Guidance on Early Access tools – Revision based on experience gain

News

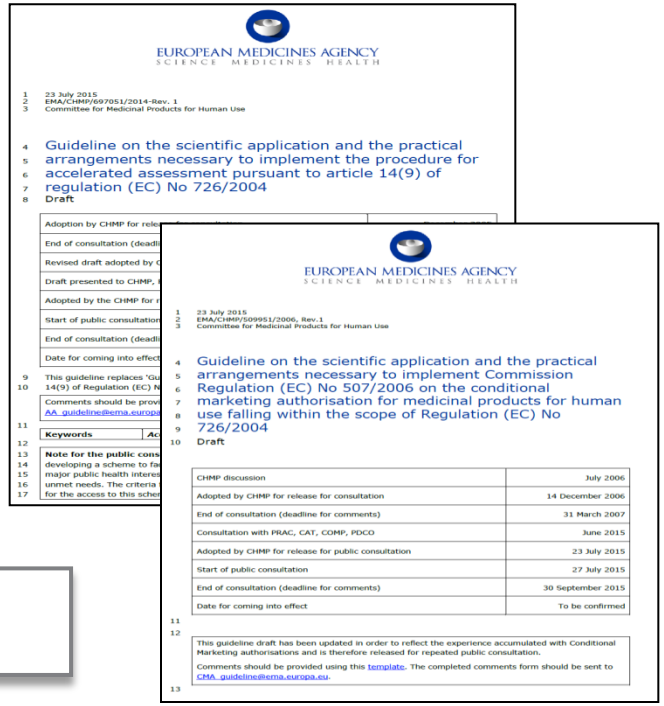
27/07/2015

Fast track routes for medicines that address unmet medical needs

Launch of two-month public consultations on revised guidelines on accelerated assessment and conditional marketing authorisation

The European Medicines Agency (EMA) has revised its guidelines on the implementation of accelerated assessment and conditional marketing authorisation, two key tools in the European legislation to accelerate patients' access to medicines that address unmet medical needs.

EMA/CHMP/697051/2014 Rev. 1
EMA/CHMP/509951/2006 Rev. 1


EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 July 2015
EMA/CHMP/697051/2014-Rev. 1
Committee for Medicinal Products for Human Use

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 July 2015
EMA/CHMP/509951/2006, 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
Draft

CHMP discussion	July 2006
Adopted by CHMP for release for consultation	14 December 2006
End of consultation (deadline for comments)	31 March 2007
Consultation with PRAC, CAT, COMP, PDCO	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
Date for coming into effect	To be confirmed

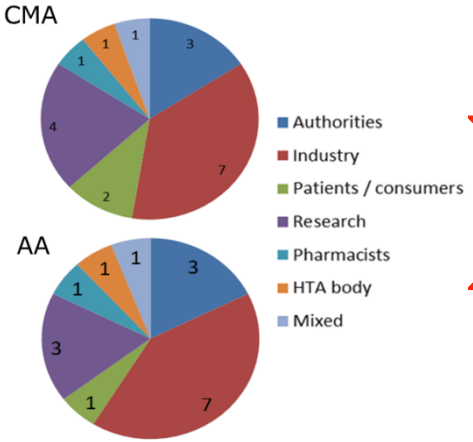
This guideline draft has been updated in order to reflect the experience accumulated with Conditional Marketing authorisations and is therefore released for repeated public consultation.

Comments should be provided using this template. The completed comments form should be sent to CMA_guideline@ema.europa.eu.

Publication of the final revision of these guidelines following the public consultation is foreseen in 1Q16.

Contributions from various stakeholders during the process for the revision

Reflections on experience with AA and CMA[#] → Drafting of guideline updates → Consultation with other committees → Public consultation



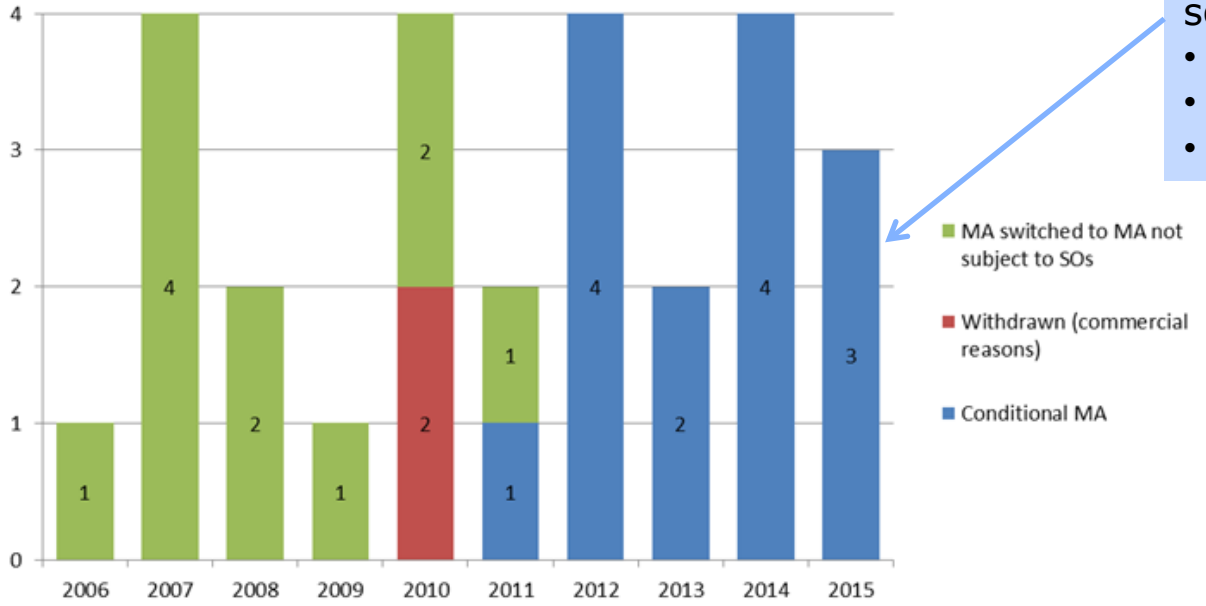
currently

Review of comments and revision of the guidelines → Favourable opinion of the European Commission* → Finalisation and adoption of the guidelines

[#] AA = Accelerated assessment; CMA = Conditional marketing authorisation

* For the Guideline on Conditional marketing authorisation only

Conditional Marketing Authorisation granted in the centralised procedure



Conditional Marketing Authorisations in 2015 so far:

- Holoclar
- Zykadia
- Blincyto

Experience with Conditional Marketing Authorisations (CMAs) so far in 2015

New CMAs authorised

Zykadia (ceritinib)	(ALK)-positive advanced non-small cell lung cancer (NSCLC) in patients previously treated with crizotinib
Holoclar (autologous human corneal epithelial cells containing stem cells)	Treatment of moderate to severe limbal stem cell deficiency, unilateral or bilateral, due to physical or chemical ocular burns
Blincyto (blinatumomab)	Philadelphia chromosome negative relapsed or refractory B-precursor acute lymphoblastic leukaemia

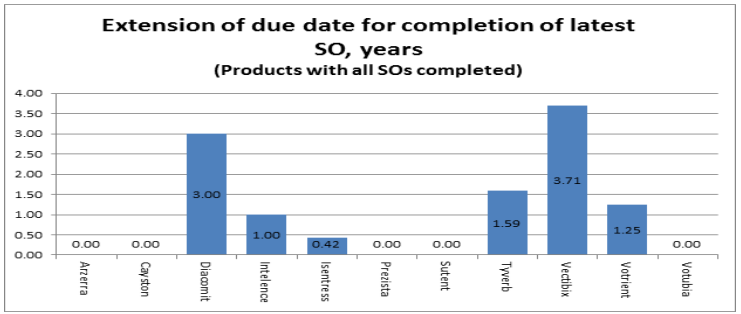
Switch of CMAs

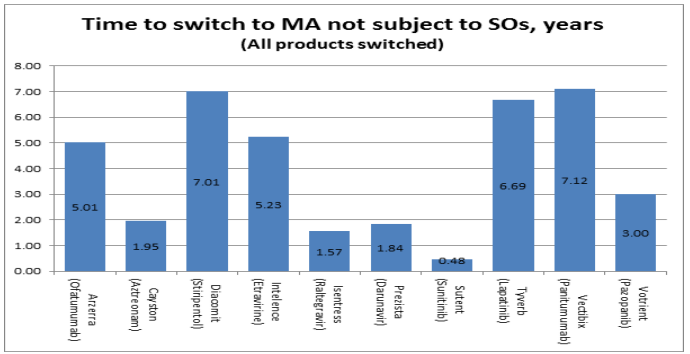
Vectibix (Panitumumab)	15/01/2015
Tyverb (Lapatinib)	17/02/2015
Arzerra (Ofatumumab)	24/04/2015
Votubia (Everolimus)	16/11/2015

Conditional marketing authorisations are aimed at being switched to full marketing authorisations once comprehensive data was generated, and this is followed up closely.

Overall experience with time to 'switch' from conditional to full marketing authorisation

- Approximately half of the products had changes to the scope and/or deadline of at least one of the specific obligations
- For 11 products with Specific Obligations (SOs) completed, on average the due date for completion of the **last SO was extended by 1 year**
- For 10 products that currently have a full MA (i.e. no longer subject to SOs), the switch was granted **on average after 4 years**





Note: data lock September 2015

Based on experience: Draft revision of the guideline on conditional marketing authorisation (CMA)

High-level summary of changes

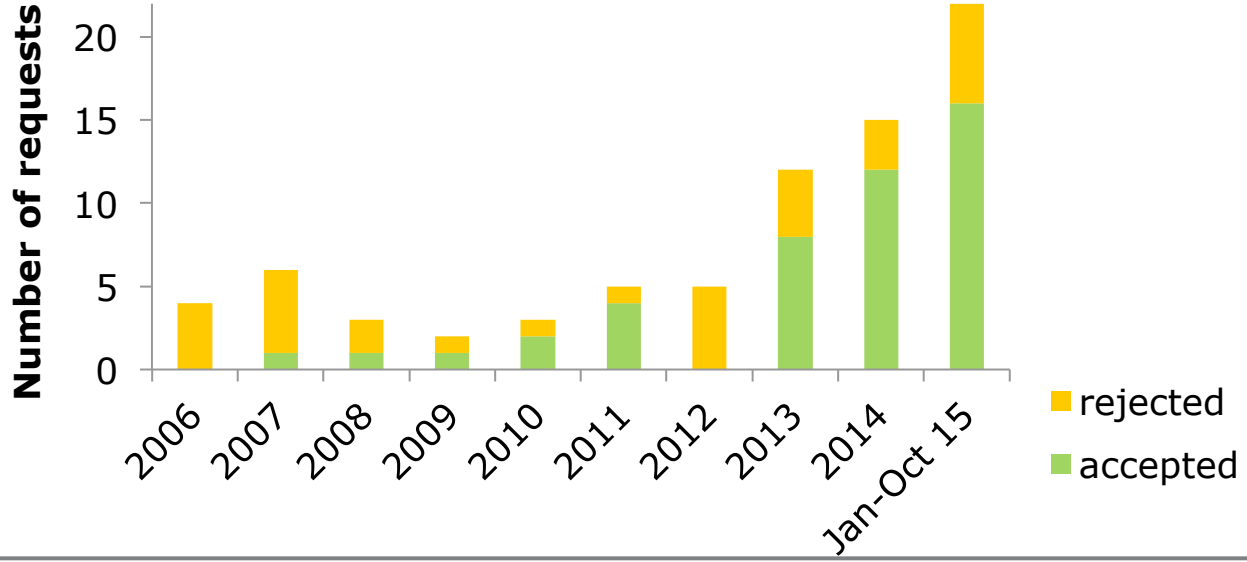
Content

- Clarification how a positive benefit-risk balance should be substantiated where there are less complete data
- Examples and further guidance on the level of evidence that must be provided at the time of authorisation and data that can be provided post-authorisation
- Guidance on when a condition could be considered life threatening or seriously debilitating if these effects are in the long-term
- Clarification on fulfilment of unmet medical needs, i.e. medicines providing major improvements in patient care over existing therapies can be eligible in certain cases

Planning and submission requirements

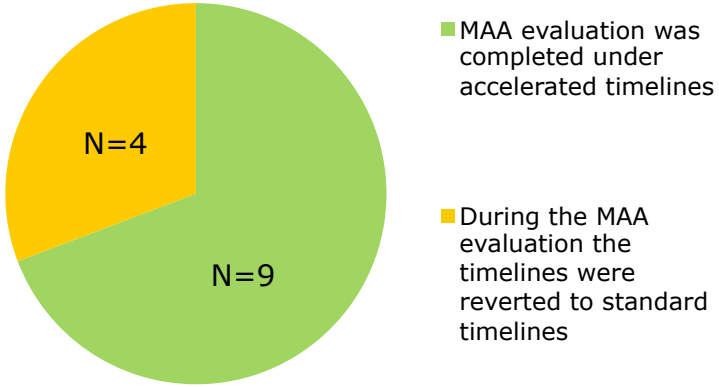
- Emphasis on importance of planning conditional marketing authorisation prospectively to ensure swift assessment procedure
- Emphasis on advantages of engaging in early dialogue with EMA on the development programme, in particular in the context of parallel scientific advice with health technology assessment bodies
- Updated guidance on extent and type of data required to be included in annual renewal submissions

Experience with Accelerated Assessment: Number of requests and acceptance rates



An increase in requests for accelerated assessment was observed over the last years along with a increase of acceptance rate of such requests.

Adherence to the accelerated review during the evaluation of the marketing authorisation



Reasons for reverting to standard timelines during the MAA evaluation:

- Critical GCP issues identified in inspections
- Major objection on adequacy of extrapolation
- Need for a GMP inspection
- Major clinical objection questioning the clinical relevance of the effects
- Numerous major objections including need for re-analysis of efficacy data
- Significant quality major objection

Note: Data analysed concerns MAAs with Opinions in 01/2014-10/2015, for which a request for accelerated assessment was accepted.

Robust decision making under accelerated timelines requires a mature submission, which should be subject to pre-filing discussions.

Based on experience : Draft revision of the guideline on accelerated assessment (AA)

High-level summary of changes

Content

- More detailed guidance on how to justify major public health interest (unmet medical need, strength of evidence)
- Acknowledgment that comprehensive clinical data may not be available in certain situations, allowing accelerated assessment in the context of a conditional marketing authorisation for example

Process

- Intent to request accelerated assessment to be indicated 6-7 months in advance and submission of accelerated assessment request to take place 2-3 months ahead of marketing authorisation application
- Importance of early dialogue / pre-submission discussions.
- Optimisation of the assessment timetable by better balancing evaluation phases to reach a CHMP opinion within 150 days

PRIME scheme to reinforce scientific and regulatory support to medicines of major public health interest

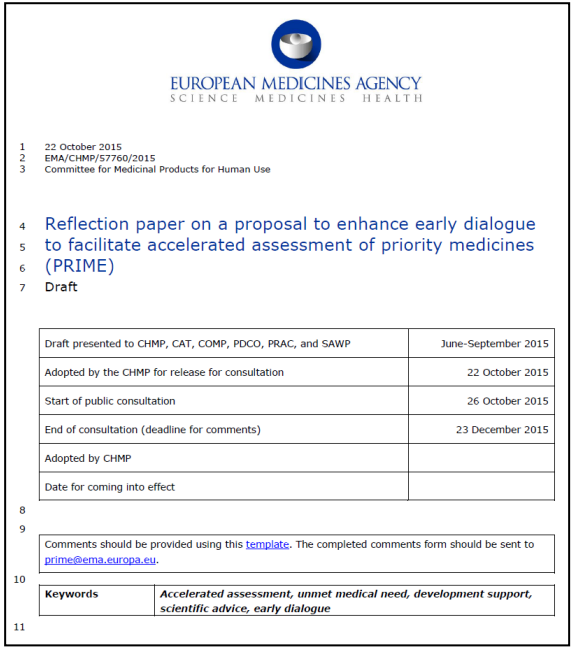
26/10/2015

Public consultation starts on PRIME - a new scheme to optimise development of priority medicines and facilitate patients' access

PRIME aims to reinforce scientific and regulatory support to medicines of major public health interest

New development to strengthen support to medicines that have the potential to benefit patients who presently have no treatment options, or that may offer a major therapeutic advantage over existing treatments.

Under public consultation until 23 December 2015.



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22 October 2015
EMA/CHMP/57760/2015
Committee for Medicinal Products for Human Use

Reflection paper on a proposal to enhance early dialogue to facilitate accelerated assessment of priority medicines (PRIME)

Draft

Draft presented to CHMP, CAT, COMP, PDCO, 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	
Date for coming into effect	

Comments should be provided using this template. The completed comments form should be sent to prime@ema.europa.eu.

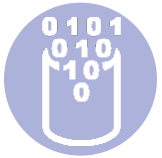
Keywords	***Accelerated assessment, unmet medical need, development support, scientific advice, early dialogue***

Goal and scope of the PRIME scheme

To foster the development of ***medicines with high public health potential.***

Reinforce scientific and regulatory advice

- *Foster and facilitate early interaction*
- *Raise awareness of requirements earlier in development*



Optimise development for robust data generation

- *Focus efficient development*
- *Promote robust data generation*

Enable accelerated assessment

- *Promote generation of high quality data*
- *Facilitated by knowledge gained throughout development*

Building on existing framework;

Eligibility according to existing Accelerated Assessment criteria.

Eligibility to PRIME scheme

For products under development which are yet to be placed on the EU market.

- *Entry to scheme at two different stages in development:*
  - *at the earlier stage of **proof of principle** (prior to phase II/ exploratory clinical studies) focusing on SMEs.*
  - *at **proof of concept** (prior to phase III/confirmatory clinical studies).*
- *Must be based on adequate data to justify a potential major public health interest.*

Applicants not eligible to PRIME can still request accelerated assessment.
Guideline of the procedure for Accelerated Assessment pursuant to Article 14(9) of Regulation (EC) No 726/2004.

Benefits of the PRIME scheme

Early access tool, supporting patient access to innovative medicines.

- *Early confirmation of potential for accelerated assessment;*
- *Written confirmation of PRIME eligibility;*
- *Timely CHMP Rapporteur appointment;*
- *Scientific advice at key development milestones/decision points;*
- *Early, proactive, continuous and strengthened regulatory support;*
- *Promote awareness and better use of existing development and authorisation tools;*
- *EMA dedicated entry point;*
- *Complementarity and collaboration with National innovation schemes;*
- *Fee incentives for SMEs on Scientific Advice requests.*

Early access tools: Overview

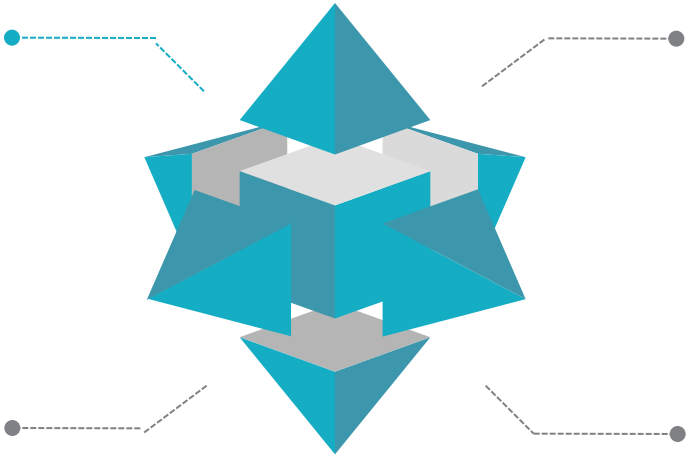
PRIME

Major public health interest, unmet medical need.

Dedicated and reinforced support.

Enable accelerated assessment.

Better use of existing regulatory & procedural tools.



Adaptive Pathways

Scientific concept of development and data generation.

Iterative development with use of real-life data.

Engagement with other healthcare-decision makers.

Accelerated Assessment

Major public health interest, unmet medical need.

Reduce assessment time to 150 days.

Conditional MA

Unmet medical need, seriously debilitating or life-threatening disease, a rare disease or use in emergency situations.

Early approval of a medicine on the basis of less complete clinical data.

Take home messages: EU early medicinal product access tools

- European medicines regulation has established early access tools to ensure timely approval and patient access to important new medicines;
- Continuous improvement based on experience is ongoing to promote better use of existing tools;
- Further support is developed to optimise current regulatory tools by increasing efficiency of development and quality of data;

Plans for 1st quarter 2016: Finalisation of the revised guidance on early access tools and launch of the PRIME scheme.

Thank you for your attention

Further information

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