EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Human Medicines Evaluation Division

Report on the European Medicines Agency meeting with stakeholders - First anniversary of PRIME

19 May 2017

1. Introduction

The European Medicines Agency (EMA) launched the PRIority Medicines (PRIME) scheme in March 2016. The scheme provides early and enhanced support to medicines that have the potential to significantly address patients' unmet medical needs. The first anniversary meeting was organised by EMA to review the experience gained with PRIME one year after its implementation. The meeting was an opportunity to receive feedback from users and potential users of the scheme, discuss on how the criteria for eligibility have been applied and what types of support applicants have received so far and review practical examples that illustrate the benefits of PRIME and how the scheme makes optimal use of existing tools supporting regulatory and scientific advice.

2. Eligibility to PRIME

Overview of one-year experience of PRIME eligibility assessments – Robert Hemmings

Robert Hemmings, chair of the Scientific Advice Working party and member of the CHMP, presented the experience of the assessment of PRIME eligibility requests received during the first year from launch (see presentation for details).

An overview of the steps taken and committees involved in the review of requests for eligibility to PRIME was presented, highlighting the lean process that has been put in place to enable a robust assessment. Overall the experience shows that a review of the written arguments presented by the applicants is sufficient to conclude on the eligibility request.

As indicated at the time of launch of the scheme, an oversight group, composed of the Agency's scientific committees' chairs, SAWP reviewers and EMA, has been put in place to provide guidance on any policy aspects that occurred during the review of PRIME eligibility requests. Examples of policy matters and decisions from the oversight group were presented. A recurrent issue has been whether to grant or deny eligibility for products already advanced in their development: the group considered that in such cases, it should be considered whether benefits are still to be expected from the PRIME scheme.

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Details on the content of eligibility requests received and the main reasons for denying eligibility to PRIME were presented. In many of the requests denied, issues with robustness of the supportive data did not allow to substantiate the conclusion that the product had the potential to bring a major therapeutic advantage. Particularly, while external comparisons are acceptable in the context of PRIME, they were either not sufficiently characterised or representative of the target population. Updates to existing guidance document may be considered as a result of the review of this first year of experience.

Industry experience and feedback on the eligibility procedure – Aimad Torqui

Aimad Torqui presented, on behalf of industry stakeholder associations, the results of a survey conducted on the initial decision to participate in the PRIME scheme. The survey has been completed by 19 companies (see presentation for details) and presents industry's experience around eligibility. The following key points and suggestions were highlighted:

- Guidance and process around eligibility are considered clear and understandable.
- Challenges were highlighted to find the suitable timing to submit a request, with medicines with non-standard development plans having a narrow window of opportunity for entering PRIME.
- Some applicants remain uncertain of the value of the scheme which is perceived to limit their flexibility of interactions within the EU regulatory network.
- Suggestions were made for pre-submission interaction based on a 2-page summary for applicant to understand whether they would meet the eligibility criteria and whether PRIME adds value to development program.
- Possibility for a teleconference in case of rejection to provide more details and clarity around the reasons for rejection.

Discussion

The Agency took note of the suggestion to include a subheading in the justification template for the applicant to highlight particular characteristics of the development that warrant further support through PRIME.

With regards to the proposal for a pre-submission interaction, it was highlighted that applicants can contact the Agency for general guidance, e.g. whether the timing would be appropriate for inclusion in the scheme. However, it was not considered appropriate to provide preliminary feedback on the basis of a 2-page summary, as the information would be too limited and would be based on individuals' view rather than a scientific committee position.

With regards to the reasons for denial, the Agency indicated that each applicant receives an outcome letter indicating the reasons for denial. The Agency will explore how to provide more comprehensive feedback in the outcome letter; nevertheless applicants have the possibility to contact the Agency should the letter be not sufficiently clear.

3. Kick-off meetings and support to PRIME medicines

How have eligible products benefited from PRIME so far? - Jordi Llinares Garcia

Jordi Llinares presented the experience on the support provided to PRIME eligible products (see presentation for details). This included information on how kick-off meetings are organised, feedback on the experience from PRIME Rapporteurs, on the iterative scientific advices that have been requested

as a follow-up to kick-off meetings and how other interactions are handled, with meetings or teleconferences held on ad hoc basis.

Overall, the experience so far meets the Agency's expectations, with the kick-off meeting and early Rapporteur appointment being considered as key features of the scheme in facilitating interactions and enabling to flag issues early in the development. Support has also been provided in excellent collaboration across committees.

An area for improvement has however been noted by the Agency, as applicants need to be prompted to provide regular updates on development progress and milestones after the kick-off meeting or scientific advice procedures. The Agency will consider further guidance on the kick-off meeting and expectations around additional interactions with the Rapporteur and EMA.

Industry perspective

Experiences from applicants of two products that were granted eligibility to PRIME in May 2016 were presented: from representatives of Kite Pharma on KTE-C19 and Biogen on aducanumab. This was supplemented by a joint presentation on behalf of trade associations which included the feedback from a survey conducted amongst 8 companies developing PRIME eligible products.

The following key points and suggestions were highlighted in these presentations:

- Suggestions around organisational aspects of the kick-off meetings were made.
- Importance to maintain the option of informal discussions with the Rapporteur as well as national scientific advice.
- Suggestion for shorter process for scientific advice.
- A question was raised on the processes for transfer of knowledge to Co-Rapporteur and EMA Product team.
- Suggestion for "automatic" access to accelerated assessment.

Discussion

The Agency took note of the suggestions regarding the kick-off meetings, which will be considered in future guidance.

The Agency also clarified that while major/key issues should be addressed as part of scientific advice requests, meetings can be organised with the Rapporteur and EMA on an ad hoc basis. Also, applicants may still request national scientific advice, as long as transparency of these interactions and its outcome is ensured.

With regards to the suggestion for shorter scientific advice process, the Agency clarified that flexibility for shorter pre-submission timing or processes can be applied on a case by case basis, provided that this does not impair the quality of the advice.

It was clarified that minutes of kick-off meeting are shared with all committee members and that most scientific advices on PRIME products are discussed during the CAT and CHMP plenary meetings, thus facilitating the sharing of knowledge with all committee members. Furthermore, the Co-Rapporteur is appointed 6-7 months prior to the marketing authorisation application (MAA) submission. The Agency has also put a process in place to transfer knowledge to the product team as the product reaches the pre-submission phase.

The Agency did not agree on automatic accelerated assessment as it needs to be confirmed prior to the marketing authorisation application that the criteria are still met.

The discussion highlighted the need to enhance the interaction with other stakeholders, in particular health technology assessment bodies and patients, allowing for a more comprehensive discussion on data generation needs to facilitate patient access.

4. Panel discussion

A panel of representatives from different interested parties was gathered to trigger a discussion. The panellists were: Emma Du Four (EFPIA) Robert Hemmings (SAWP chair) Jordi Llinares Garcia (EMA) François Meyer (HAS) Martina Schüßler-Lenz (CAT chair) Ad Schuurman (MEDEV) Christos Sotirelis (EURORDIS) Spiros Vamvakas (EMA).

Stakeholders general comments

Emma Du Four (EFPIA), representing industry trade organisations, indicated the value of PRIME, whilst applicants face challenges to find the right timing to engage into the scheme. She indicated that the discussion during the meeting helped to understand that interaction with EMA, its committees and the Rapporteur in the context of PRIME can be flexible, which was not previously perceived.

Francois Meyer (HAS), representing EUnetHTA, highlighted the importance and interest for health technology assessment bodies (HTABs) to be involved in early dialogue for products that are likely to have significant clinical benefits. He indicated that collaboration can be further explored through the EUnetHTA Joint Action 3 Work package P5 activities on Early Dialogues and Post Launch Evidence Generation.

Martina Schüßler-Lenz (chair of the CAT), noted that the majority of products in the scheme are, not surprisingly, advanced therapies, which receive dedicated support from the CAT. She indicated that the kick-off meeting is an excellent opportunity to interact and that applicants are expected to provide regular updates as they further progress the development, in order to make full advantage of the scheme.

Ad Schuurman (MEDEV), noted that whilst products in the scheme are still far away from reaching the payers, possible collaboration and early dialogue on PRIME products may be considered within the Mechanism of Coordinated Access to orphan medicinal products (MoCA), bearing in mind the limited resources.

Chris Sotirelis (EURORDIS), pointed to the need to emphasize the integration of all other stakeholders involved in pricing and reimbursement. He also advised the Agency to ensure good interface across other procedures (e.g. Innovation Task Force, ATMP classification, adaptive pathways) in order to direct relevant applicants towards PRIME. He also highlighted the need to integrate the patients' perspective, not only through the scientific advice procedures but also through involvement in the eligibility procedures.

The panel then discussed a number of topics. Highlights are summarised below.

Definition of unmet medical need

- Unmet medical need criteria is already considered by many HTABs, most often in a context of innovation procedures and early dialogues. Other priority criteria considered by HTABs include: potential to offer a major advantage, SMEs/academic origin of the proposal, very severe condition and rare disease, high effectiveness coupled with fair price.
- From the patient's perspective, it is important to also consider the unmet medical need for HTABs and the payers and reference was made to the MOCA. Challenges of quantifying the unmet medical need were also highlighted as the highest medical need may only be in a subset of the indication.

- Payers would appreciate a sharper definition, limited to life threatening and seriously debilitating conditions.

Distribution across therapeutic area and type of products

- Spiros Vamvakas (EMA) commented that denial of eligibility to PRIME is not a judgement on the value of the development proposal.
- The Agency noted a high proportion of applications in oncology or haematology. On the other hand, the Agency has not yet seen important developments in other priority areas of unmet need such as antimicrobial resistance. Industry considered that while the scheme can encourage applicants, it will not on its own incentivise development in a specific area.

Challenge of finding the optimal time to engage into PRIME

- Industry would welcome an early entry point to the scheme independent of the size of the company, particularly if justified for those developments that are innovative and rapid, when early engagement is necessary. It was clarified that the early entry stage provides support to SMEs and academics, mainly at EMA level (as the Rapporteur is not yet appointed and no kick-off meeting is organised), to help the applicant to progress to the proof of concept stage.
- Industry would also like PRIME to include products already authorised in the EEA that could address unmet medical need (e.g. new indications). On that matter, EMA considered that PRIME would not be of benefit as Rapporteurs are already appointed and applicants can request scientific advice. Involvement of relevant committees (e.g. COMP, PDCO) can also be considered on an ad hoc basis after discussion with EMA.
- From a patient point of view, the timing of entry into the scheme was not a major issue. However, the patients consider the early Rapporteur appointment of high importance as it allows not only for the Rapporteur to familiarise with the medicine but importantly to have a better understanding of the disease.

Importance of prospective planning of paediatric, orphan and post-authorisation aspects

- Dirk Mentzer, chair of the PDCO, indicated that PRIME is very useful in helping interactions across committees and for PDCO to initiate discussions on the PIP.
- From the Agency's perspective, a key learning is that applicants need to consider post-authorisation planning earlier. From the Industry's perspective, it was argued that while such commitments are difficult to make early, they are open for such discussion to take place in coming years before MAA.

Interactions with the Rapporteur

- The Agency reiterated that while major/key issues should be addressed as part of scientific advice requests, meetings can be organised with the Rapporteur and EMA on an ad hoc basis. Also, applicants may still request national scientific advice, as long as transparency of interactions is ensured.
- June Raine, chair of the PRAC, clarified the PRAC's involvement in PRIME through the participation of a member at kick-off meetings and the pilot process of involvement of PRAC on scientific advice. Emphasis was made on the benefits of early planning for post marketing data generation which most likely will be of key importance for medicines in the PRIME scheme.

5. Closing remarks (by Jordi Llinares)

Overall, the Agency has successfully delivered and implemented the PRIME scheme, with the review of first year of experience and stakeholder meeting giving positive feedback on its performance.

The Agency highlighted that, despite the very positive results of the first phases of implementation, the ultimate benefit of PRIME cannot be assessed yet as there is no experience with marketing authorisation applications for PRIME products and therefore whether PRIME facilitates an accelerated assessment is still an assumption.

It is recognised that regular updates from sponsors is key to ensure adequate provision of advice and keeping the regulatory system up to date on development milestones. In addition, there is a need for further engagement with key stakeholders such as HTA and patients in order to facilitate data generation that addresses timely access of medicines to patients.

The Agency took note of the feedback collected during the meeting and will consider whether updates or new guidance are required in due course. Further discussion will take place in future industry platform meetings that the Agency organises regularly with stakeholders.