awareness to PRIME, exchange of information

### HTA
EMA to encourage use of relevant tools supporting early dialogue with HTAs

### International cooperation
Global development context and confidentiality arrangements

### Collaboration

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<td><strong>Innovation offices</strong> exist in a number of EU Member States. These offices are in contact and support applicants in very early stages of developments. They will have an important role in raising awareness to PRIME and directing possible candidates towards the scheme. The Agency collaborates with the Innovation offices and will exchange information on the scheme and its output on a regular basis.</td>
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<td><strong>EMA</strong> is committed to facilitating as much as possible the assessment of priority medicines done by <strong>health technology assessment (HTA) bodies</strong>, which inform reimbursement decisions by Member States. This is vital so that patients can access new medicines in a timely manner. In the last years the Agency has launched various initiatives to strengthen collaboration with these bodies. In view of its aim to promote the possibility of earlier patients’ access, as part of PRIME, EMA will encourage medicine developers to make use of relevant tools supporting early dialogue with HTAs, such as the parallel EMA/HTA advice.</td>
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<td>The importance of considering PRIME in the context of global developments and <strong>international cooperation</strong> is acknowledged. As part of their confidentiality agreements, EMA and other agencies may exchange information on specific medicines’ development and experience on development support tools.</td>
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Update of CHMP Guidelines on accelerated assessment and conditional MA

- Reflections on the experience
- Drafting of guideline update
- Consultation with other committees
- Public consultation
- Review of comments and revision of the guideline
- Favourable opinion of the European Commission*
- Finalisation and adoption of the guideline February 2016

* for CMA guideline only

Update provided to STAMP

Update on PRIME and CHMP Guidelines for early access tools
Key changes to CHMP Guideline on conditional MA

- Encouragement of early dialogue and **prospective planning**
- **‘Positive benefit-risk balance’** vs. comprehensive dossier
- Scope of CMA to cover serious debilitation and life-threatening effects also in the **long-term**
- Exceptionally, **improvements in patient care** as a possible major therapeutic advantage
- Guidance on situations when a **second product** can still address the same unmet medical need
- Confirmation of **significant benefit for orphan medicinal products**
- Clarifications on some further aspects (e.g. compatibility with **accelerated assessment**)

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Revisions to CHMP Guideline on accelerated assessment

• Stressing the importance of proactive **early dialogue** to advise on MAA submission strategy

• More detailed guidance **how to justify** major public health interest based on the existing three key elements (existing methods, unmet medical need, and strength of evidence)

• Optimisation of the **evaluation phases** to reach a CHMP opinion within 150 days (now 90 + 30 + 30 days)*

• Acknowledgment that **comprehensive clinical data** may not be available in certain situations (e.g. accelerated assessment for conditional marketing authorisation applications)

* For ATMPs, timetable will be arranged to include review by the Committee for Advanced Therapies

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One step towards EU network strategy to 2020 objectives

- Better overview of existing tools
- Encourage early dialogue
- Improved accelerated assessment procedure
- Prospective planning and optimisation of use of CMA
- Consolidation through PRIME for priority medicines

Update on PRIME and CHMP Guidelines for early access tools
Thank you for your attention

Further information

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