



European Medicines Agency
Post-authorisation Evaluation of Medicines for Human Use

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POST-AUTHORISATION GUIDANCE

Human Medicinal Products

QUESTIONS AND ANSWERS ON NOTIFICATION TO THE EMEA OF ACTUAL MARKETING AND CESSATION OF PLACING ON THE MARKET FOR CENTRALLY AUTHORISED MEDICINAL PRODUCTS

Please note that the final version of this document will also be integrated in the EMEA post-authorisation guidance.

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1. INTRODUCTION

This guidance document addresses questions that a Marketing Authorisation Holder (MAH) may have on this topic and gives practical aspects on notification to the EMEA of the dates of actual marketing for a centralised medicinal product per presentation in the various Member States as well as the temporary or permanent cessation/interruption of marketing within at least 2 months before such cessation occurs.

This guidance only focuses on marketing and cessation information but does not address the requirements to provide, in the context of pharmacovigilance, the volume of sales and volume of prescriptions.

To make the reporting for the MAH easier and to facilitate the tracking of this information by the EMEA for the purpose of the sunset clause monitoring, the Agency would like to collect data electronically through the EudraVigilance Medicinal Product Dictionary (EVMPD). EVMPD extension will allow a direct and up-to-date reporting by the MAH to the Agency with a view to track a three-year period without marketing so-called “sunset period” and to make the marketing status information public.

In addition to guidance on the details of requirements to notify to the Agency, recommendations are given in this document regarding the format and timelines to follow for the marketing status reporting until availability of this particular functionality within EVMPD.

This guidance document needs to be read in conjunction with the post-authorisation Q&A guidance document on ‘*the application of the so-called “sunset clause” to centrally authorised medicinal products*’ (Doc.Ref. EMEA/180079/2005) and in the future with a procedure which will relate to the data reporting in EVMPD.

2. WHAT IS THE LEGAL BASIS?

First and second paragraphs of Article 13(4) of Regulation (EC) No 726/2004 introduces the obligation as of 20 November 2005 for all Marketing Authorisation Holders, after the granting of a Marketing Authorisation (MA) for a centrally authorised medicinal product for human use:

- to inform the Agency of the dates of actual marketing of the medicinal product for human use in the Member States, taking into account the various presentations authorised;
- to notify the Agency if the product ceases to be placed on the market, either temporarily or permanently. Such notification shall, otherwise than in exceptional circumstances, be made no less than 2 months before the interruption in the placing on the market of the product.

This provision is also referred to in article 23a of Directive 2001/83/EC, as amended.

In this guidance document, the third paragraph of this article related to the volume of sales and volume of prescriptions is not addressed.

3. DOES IT APPLY TO EXISTING PRODUCTS?

This provision applies to all centrally authorised medicinal products from the date of entry into force of the Regulation i.e. 20 November 2005.

From this date, MAHs have the obligation to inform the EMEA of the actual marketing and cessation for all the various presentations of their medicinal product per Member State.

4. WHAT ARE THE DEFINITIONS?

The definitions below are based on the general principles outlined in the Chapter 1 of volume 2A of the Notice to Applicants.

4.1 What is the meaning of ‘actual marketing’ / ‘placing on the market’?

The terms ‘actual marketing’ and “placing on the market” as referred to in Article 13(4) of Regulation (EC) No 726/2004 should be defined as when the medicinal product is ‘released into the distribution chain’ i.e. out of the direct control of the Marketing Authorisation Holder.

4.2 What is the meaning of “cessation of placing on the market”?

The ‘cessation of placing on the market’ shall be defined by analogy to the placing on the market, as the ‘cessation of release into the distribution chain’ with the consequence that the concerned product is no longer available for the supply to the patients.

It means that the date of cessation shall be the date of the last release into the distribution chain.

5. WHAT ARE THE REQUIREMENTS FOR NOTIFICATION OF ACTUAL MARKETING AND CESSATION?

5.1 What information should be reported to the Agency on the medicinal product marketing status?

Pursuant to Article 13 (4), first paragraph of the Regulation, the actual marketing of a medicinal product shall be reported to the Agency per presentation and per Member State. For centrally authorised medicinal products, presentation corresponds to pack-size.

The Marketing Authorisation Holder shall also notify the Agency of a cessation (temporary/permanent) in marketing their medicinal product.

Temporary cessation should only be reported when it may cause a public health concern. The MAH has to exercise his best judgement to determine when it is appropriate to report such a cessation but can always seek advice from the EMEA, when required.

MAHs are advised that where cessation is due to efficacy, safety and/or quality related issues for which already particular procedures are established, reporting of such cessation is without prejudice to applying the other specific related procedures (e.g. quality defect, pharmacovigilance issues, etc.), as appropriate.

In accordance with Article 13(4), first paragraph of the Regulation, a date is to be reported for actual marketing which shall be defined as Day/Month/Year. By analogy, a cessation in placing on the market should also be defined as an exact date. If MAHs experience difficulties in identifying the exact date, the cessation date should still be defined as D/M/Y, mentioning the last day of the nearest week or month for the purpose of the sunset clause monitoring.

5.2 When to report to the Agency?

5.2.1 *The marketing status overview*

The so-called marketing status overview refers to the picture of the marketing situation of a specific product, at one time point of the product life-cycle, per presentation and per Member States.

Until availability of the EVMPD extension, MAHs should inform the EMEA of the marketing status of their medicinal product(s) reflecting on the different situations detailed above, according to the timelines given hereafter and using the [electronic tabular](#) format that is provided to MAHs on the EMEA website.

The MAH should notify the Agency within 30 days of the initial placing on the market of the product within the Community. Thereafter, any subsequent placing on the market or change in the marketing status should be reported through updates provided following the PSUR-cycle timelines and after renewal, annually in accordance with anniversary of the Commission Decision date. The reporting table should be attached to the cover letter.

Furthermore, in addition to these regular updates when there is a cessation which may cause a public health concern, the MAH should notify the Agency as detailed below.

When addressing such a notification cessation, the MAH should provide in addition a full updated table of the product marketing status.

5.2.2 *Cessation*

Permanent and temporary cessations where the MAH identifies that there may be a public health concern should be notified to the Agency at least 2 months in advance of the cessation, unless exceptional circumstances apply. However, the MAH is advised to inform the Agency at the earliest possible opportunity i.e. as soon as the interruption is foreseen. If the MAH was thinking of ceasing to market a product several months beforehand, but did not have an exact date defined, the MAH could give the EMEA a provisional date and then subsequently update it with more precise information.

It is anticipated that the MAH provides detailed information to the Agency to deal with such cessation. This should include e.g. grounds, length of cessation period, Members State(s) concerned, company's intention to provide information to prescribers and patients, etc.

MAHs are advised that reporting is without prejudice to other procedures. Where cessation is due to efficacy, safety and/or quality related issues for which particular procedures are established, the specific related procedure should be followed in addition (e.g. quality defect, pharmacovigilance issues, etc.).

The 2-month notice period for notifying to the Agency a cessation in placing on the market which might be of public health concern may not be met in exceptional circumstances.

It is recognised that there are some cases where the MAH cannot anticipate the interruption of the placing on the market of the medicinal product within the required timeframe as reasons for the interruption are outside of their control. Cases should be considered on a case-by-case basis.

This includes cases of 'force majeure' (e.g. burning down of manufacturing site, natural disaster, major manufacturing difficulties, out of stock of active substance or any ingredient of the medicinal product including packaging material, urgent safety and quality concerns...), as well as the cases referred to in article 20 of the Regulation (EC) No 726/2004 and article 107(2) of the Directive 2001/83/EC as amended concerning urgent provisional measures, and articles 116 and 117 of the Directive 2001/83/EC as amended concerning suspension.

However, when the 2-month notice period cannot be respected, the MAH shall inform the Agency as soon as the interruption is considered likely or known.

Permanent cessations in placing on the market of any presentation in any Member State where no potential public health concern is identified by the MAH should be reported at the time of the reporting of the marketing status overview.

5.3 What is the reporting format to the Agency?

Until availability of the EVMPD extension, MAHs should inform the EMEA of the marketing status of their medicinal product(s) using the [electronic template](#) which is provided on the EMEA website.

Two paper copies of the completed table and any subsequent updates are to be returned to the EMEA (via their Project Team Leader - PTL) as well as the electronic version of the table via e-mail. For updates provided at the time of PSUR submission, the paper version of the reporting table should be attached to the cover letter.

In addition, where the MAH identifies that there may be a public health issue with a cessation, the MAH should inform the EMEA (PTL) as detailed above and provide a full updated table of the marketing status.

6. DOES THE EMEA INTEND TO PUBLISH INFORMATION ABOUT MARKETING STATUS OF THE MEDICINAL PRODUCTS?

MAHs should be aware that when the electronic reporting will be in place, the information on availability of the medicinal product and its various presentations per Member State will be made public by the EMEA as “marketed” / “not marketed” based on the data provided in EVMPD by the MAH.