February 2021

CMDh/378/2018, Rev. 2

<Preliminary> <Updated> <Final> Lead Member State

PSUR Follow-Up assessment report

Active substance(s):

Procedure No.: MS/H/PSUFU/xxxxxxxx/yyyymm

| Procedure resources |  |
| --- | --- |
| Lead Member State (LMS) | <Two letter country code> |
| LMS Contact person | Name:  Tel:  Email: |
| LMS Assessor(s) | Name:  Tel:  Email: |

| Status of this report and steps taken for the assessment¹ | | | | |
| --- | --- | --- | --- | --- |
| Current step | Description | Day | Planned date | Actual date |
|  | Start of procedure | 0 |  |  |
|  | LMS preliminary assessment report (AR) | 36 |  |  |
|  | Submission of MS request for PRAC advice | 36 |  |  |
|  | CMS comments | 50 |  |  |
|  | LMS updated response assessment report following comments (with an updated MS’s request for PRAC advice if a need to refine the questions to PRAC is identified) | 53 |  |  |
|  | PRAC advice | 60 |  |  |
|  | LMS updated assessment report following PRAC advice | 60 |  |  |
|  | **In case the procedure can be finalised:** |  |  |  |
|  | LMS circulates the updated AR (FAR) including the PRAC advice to CMDh together with the summary AR for publication | 60 |  |  |
|  | CMDh discussion/adoption | 74 |  |  |
|  | Publication of the outcome/summary of the FAR | Post day 74 |  |  |
|  | **In case PRAC advises for a RfSI:** |  |  |  |
|  | RfSI submitted to MAH(s) procedure goes into clock stop | 60 |  |  |
|  | Submission of responses to RfSI by MAH(s) | 75 |  |  |
|  | LMS response assessment report | 111 |  |  |
|  | CMS comments | 125 |  |  |
|  | LMS updated response assessment report following comments | 128 |  |  |
|  | PRAC advice | 135 |  |  |
|  | LMS updated assessment report following PRAC advice | 135 |  |  |
|  | LMS circulates the updated AR (FAR) including the PRAC advice to CMDh together with the summary AR for publication | 135 |  |  |
|  | CMDh discussion/adoption | 149 |  |  |
|  | Publication of the outcome/summary of the FAR | post day 149 |  |  |

¹Tick the box corresponding to the applicable step – do not delete any of the steps. If not applicable, add N/A instead of the date

Declarations

*In order to facilitate the redaction of potentially commercially confidential information the assessor should confirm by ticking the below box whether the report contains any of the below data/information. This does not preclude the assessor from including this information if needed for the assessment; however, if the boxes are un-ticked, the P-RMS will review and redact the report accordingly prior to circulation to the MAH(s):*

The assessor confirms that reference to ongoing assessments, development plans (including Scientific Advice/Protocol assistance) or pharmacovigilance inspections are not included in this assessment report.

Whenever the above boxes are un-ticked please indicate the section and page where the confidential information is located here: …

**General guidance**

This PSUR Follow-Up AR template should be used by the Lead Member State (LMS) for informal Work-Sharing procedure for follow-up for PSUSA for NAPs.

**As a reminder, the informal worksharing procedure for the submission and assessment of follow-up after a PSUSA for NAPs is for exceptional use only and will not be used for issues that could/should have been dealt with and resolved within the PSUSA procedure. Such issues should be dealt with in the PSUSA procedure.**

Use INN/name of active substance when referring to other products/comparators rather than invented names.

**Further guidance**

\* Taking into consideration the principles established in the HMA/EMEA recommendations on the handling of requests for access to PSURs (EMEA/743133/2009), it is not expected that the LMS PSUFU AR would contain commercially confidential information. As per the HMA/EMEA recommendations, exposure data are not considered confidential.

**Publication of the AR after finalisation of the PSUFU procedure**The sections 1-5, as well as a summary of the PRAC advice which will be included in section 3, will be published on the CMDh website after finalisation. NB: the time table, the table “Procedure resources” on the cover page (i.e. LMS and names/contact details of the LMS’s contact person and assessor) and the section “declarations” should be deleted from the AR once it is finalised before publication

**List of data sources available for guidance**

The Informal Work-Sharing procedure for follow-up for PSUSA for NAPs is described in more detail in the [include name of document and web link if published on CMDh website].

GVP Module VII – Periodic safety update report <https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-pharmacovigilance-practices-gvp-module-vii-periodic-safety-update-report_en.pdf>

GVP Module V - Risk management systems

<https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-pharmacovigilance-practices-module-v-risk-management-systems-rev-2_en.pdf>

GVP Module VIII – Post-authorisation safety studies <https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-pharmacovigilance-practices-gvp-module-viii-post-authorisation-safety-studies-rev-3_en.pdf>

<https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-pharmacovigilance-practices-gvp-module-viii-addendum-i-requirements-and-recommendations-submission-information-non-interventional-post-authorisation-safety-studies-rev-3_en.pdf>

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1. Background information on the procedure

This is the assessment of Follow-Up information for <active substance> <combination of active substances> as agreed with the PSUSA assessment <PSUSA/xxxxxxxxx/yyyymm>.

CMDh adopted the following question(s) to the MAH(s):

Copy and paste LoQ(s) as agreed by CMDh

CMDh agreed that the response(s) are submitted and assessed within an informal work-sharing procedure for follow-up for PSUSA for NAPs and appointed [MS] as Lead Member State.

1. Assessment conclusions and actions

* In this section, the LMS should summarise the assessment conclusions and relevant comments highlighted in the AR. Further to the receipt of MAH and Member States comments, the LMS should provide an update of this section, reflecting the received comments and providing the final position of the LMS.
* This section should start with a very brief overview of the active substance/product(s) and its stage in the lifecycle (when the product was authorised first, its indication and how extensively it is used).
* This section should briefly summarise the outstanding issue from the PSUSA that warranted submission of additional data within this informal work-sharing procedure.
* It should summarise the data submitted by the MAH(s) and the LMS assessment conclusion thereof.
* The overall conclusion should be whether the MAH(s) provided satisfactory responses and whether changes to the product information or RMP are warranted.
* Changes in PSUR frequency: Any proposals for changes of the PSUR frequency, and/or scope of the single assessment procedure, i.e. requirements for generics should be discussed based on data/information presented in the PSURs. Proposals for any changes should be clearly justified.
* The comments should be active substance specific rather than product specific.
* Although an RMP cannot be submitted with a follow-up procedure for PSUSA for NAPs, the LMS may provide comments, based on the data submitted, to be addressed in the next RMP update to be provided separately with the next regulatory procedure affecting the RMP or within a specified timeframe. Please note that the timeframe should be realistic and that 6 months are usually considered adequate (this could be longer depending on the issue). As such, any impacts on the RMP or the need for further studies or risk minimisation measures, monitoring or signal evaluation should be reflected in this section, including clear expectations for follow-up actions.
* If it is considered that action needs to be taken with regards to the safety specification in existing RMPs, this should be explicitly highlighted to CMDh.

**[In case of recommendation to update the product information and/or RMP only.]**

**<Scientific conclusions and grounds for a recommendation to update the product information and/or RMP>**

In case a change(s) the product information and/or RMP is recommended, the scientific grounds need to be clearly documented i.e. a short summary of the evidence/data underlining the proposed changes (not just a copy of the scope) should be included here. This should give the scientific motivation for the recommendation in a concise manner (recommended maximum size of ½ page). A more detailed discussion on the issue(s) underlying the variation should be provided in the Assessment conclusions and actions section above.

1. Recommendations

The Recommendation should be based on the data submitted and not on other information related to the active substance but not submitted within the ongoing procedure.

**[In case of recommendation that no changes to product information or RMP are needed]**

Based on the review of data submitted, the LMS considers that the MAH(s) provided satisfactory responses and no changes to the product information or risk management plan are warranted.

**For preliminary conclusion only:**

<However, the Lead Member State considered that the MAH(s) should provide satisfactory responses to the <request for supplementary information> detailed in annex.>

**[In case of recommendation to update the product information]**

Based on the review of data submitted, the LMS considers that the product information should be updated as follows:

[Where the product/active substance is involved in a referral procedure, the following statement should be added as part of the Recommendation section:]

<This recommendation is without prejudice to the final conclusions of the ongoing referral procedure under [legal basis] for [name of procedure].>

[The scope of changes to the SmPCs and Package leaflets should be highlighted here.

Please do not change the layout and style of the next section and use the proposed way to highlight changes].

Update of section X and X of the SmPC to add <the adverse reaction x with a frequency y> <to add a warning on…>. The Package leaflet is updated accordingly.

The following changes to the product information of medicinal products containing the active substance <name of active substance> are recommended (new text **underlined and in bold**, deleted text ~~strike through~~):

**Summary of Product Characteristics**

[Add sections as relevant]

• Section 4.4

A warning should be <added> <revised> as follows:

<Exact wording of final warning>

• Section 4.8

<The following adverse reaction(s) should be added under the SOC <name of SOC> with a frequency <frequency>:

< The frequency of the adverse reaction <name of ADR> should be changed to <very common> <common etc…>

• Section x.y

**Package Leaflet**

[Add sections as relevant, ensuring that the above proposed changes to the SmPC are adequately reflected in lay terms in the package leaflet]

**For preliminary conclusion only:**

<However, the LMS considered that the MAH(s) should provide satisfactory responses to the <request for supplementary information> detailed in annex.>

**RMP Update**

**[In case of recommendation to update the Risk Management Plan]**

Based on the review of data submitted, the LMS considers that the RMP should be updated as follows:

[detail changes to be made to the RMP here]

**MS PRAC advice**

*The outcome of the MS PRAC advice should be added in section 3 when finalising the conclusion and before sending the AR to CMDh for adoption*

1. <Issues to be addressed in the next PSUR:>

**[In addition, issues to be addressed as a follow-up of this assessment should be added here, if applicable. These should be requested by default in the next PSUR, unless otherwise justified.]**

*The LMS should follow a risk based approach to limit the number of follow-up requests to a PSUSA assessment. Requests for follow-up review need to be justified and be clear on exactly what further data need to be submitted. The wording for any cumulative review request should be explicit in terms of the search strategy, preferred terms, MedDRA catalogue etc. This will ensure that the review(s) is structured correctly, allowing for a single assessment across all submissions.*

<In addition, the MAH(s) should also address the following issues in the next PSUR:>

1. PSUR frequency <and other changes to the EURD list>

If no changes to the PSUR frequency

<The next PSUR should be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.>

If changes of PSUR frequency are proposed – these should be justified. However, for the substances included in these work sharing procedures, it is unlikely that the PSUR frequency will be changed.

Annex: <Preliminary> <Updated> <Final> Lead Member State assessment comments on follow-up data

1. Introduction

This section should provide a brief statement on the active substances, their pharmacotherapeutic action and approved indication, posology, pharmaceutical forms and strengths.

It should also include information on the IBD/EURD, interval and cumulative periods covered by the PSUR.

It should also include the PSUSA procedure from which this informal work-sharing procedure for follow-up for PSUSA for NAPs originates ([PSUSA/xxxxxxxxx/yyyymm]) and paste the LoQ(s) as agreed by CMDh

It should also highlight any changes proposed by the MAH(s) to the product information as part of the submission.

1. Overview of MAHs (and medicinal products) involved with status of data submission

The below table should list all MAHs to which the request for follow-up data was made and indicate whether data were submitted.

|  |  |  |
| --- | --- | --- |
| **MAH or group of MAHs** | **Medicinal product(s)** | **Data submitted** |
|  |  | Y / N |
|  |  | Y / N |
|  |  | Y / N |
|  |  | Y / N |

1. Assessment of data submitted by the MAH

This section should summarise the data submitted by the MAH within the PSUFU procedure. Relevant assessor’s comments should be placed in boxes.

Subheadings can be introduced as appropriate, since they may vary due to the different nature of follow-up for PSUSA for NAPs.

1. LMS conclusion

The overall conclusion should be whether the MAH(s) provided satisfactory responses and whether changes to the product information and/or RMP are warranted.

The scope of changes to the SmPCs and Package leaflets should be highlighted here.

The changes proposed to the RMP should be highlighted here.

1. <LMS Request for supplementary information>

This section should be included in the LMS’s preliminary AR for the MAH(s) to address during the commenting phase.

1. <Comments from Member States>

This section should summarise the comments from Member States

*Lead Member State assessment comment:*

1. <MAH(s) responses to Request for supplementary information>

*Lead Member State assessment comment:*