EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Implementation of the 2016 Notice on the application of the Orphan Regulation

Approach to the implementation with regard to procedural, regulatory and scientific elements

Industry stakeholder platform on research and development support

Presented by Kristina Larsson on 25 April 2017
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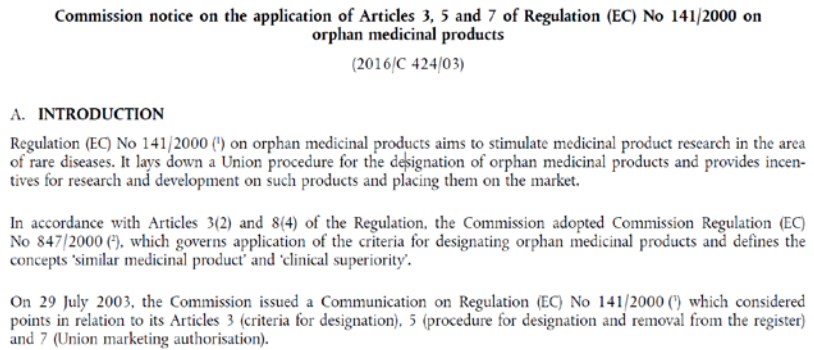
Commission notice on the application of Articles 3, 5 and 7 of Regulation (EC) No 141/2000 on orphan medicinal products



Commission notice on the application of Articles 3, 5 and 7 of Regulation (EC) No 141/2000 on orphan medicinal products

(2016/C 424/03)

A. **INTRODUCTION**

Regulation (EC) No 141/2000 [1] on orphan medicinal products aims to stimulate medicinal product research in the area of rare diseases. It lays down a Union procedure for the designation of orphan medicinal products and provides incentives for research and development on such products and placing them on the market.

In accordance with Articles 3(2) and 8(4) of the Regulation, the Commission adopted Commission Regulation (EC) No 847/2000 [2], which governs application of the criteria for designating orphan medicinal products and defines the concepts 'similar medicinal product' and 'clinical superiority'.

On 29 July 2003, the Commission issued a Communication on Regulation (EC) No 141/2000 [3] which considered points in relation to its Articles 3 (criteria for designation), 5 (procedure for designation and removal from the register) and 7 (Union marketing authorisation).

- Replacing 'Communication from the commission regulation (EC) No 141/2000, 2003/C 178/02'
- Published in November 2016
- Updated guidance on the application of the orphan regulation (EC) No 141/2000

Significant benefit

The criteria for significant benefit are further outlined in the Commission notice.

"Significant benefit' is established by means of comparison with existing authorised medicinal products or methods, not just by assessing the intrinsic qualities of the product in question"….

"the spirit underlying the system it establishes that the criteria for a finding of significant benefit are strict"

- Claims at time of MAA should be based on clinical data.
- Should include a quantitative element that allows the COMP to measure magnitude of effect as compared with an already authorised product.

Significant benefit cont.

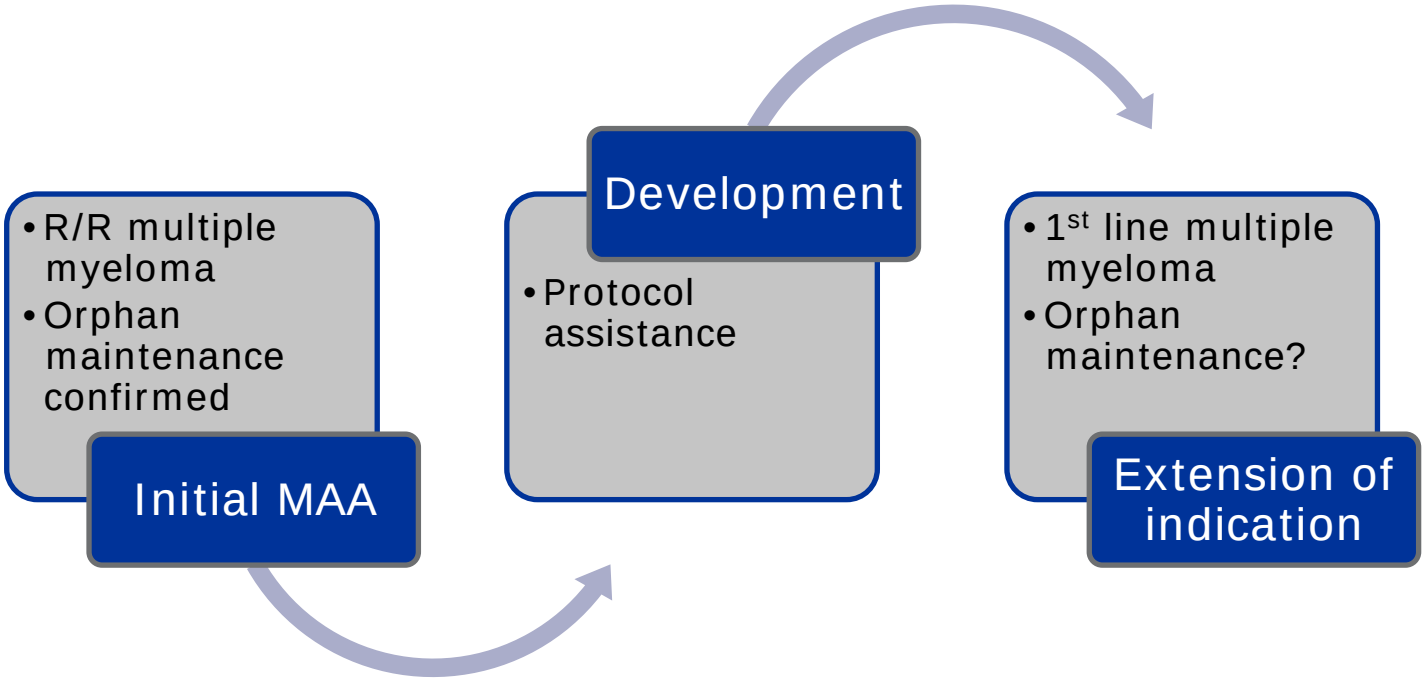
Should not be based on:

- possible increased supply/availability due to shortages of existing authorised products or to existing products being authorised in only one or a limited number of Member States (except evidence of patient harm).
- a new pharmaceutical form, a new strength or a new route of administration unless it brings major contribution to patent care.
- an alternative mechanism of action *per se*.

Parallel applications

- The sponsor of the 2nd product should not be asked to show significant benefit over the 1st product.
- BUT: if the notification of marketing authorisation of 1st product is published in the Official Journal of the EU at the time of re-evaluation of the orphan drug criteria, the sponsor of the 2nd product should show data supporting significant benefit as compared with the 1st product.

Reassessment at extension/modification of indication



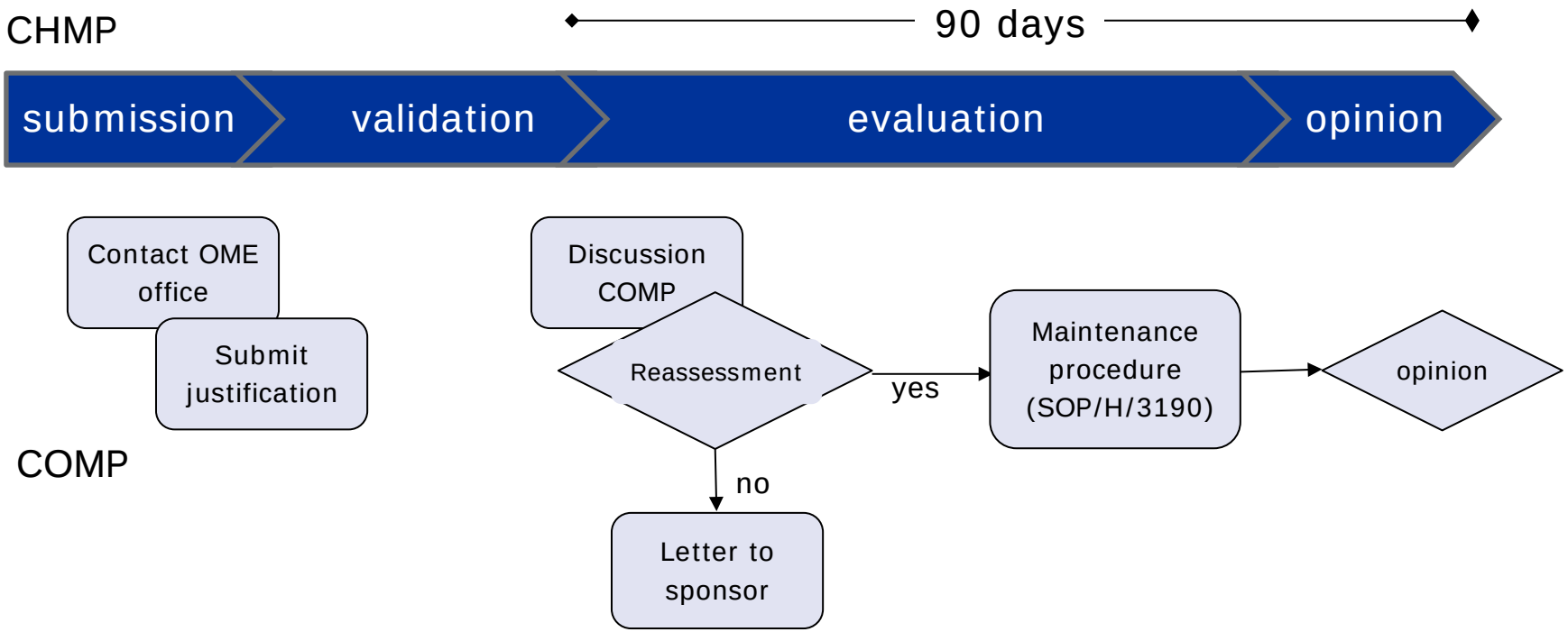
Consequences of non-confirmation of orphan status

Split Marketing authorisation:

One orphan and one non-orphan

Withdraw orphan status and have non-orphan product with extended indication.

Process for reassessment, extension/modification of indication



One approval per medicinal product and condition

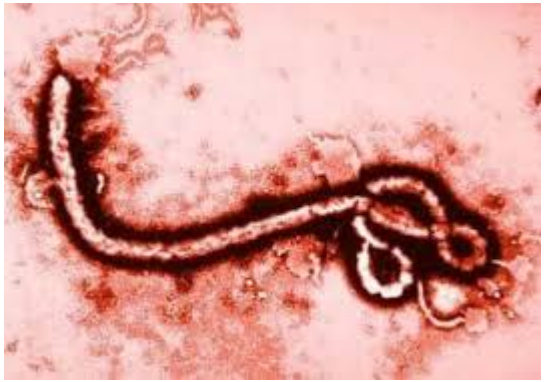
- One orphan designation per condition/active ingredient/sponsor for any given medicinal product.
- New subsequent formulations and routes of administration fall within the scope of the existing orphan designation.
- Not possible to transfer an orphan designation to a sponsor who already has a marketing authorisation for the same medicinal product and condition.

Hospital preparations

- In certain cases, medicinal products prepared for an individual patient in a pharmacy according to a medical prescription ‘magistral formula’ / ‘officinal formula’, may be considered as satisfactory treatment.
- Even if the product is not placed on the market, patients would still be treated with a hospital formulation.
- A product prepared in a hospital under a hospital exemption scheme (ATMPs) should not be considered a satisfactory method.

Prevalence “0”

- Communicable diseases can very rapidly become a serious threat to public health.
- A prevalence of approximately zero in the EU, may be eligible for designation.
- Where prevalence in the EU is currently approximately zero, account should be taken of the risk that persons in the EU may become affected.



Conclusions

- The “Notice” gives updated guidance on the orphan legislation.
- Most important aspect of the Notice is the procedure for reassessment at extension of indication.
- There is untapped potential in terms of guidance on evidence generation through protocol assistance and developers are encouraged to use these opportunities.
- The OME office is always happy to help, do contact us if you have any questions.