Policy document MEB 42

Renewal of medicinal products for human use authorised through the national procedure

3 August 2022

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2 Introduction

Section 47 of the Dutch Medicines Act (effective date 1 July 2007) stipulates that a marketing authorisation has a limited period of validity when first granted. After five years, the Medicines Evaluation Board (MEB) must carry out a benefit/risk assessment to decide whether this authorisation may be renewed and, if so, whether the renewal will be granted for an indefinite period or, in connection with pharmacovigilance, for one additional period of five years.

For each product authorised through the national procedure (hereinafter referred to as 'strictly national products'), the MEB will make a decision regarding renewal of the marketing authorisation. Replica authorisations are given the authorisation date as assigned for the reference product.

3 Renewal procedure

Each year the MEB compiles a list of all strictly national products whose marketing authorisation expires in the relevant year. Exempted from this are parallel authorisations, replica authorisations and products which have undergone a Mutual Recognition Procedure (MRP).

For each product on the list, the MEB determines whether the marketing authorisation can be renewed based on the available data in the dossier and current knowledge about the active ingredient(s) in relation to the indication(s) of the product concerned (including PSUSA data). If the available data in relation to the indication(s) do not give reason to revise the benefit/risk balance of the product concerned, the marketing authorisation will be renewed. Based on the criteria as described in the EMA Reflection Paper '*Criteria for requiring one additional five-year renewal*' (see §3.1), the MEB determines whether the marketing authorisation will be renewed for an indefinite period or for one additional period of five years.

The holder of the marketing authorisation does not need to submit a renewal request/renewal dossier. The data on which the MEB will base its decision regarding renewal and type of renewal (indefinite period or five years) are already available. In making its decision, the MEB will take into account current knowledge about the active ingredient(s) in relation to the indication(s).

The date of renewal is five years after the date on which the marketing authorisation was granted.

<u>Follow-up action in the event of five-year renewal</u>

Renewal of the authorisation will be granted for an indefinite period unless, based on justified grounds relating to pharmacovigilance, the decision is made to renew the authorisation for one additional five-year period (see §3.1). If the MEB decides to renew for a five-year period, the marketing authorisation holder will receive an explanation of this decision from the MEB.

The marketing authorisation holder must then submit a renewal request to the MEB at least nine months before the authorisation expires (i.e. four years and three months after the renewal date), together with a version of the dossier which refers to the quality, safety and efficacy of the medicinal product (including the changes which have been made in relation to these aspects since the marketing

authorisation was granted) (Section 47 of the Dutch Medicines Act and Article 24 of Directive 2001/83/EC). This means that a renewal dossier must be submitted which complies with the requirements in Annex 3 (*'Documents to submit'*) of the CMDh's *'Best Practice Guide on the Processing of Renewals in the Mutual Recognition and Decentralised Procedures'*. Based on the information provided and current knowledge about the active ingredient(s) in relation to the indication(s), the MEB will decide either to grant renewal for an indefinite period (in the event of a positive benefit/risk balance) or express the intention to revoke the authorisation (in the event of a negative benefit/risk balance).

Follow-up action in the event of negative benefit/risk balance

If, based on the available data in relation to the indication(s), the MEB determines that for reasons of pharmacovigilance the benefit/risk balance is no longer positive, an intention to revoke the authorisation, along with an accompanying explanation, will be sent to the marketing authorisation holder. The marketing authorisation holder will then be given the opportunity to submit additional information and/or argumentation within one month of the date of the letter from the MEB in order to respond to the MEB's explanation of the negative benefit/risk balance. The MEB will determine whether the additional information and/or argumentation affects its assessment of the benefit/risk balance and whether the authorisation should still be revoked or, subject to certain restrictions/conditions or otherwise, that it is possible to instead grant a renewal for five years or for an indefinite period.

Communication in the event of renewal

Each year, a list of strictly national products whose marketing authorisation has been renewed for an indefinite period or for a period of five years is published in the Dutch Government Gazette.

The holders of the marketing authorisations, which have been renewed for an indefinite period or for five years, are also informed of this in a letter from the MEB. The letter states the product names and RVG numbers of the products whose authorisation has been renewed. The renewal date and renewal period are included in the letter as well.

If renewal has been granted for a five-year period instead of for an indefinite period, the letter will be supplemented with an explanation of the MEB's decision, along with the notification that the marketing authorisation holder must submit a renewal request at least nine months before the authorisation expires.

Marketing authorisation and SmPC

In principle, the marketing authorisation and SmPC will not be amended during the renewal procedure:

- With the next variation affecting the SmPC, the marketing authorisation holder is asked to state the granted renewal date of the authorisation in Section 9, and additionally to state in Section 10 that Section 9 has been amended. In the context of the renewal procedure, it is not possible for the marketing authorisation holder to submit an SmPC with amended Sections 9 and 10, or to submit a separate variation in which no amendments are presented in the dossier other than entry of the renewal date in the SmPC.
- When the marketing authorisation is next revised, the renewal date and type (indefinite period or five years) will be stated on the marketing authorisation.

The MEB will only request an amendment to the SmPC in those exceptional cases where this amendment is necessary to maintain a positive benefit/risk balance.

4 Assessment criteria

4.1 Criteria for five-year renewal

In accordance with current European and Dutch legislation (Article 24.3 of Directive 2001/83/EC and Section 47.3 of the Dutch Medicines Act, respectively), renewal will be granted for an indefinite period unless, based on justified grounds relating to pharmacovigilance, the decision is made to renew for five years.

The EMA Reflection Paper *'Criteria for requiring one additional five-year renewal'* provides a more detailed explanation of these grounds for granting a renewal for five years.
As with renewal procedures for MRP/DCP products, for which the Netherlands is the Reference Member State (RMS), the MEB applies the criteria as described in this EMA Reflection Paper as grounds for granting renewal for a period of five years during the renewal procedure for strictly national products.

4.2 Criteria for denial of renewal

If, after assessing the available information about the active ingredient(s) in relation to the indication(s), the MEB concludes that the benefit/risk balance is no longer positive, the decision will be made to express the intentions to revoke the authorisation. Article 116 of Directive 2001/83/EC provides a more detailed explanation of the grounds for denial of renewal. As with renewal procedures for MRP/DCP products, in which the Netherlands is a Reference Member State (RMS), the MEB will apply the grounds described here when deciding whether to revoke an authorisation.

5 In closing

The MEB always has access to sufficient and up-to-date information about the efficacy, safety and quality of the medicinal products which have been granted a marketing authorisation. The benefit/risk balance is continuously monitored through active pharmacovigilance. In addition, the dossiers of authorised products are always kept up-to-date through such efforts as the abovementioned active pharmacovigilance, the risk-based updating programme, the harmonisation of product information initiated by the MEB for the purpose of implementing class-labelling effects (clean-ups) and variations initiated by marketing authorisation holders. Monitoring of the benefit/risk balance therefore does not stop after renewal, but is instead a continuous process from the moment a marketing authorisation is granted until the authorisation is withdrawn. Renewal is only a snapshot of five years, or a multiple thereof, after authorisation Furthermore, the marketing authorisation holder is required to inform the MEB if and as soon as he/she obtains information that could affect the benefit/risk balance of the product. This obligation continues to apply even after renewal of the authorisation, until the marketing authorisation has been withdrawn.

6 Information on this document

6.1 Characteristics

Responsible department/working group	National Working Group
Responsible department/working group is mandated by	MT
Email address for responses to this document:	DienstpostbusNationaleWerkgroep@cbg-meb.nl
Which information in this document has to remain within the MEB? (in other words what must not be made public during a Freedom of Information Act (WOB)-request)	N/A
Does the document have to be translated and placed on the website?	Yes
Is/was public consultation necessary?	No

6.2 History

Who, when	**What**
14 March 2013	Initial version on the basis of • New policy of renewal of national marketing authorisations Approved by/coordinated with: • MT, DT, MEB Method of communicating about the changes to the document • Via intranet message (from Editing Handbook)
3 August 2022	Reason for revision: • Background information removed which is no longer relevant. Approved by/coordinated with: • MT, DT, secretaries, CCR Method of communicating about the changes to the document • Via intranet message (from Editing Handbook)