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Reflection Paper
Criteria for requiring one additional five-year renewal for Centrally Authorised Medicinal Products

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Background

According to Art 14.3 of Regulation EC (No) 726/2004, a marketing authorisation...

> *…. once renewed, shall be valid for an unlimited period, unless the Commission decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal.*

Art 16.2 of Regulation EC (No) 726/2004 also states that

> *…. In order that the risk-benefit balance may be continuously assessed, the Agency may at any time ask the MAH to forward data demonstrating that the risk-benefit balance remains favourable ……..…..*

The CHMP/NTA Guideline on the processing of renewals in the Centralised Procedure (EMEA/2990/00 rev. 03), indicated in section 3.4 that

> *… guidance on the criteria or factors considered by CHMP when requiring one additional five-year renewal will be provided in due time taking into account experience gained.*

Since September 2005, EMEA/CHMP has been adopting renewal opinions according to the new legal provisions, recommending unlimited validity or one additional renewal.

The purpose of this document is to set-out criteria/factors which will be considered by CHMP when determining the need for one additional renewal of the product concerned, based on pharmacovigilance grounds.

Criteria/factors

In general, if the safety profile of a product should be closely monitored this could be obtained by requiring an increased PSUR frequency reporting, by requiring specific post-marketing studies or a pharmacovigilance inspection (e.g. in case of concerns regarding the MAH's pharmacovigilance system). As a further tool, CHMP could consider requiring one additional five-year renewal which would provide for an additional benefit-risk assessment.

The following criteria/factors should be considered:

1. Limited exposure

- Medicinal products for which limited safety information is available because of limited exposure due to e.g.
  - recent marketing of the medicinal product
  - limited marketing of the medicinal product (e.g. only in a few member states, only few presentations marketed).
  - limited use in a recently approved new indication.

  Based on the new PSUR requirements, a recently marketed product would still fall within the 6-monthly or yearly reporting frequency at the time of renewal.
  Note: This would however not mean that orphan drugs, due to the low prevalence of the disease, would always require an additional renewal.

- Medicinal products for which the marketing authorisation, or any of its indications, had been suspended.

- Medicinal product currently not marketed as it is intended only to be used in emergency situations, in response to public health threats duly recognised either by the WHO or by the Community (Decision No. 2119/98/EC).

2. Safety concerns

- Medicinal products with a particular safety issue which could impact on the benefit-risk balance of the product, e.g. those for which specific measures need to be taken and which need to be monitored in order to manage the risks (i.e. specific risk minimisation measures).

- Medicinal products for which post-marketing studies are ongoing/ planned[1], the results of which are expected to yield important new safety data which could impact on the benefit-risk balance of the product.

- Medicinal products for which a class review of a serious safety issue is ongoing or imminent.

3. Other

- Medicinal products authorised under exceptional circumstances: if the renewal opinion recommends that the MA should be maintained under exceptional circumstances since a (number of) specific obligation(s) are still outstanding, an additional renewal may be appropriate in case of remaining pharmacovigilance concerns, before granting unlimited validity. If the renewal opinion recommends a switch to a "normal MA", CHMP could recommend unlimited validity or could consider requiring one additional 5-year renewal taking into account the above-mentioned criteria (as for any other product with a 'normal' MA).

- Medicinal products authorised as a conditional MA will require a yearly renewal until they are switched to a 'normal' MA. In such a case, the 'normal' MA will be valid for 5-years and at the time of renewal, CHMP could recommend unlimited validity or could consider requiring one additional 5-year renewal taking into account the above-mentioned criteria (as for any other product with a 'normal' MA).

[1] Where possible, the renewal date should be considered when agreeing the timing for such studies with MAHs.