

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Update on PRIME and CHMP Guidelines for early access tools

4th STAMP meeting, 10 March 2016

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Human Medicines Research and Development Support Division

An agency of the European Union





Launch of PRIME and updated guidelines



- Pre-authorisation
- Post-opinion
- Post-authorisation
- Product information
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Support for early access

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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.

Related content

- ▶ Adaptive pathways
- ▶ Innovation Task Force
- ▶ Scientific advice and protocol assistance
- ▶ Scientific guidelines
- ▶ SME office

Related EU legislation

- ▶ Regulation (EC) No 726/2004

Related documents

- ▶ Development support and regulatory tools for early access to medicines (07/03/2016)

Medicines approved since 2006 using early access tools



1 March 2016
EMA/531851/2015
Human Medicines Research and Development Support Division

Development support and regulatory tools for early access to medicines

The EU pharmaceutical legislation includes a number of provisions in Regulation (EC) No 726/2004 aimed at fostering patients' early access to new medicines that address public health needs and are eligible at the centralised procedure, such as:

- accelerated assessment procedure which reduces the timeframe for review of an application for marketing authorisation from a maximum of 210 days to 150 days for medicinal products of major public health interest and in particular from the viewpoint of therapeutic innovation,
- for certain categories of medicinal products, the possibility to obtain a conditional marketing authorisation on the basis of less complete data than is normally the case and subject to specific obligations and additional comprehensive data to be provided post-authorisation. Conditional marketing authorisations are valid for one year on a renewable basis,
- the possibility for a compassionate use opinion by the CHMP defining at European level the criteria and conditions for use of medicinal products which are made available to patients through national patients' access programmes (prior to a marketing authorisation).

To optimise the use of the above regulatory tools, EMA has launched the PRIME scheme to support development of medicinal products of major public health interest through early and enhanced scientific and regulatory dialogues. This tool targets support to certain type of products eligible for accelerated assessment and falling within the scope of the centralised procedure. It builds also on existing regulatory tools in place within the European Union (EU) legal framework, including scientific advice/protocol assistance.

The table overleaf provides a high-level overview of the above legislative and development support tools to help sponsors identify when and how to use them.

However, there are a number of other development support activities, not covered in this tabular overview, carried out by the Agency including the following:

- The Innovation Task Force (ITF) which is a multidisciplinary group providing a forum for informal early dialogue with applicants, in particular micro, small and medium enterprises (SMEs) and academic sponsors, to proactively identify scientific, technical and regulatory issues related to emerging therapies and technologies.

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	Development support		Early Access regulatory tools	
	PRIME	Accelerated assessment	Conditional MA	CHMP Compassionate use opinion
Which medicines	Medicinal products of a major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation (unmet medical need)	Medicinal products of a major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation (unmet medical need)	Medicinal products for: <ul style="list-style-type: none"> • Seriously debilitating diseases or life threatening diseases, • Emergency situations, • Orphan medicinal products Fulfilling all of the following criteria: <ul style="list-style-type: none"> • Positive risk-benefit balance • Applicant likely to be able to provide comprehensive data after authorisation • Fulfillment of unmet medical need • Benefits of immediate availability outweigh the risks that additional data are still required. 	Unauthorised medicinal products fulfilling the following criteria: <ul style="list-style-type: none"> • Chronically, seriously debilitating or life threatening disease, with no satisfactory treatment authorised in the EU, • For a "group of patients", • Undergoing centralised MA or clinical trials • Falling under mandatory or optional scope of centralised procedure
Key features	<ul style="list-style-type: none"> • Identify potential for accelerated assessment earlier in development • Early rapporteur appointment • Reinforced scientific and regulatory support from the SWMP, CHMP, other relevant scientific committees and EMA • Dedicated contact person within EMA 	<ul style="list-style-type: none"> • Reduced MA assessment time to maximum 150 days (compared to standard 210 days) 	<ul style="list-style-type: none"> • Earlier authorisation of medicines for patient with unmet medical needs, on the basis of less complete clinical data. • Comprehensive data generated post authorisation within agreed timeframe. 	<ul style="list-style-type: none"> • Benefit seriously ill patients who cannot be treated satisfactorily or cannot enrol in ongoing clinical trials • CHMP recommendations to MS to harmonise the conditions of use, distribution and the target population.

Development support and regulatory tools for early access to medicines
EMA/531851/2015

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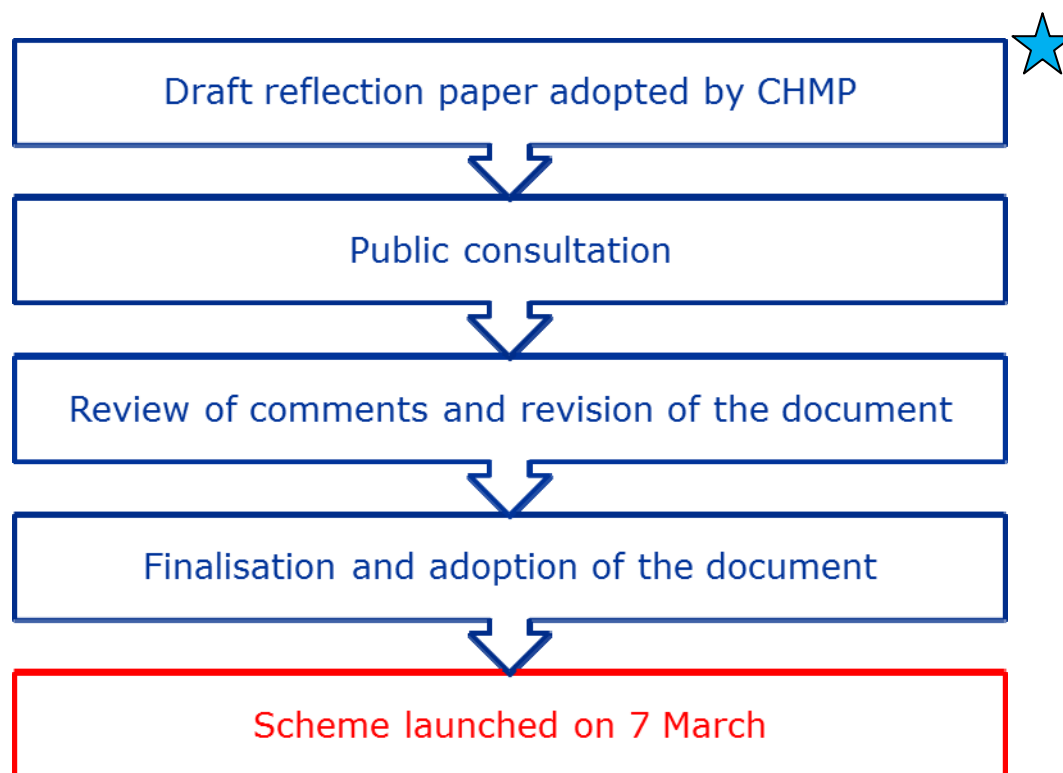
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1 Update on PRIME and CHMP Guidelines for early access tools



PRIME

After discussions at all STAMP 2015 meetings



25 February 2016
EMA/CHMP/57760/2015
Committee for Medicinal Products for Human Use

Enhanced early dialogue to facilitate accelerated assessment of priority medicines (PRIME)

Draft presented to CHMP, CAT, COMP, PDCD, PRAC, and SAWP	June-September 2015
Adopted by the CHMP for release for consultation	22 October 2015
Start of public consultation	26 October 2015
End of consultation (deadline for comments)	23 December 2015
Adopted by CHMP	25 February 2016
Date for coming into effect	7 March 2016

Keywords Accelerated assessment, unmet medical need, development support, scientific advice, early dialogue

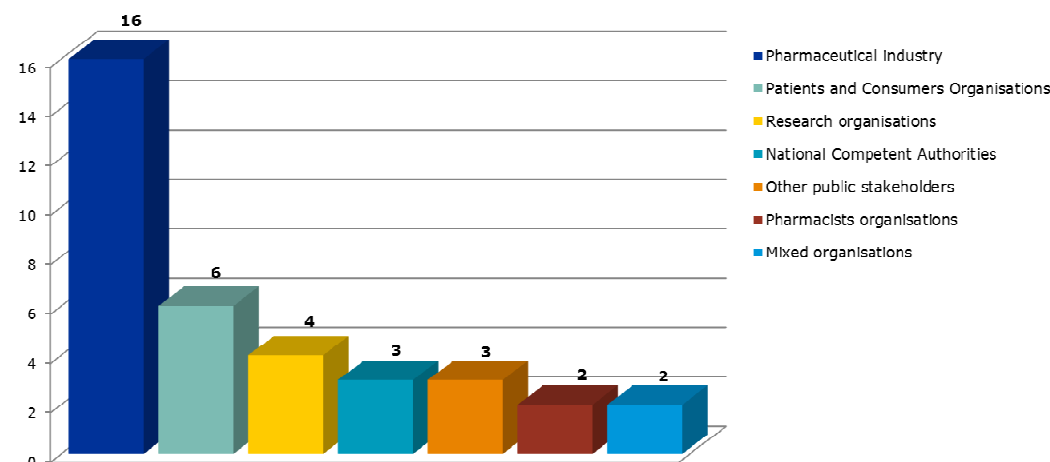
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Public consultation on PRIME

- 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 fulfil 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.



PRIME - Main changes after public consultation (2)

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.



PRIME - Main changes after public consultation (3)

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

In early stages of development, following demonstrated proof of principle, focusing on SMEs and applicants from the academic sector:

- Raising awareness of regulatory requirements early in the development, by providing scientific and regulatory advice on the overall development plan and at major development milestones, with the possibility to involve multiple stakeholders (e.g. Health Technology Assessment (HTA) bodies, patients).
- Eligibility to PRIME may help these applicants to overcome financial hurdles³ to progress through later stages of the development.
- Upon request, SMEs and applicants from the academic sector⁴ may also be eligible for fee reductions on their scientific advice requests, upon case-by-case decisions.



PRIME - Main changes after public consultation (4)

New section to highlight importance of collaborations

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

7. Collaboration

Innovation offices 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.

EMA is committed to facilitating as much as possible the assessment of priority medicines done by **health technology assessment (HTA) bodies**, 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.

The importance of considering PRIME in the context of global developments and **international cooperation** 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.



PRIME webpage and supporting documents

The screenshot shows the PRIME webpage interface. At the top, it identifies the agency as 'An agency of the European Union'. The main navigation bar includes links for Home, Find medicine, Human regulatory (selected), Veterinary regulatory, Committees, News & events, Partners & networks, and About us. A sidebar on the left lists various regulatory and support services, with 'Support for early access' highlighted. The main content area features a header for 'PRIME: priority medicines' and a large graphic with the text 'PRIME - PRIORITY MEDICINES'. Below this, a paragraph explains that PRIME is a scheme launched by the EMA to enhance support for the development of medicines that target an unmet medical need. It is based on enhanced interaction and early dialogue with developers of promising medicines to optimise development plans and speed up evaluation so these medicines can reach patients earlier. Further down, there are sections for 'Accelerated assessment', 'Fostering early dialogue', and 'Related content' which includes links to 'Support for early access' and 'Launch of PRIME - Paving the way for promising medicines for patients (07/03/2016)'. A 'PRIME at a glance - Factsheet' is also visible.

The factsheet graphic is titled 'PRIME - PRIORITY MEDICINES' and 'Paving the way for promising medicines for patients'. It features a blue and white color scheme with a molecular structure background. Key sections include:

- Why PRIME is needed:** Many patients with serious diseases have no or only unsatisfactory therapeutic options and should be able to benefit from scientific advancement and cutting-edge medicines as early as possible.
- Benefits of PRIME:**
 - FOR PATIENTS:**
 - PRIME is driven by patients' needs.
 - It focuses on medicines that address an unmet medical need, or offer a major therapeutic advantage over existing treatments, or benefit patients with no current treatment options for their disease.
 - It helps to translate research into the development of medicines with meeting regulatory requirements.
 - It aims to bring promising treatments to patients earlier, without compromising the evaluation standards in post-market safety.
 - FOR MEDICINE DEVELOPERS:**
 - PRIME helps developers of promising new medicines to complete development plans.
 - It fosters early dialogue with EMA to facilitate critical data collection and high quality marketing authorisation applications.
 - It speeds up evaluation so that medicines can reach patients earlier.
 - It encourages developers to focus resources on medicines likely to make a real difference to patients' lives.
- PRIME: in brief:** Medicines eligible for PRIME must address an unmet medical need. Preliminary data must be available showing the potential to address this need and bring a major therapeutic advantage to patients. EMA will provide early and enhanced support to streamline the development of eligible medicines, based on their evaluation and contribute to timely patient access.

**Factsheet
in lay
language**

**Q&A,
templates,
application
form for
applicants**

The screenshot shows the 'European Medicines Agency Guidance for applicants seeking access to PRIME scheme'. It is dated 7 March 2016 (EMA/15104/2015) and issued by the Human Medicines Research and Development Support Division. The document addresses questions that applicants seeking support through the PRIME scheme may have. It explains the scope and features of PRIME, provides an overview of the procedure to obtain support, and gives guidance to companies in preparing their requests. The guidance will be updated regularly to reflect new developments as experience is gained with the scheme. It should be read in conjunction with:

- [Enhanced early dialogue to facilitate accelerated assessment of Priority Medicines \(PRIME\)](#)
- [Guidance on accelerated assessment](#)
- [European Medicines Agency guidance for applicants seeking scientific advice and promote assistance](#)

 If you require further information on any of the included topics, do not hesitate to send your request to primo@ema.europa.eu and we will deal with your query in a timely manner.



Update of CHMP Guidelines on accelerated assessment and conditional MA



* for CMA guideline only

★ Update provided to STAMP

9 Update on PRIME and CHMP Guidelines for early access tools

25 February 2016
EMA/CHMP/007031/2014-Rev. 1

Guideline on the scientific application and the practical arrangements necessary to implement the procedure for accelerated assessment pursuant to article 14(9) of regulation (EC) No 726/2004

Draft presented to CHMP, PRAC and CAT	May/June 2015
Adopted by the CHMP for release for consultation	23 July 2015
Start of public consultation	27 July 2015

25 February 2016
EMA/CHMP/009931/2006, Rev.1
Committee for Medicinal Products for Human Use

Guideline on the scientific application and the practical arrangements necessary to implement Commission Regulation (EC) No 507/2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004

CHMP discussion	July 2006
Adopted by CHMP for release for consultation	14 December 2006
End of consultation (deadline for comments)	31 March 2007
Drafting of revision 1 of the guideline	January – May 2015
Consultation with PRAC, CAT, COMP, PDCCO	June 2015
Adopted by CHMP for release for public consultation	23 July 2015
Start of public consultation	27 July 2015
End of consultation (deadline for comments)	30 September 2015
Receipt of a favourable opinion of the European Commission	22 February 2016
Final guideline adopted by the CHMP	25 February 2016
Date for coming into effect	1 June 2016

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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**)



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



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

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Compassionate use
Adaptive pathways
Scientific guidelines
Innovation Task Force
SME office
Paediatric medicine
Geriatric medicine
Orphan designation
Herbal products

Support for early access

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Medicines approved since 2006 using early access tools

28 Opinions for conditional marketing authorisations

22 Medicines evaluated under accelerated assessment



Thank you for your attention

Further information

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