*CMDh/359/2017*

*March 2017*

<Preliminary> <Final> < Reference Member State> PSUR assessment report

Active substance(s):

Procedure No.:

PSUR Period: <dd.mm.yyyy to dd.mm.yyyy >

| Status of this report and steps taken for the assessment¹ | | | |
| --- | --- | --- | --- |
| Current step | Description | Planned date | Actual Date |
|  | Start of procedure |  |  |
|  | P-Reference Member State preliminary assessment report (AR) |  |  |
|  | CMS and MAH comments |  |  |
|  | P-RMS final assessment report following comments |  |  |

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

| Procedure resources |  |
| --- | --- |
| P-RMS | <Two letter country code> |
| P-RMS Contact person | Name:  Tel:  Email: |
| P-RMS Assessor | Name:  Tel:  Email: |

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 AR template should be used by the PSUR Reference Member State (P-RMS) for PSUR assessments with nationally authorised medicinal products (NAPs) for whom the EURD-list is not yet legally binding.

Further to the receipt of comments from the MAH(s) and other Member States, the P-RMS should circulate a final AR (FAR). In the FAR, the assessment conclusions should be updated in order to fully integrate the comments received and to reflect the final position of the P-RMS. The Summary AR will then be sent to the CMDh for adoption.

It is essential that new information presented in the PSUR requiring updates to product information are highlighted in the relevant sections and particularly in section 2, Assessment conclusions and actions. It should always be ensured that the recommendations for SmPC and package leaflet changes are fully supported by the Assessment Report and data submitted with the PSUR(s).

If further data or discussion is needed from the MAH to support conclusions, they should be requested by the P-RMS in the preliminary AR (PAR). Only questions critical to the assessment of important safety issues or the benefit/risk balance should be considered during the assessment, other issues should be addressed in the next PSUR.

As a reminder, the PSUR is not the appropriate procedure for submitting final or interim study reports to the EU regulatory authorities. These reports should be submitted and assessed via the appropriate procedure in line with the Variations Classification guideline of Commission Regulation 1234/2008. However, in case a study report is able to further support either the discussion by the MAH or the P-RMS’ assessment of the PSUR sections dealing with data from clinical trials, findings from non-interventional studies, or other clinical trials and sources, the MAH may provide the study report (or relevant parts thereof) as an appendix to the PSUR.

In case a study report has been submitted by the MAH in the PSUR, the P-RMS should include in the ‘Other considerations’ section a reminder to the MAH that the study report should also have been submitted according to the Commission regulation 1234/2008 via an appropriate 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 PSUR and consequently the P-RMS PSUR AR would contain commercially confidential information. As per the HMA/EMEA recommendations, exposure data are not considered confidential.

\* Updated RMP(s) cannot be submitted and assessed with the PSUR in procedures containing NAPs. Any erroneous RMP submissions will not be subject to assessment. Updates to RMPs should be submitted to and assessed by the National Competent Authorities.

**List of data sources available for guidance**

GVP Module VII, Rev.1 – 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](https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-pharmacovigilance-practices-gvp-module-vii-periodic-safety-update-report_en.pdf%20)

GVP Module V, Rev.1 - 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, Rev. 2 – 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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Background information on the procedure

This is the assessment of PSUR(s) for <active substance> <combination of active substances>.

1. Assessment conclusions and actions

• In this section, the P-RMS should summarise the assessment conclusions and relevant comments highlighted in the AR. Further to the receipt of MAH and Member States comments, the P-RMS should provide an update of this section, reflecting the received comments and providing the final position of the P-RMS.

• 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 main safety data that became available, including through signal evaluation, during the reporting interval and cumulatively.

• This section should discuss whether the safety profile remains in accordance with the expected or whether risks have changed. If needed, discuss whether updates of the product information are necessary as well as risk minimisation activity to address specific safety concern(s).

• The overall conclusion should be whether the Benefit Risk balance remains unchanged.

• 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.

* If it is considered that action needs to be taken with regards to the safety specification in existing RMPs, this should be included in Section 6 “Other considerations” in order to highlight to CMDh the need to request changes to existing RMPs.

• Although an RMP cannot be submitted with the PSUR in a procedure which includes NAPs only, the PRAC /RMS may provide comments, based on the data submitted with the PSUR, 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. This should take into account the fact that routine updates of the RMP are no longer required in view of the new variation guideline. This request should also be flagged to CMDh via inclusion in section 6 “other considerations”.

**[In case of recommendation to vary the marketing authorisation only and /or in case of suspension/revocation. If suspension/revocation, please amend the title for the following section. Please ensure that you justify in accordance with Art. 116 of Directive 2001/83/EC.]**

**<Scientific conclusions and grounds for the variation to the terms of the Marketing Authorisation(s)>**

In case a variation to change the product information or the conditions of the MA 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 of the variation 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 current PSUR data and not on other information related to the active substance but not submitted within the ongoing procedure. Please use section 6 “Other Considerations” to reflect important issues which are unrelated to the current PSUR.

**[In case of recommendation to maintain the marketing authorisation]**

Based on the review of data on safety and efficacy the P-RMS considers that the risk-benefit balance of medicinal products containing the active substance <name of active substance> remains unchanged and therefore recommends the maintenance of the marketing authorisation(s).

**For preliminary conclusion only:**

<However, the Reference 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 vary the marketing authorisation]**

Based on the review of data on safety and efficacy the P-RMS considers that the risk-benefit balance of medicinal products containing the active substance <name of active substance> remains unchanged but recommends that the terms of the marketing authorisation(s) should be varied 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 P-RMS considered that the MAH(s) should provide satisfactory responses to the <request for supplementary information> detailed in annex.>

**<Conditions to the Marketing Authorisation(s) for nationally authorised products:>**

[In cases changes to the conditions of the marketing authorisation are recommended, these should also be highlighted here.]

[In case of imposition of conditions to the marketing authorisations e.g. PASS]

<The marketing authorisation holder(s) shall complete the below conditions, within the stated timeframe:>

**[In case of recommendation to suspend the marketing authorisation]**

Based on the review of data on safety and efficacy the P-RMS considers that the risk-benefit balance of medicinal products containing the active substance <name of active substance> is negative and recommends the suspension of the marketing authorisation(s) on the following grounds pursuant to Article 116 of Directive 2001/83/EC:

[Grounds for suspension]

[Select one or more from the below]

<{Product(s)}is/are harmful><, and>

<{Product(s)} lack(s) therapeutic efficacy><, and>

<the risk-benefit balance of {product(s)} is not favourable>

<the condition {specify the condition concerned} has not been fulfilled>,

**Conditions for lifting the suspension of the Marketing Authorisation(s)** **for nationally authorised products:**

**[In case of recommendation to revoke the marketing authorisation]**

Based on the review of data on safety and efficacy the Reference Member State considers that the risk-benefit balance of medicinal products containing the active substance <name of active substance> is negative and recommends the revocation of the marketing authorisation(s) on the following grounds pursuant to Article 116 of Directive 2001/83/EC:

[Grounds for revocation]

[Select one or more from the below]

<{Product(s)}is/are harmful><, and>

<{Product(s)} lack(s) therapeutic efficacy><, and>

<the risk-benefit balance of {product(s)} is not favourable>

<the condition {specify the condition concerned} has not been fulfilled>,

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 P-RMS 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.

1. <Other considerations>

*This section is optional and should be used to highlight to MAH issues that require follow-up outside of the PSUR procedure, which the CMDh can make public via the minutes.*

*In general, anything that is based on the scientific assessment of PSUR data should be in section 2 of the AR with, in principle, a recommendation in section 3. If such a recommendation goes beyond the (legal) scope of a PSUR procedure the information should be included only in this section. However, issues not related to data assessed in the PSUR, such as non-compliance in the implementation of previous EU regulatory procedure outcomes, should be mentioned here only.*

*Information included in this section will be automatically flagged to CMDh via email and also by the CMDh member of the P-RMS in the plenary CMDh meeting. The P-RMS should also add a note in the “additional comments” field of the PSUR Repository notification that the assessment includes issues which need flagging to CMDh.*

* *In the case of mono-components and fixed dose combinations due consideration should be given from a scientific point of view in how far the conclusion on the mono product or on the combination can also be extrapolated to the other combinations/mono products. A simple check in the EURD list using the substance name can provide a rapid overview of any other currently authorised/applicable entries in this respect. Any conclusion on extrapolation should therefore be included in this section. The scientific rationale should be provided in section 2.*

*Regardless whether covering only mono products or combination products or both - if it is not possible to extrapolate, this should be clearly stated (e.g. different dosing in the combination, different route of administration) in this section.*

* *If a new drug-drug interaction or contraindication is added, due consideration should be given as to whether the change should be extended to the other impacted products and raised to CMDh. The scientific rationale should be provided in section 2.*
* *As a general principle no follow-up measures for PSUR WS should be requested as there is no regulatory/legal framework to assess them in a consistent manner. Exceptionally, however, the P-RMS may agree on the need to urgently follow up on a potentially serious safety issue that cannot be carried over to the next planned PSUR.*

*In such cases the P-RMS assessor should indicate the route which should be followed for the submission of the data, e.g. signal, change in PSUR submission deadline or triggering of a referral procedure. Whichever route is proposed for the submission of follow up information, the PRAC should be consulted in the assessment of the data through a Member State request for PRAC advice made by the P-RMS.*

* *As a reminder, the PSUR is not the appropriate procedure for submitting final or interim study reports to the EU regulatory authorities. These reports should be submitted and assessed via the appropriate procedure in line with the Variations Classification guideline of Commission Regulation 1234/2008. However, in case a study report is able to further support either the discussion by the MAH or the P-RMS’ assessment of the PSUR sections dealing with data from clinical trials, findings from non-interventional studies, or other clinical trials and sources, the MAH may provide the study report (or relevant parts thereof) as an appendix to the PSUR.*

*In case a study report has been submitted by the MAH in the PSUR, the P-RMS should include in this section a reminder to the MAH that the study report should also have been submitted according to the Commission regulation 1234/2008 via an appropriate procedure.*

**Annex: <Preliminary> <Final> P-Reference Member State assessment comments on PSUR**

1. PSUR 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 highlight any changes proposed by the MAH to the product information as part of the submission of this PSUR (to be crosschecked with Module 1.3 of the MA and regional appendix of a PSUR).

* 1. Worldwide marketing authorisation status

This section should include brief information provided in the PSUR with regard to the date of the first authorisation worldwide, and in how many countries the product is authorised, with indications(s), authorised dose(s), if applicable.

<X was first authorised in < A on <DD Month YYYY> and> in the EU on <DD Month YYYY>. In the EU, X has been marketed in <A, B, C and D>. It is approved in a total of X countries.>

*Reference Member State assessment comment:*

* 1. Overview of exposure and safety data
     1. Actions taken in the reporting interval for safety reasons

This section should include a description of significant actions (and reasons for these actions) related to safety that have been taken worldwide during the interval since the last DLP, related to either investigational uses or marketing experience by the MAH(s), sponsors of clinical trial(s), data monitoring committees, ethics committees or competent authorities. For further details and examples of such actions, please refer to GVP Module VII on PSUR.

*Reference Member State assessment comment:*

* + 1. Changes to reference safety information

This section should highlight what Reference Safety Information is used by the MAH(s) (e.g. CCDS, SmPC) and the date of the current version.

The changes made during the reporting interval to the Reference Safety Information should be summarised.

The RMS should briefly comment whether any proposals by MAHs in terms of new safety information and key risk minimisation recommendations has been made based on the evaluation of the information provided in the PSUR and whether those are already reflected in the SmPC.

*Reference Member State assessment comment:*

* + 1. Estimated exposure and use patterns

This section should provide estimates of the size and nature of the population exposed to the medicinal product. Particularly, information should be provided on the cumulative and on-going subject exposure in clinical trials [PSUR: Section 5.1], cumulative and interval patient exposure from marketing experience and if available with special focus on the populations with no or limited exposure during clinical trials (inclusions, exclusions, limited numbers, trial setting, and use in special populations) and off-label use [PSUR: Section 5.2].

When relevant, this information should be stratified by indication, formulation or route of administration, and follow-up duration), as well as information on patterns of drug use.

*Reference Member State assessment comment:*

* + 1. Data in summary tabulations

*It is not expected to include here, or in an attachment, copies of the summary table. Further, the data presented by the MAH as cumulative summary tabulations of serious adverse events from clinical trials and cumulative and interval summary tabulations from post-marketing data sources is not intended to be used as a tool for signal detection purposes. Summary tables with number of events or cases lack sufficient detail to allow for meaningful assessment of a causal association. For signal detection, other processes are in place, which are more appropriate.*

*Reference Member State assessment comment:*

* + 1. Findings from clinical trials and other sources

This section should provide a brief summary of the clinically important emerging safety and efficacy findings obtained during the reporting interval from:

* Completed clinical trials, ongoing clinical trials, long-term follow-up, other therapeutic use of medicinal product and new safety data related to fixed combination therapies. (section 7 of the PSUR).
* non-interventional studies (section 8 of the PSUR).
* Other clinical trial/study sources (e.g. results from pooled analysis or meta-analysis of randomised clinical trials, safety information provided by co-development partners or from investigator-initiated trials, that were accessible to the MAH(s) – Section 9 of the PSUR).
* Non-clinical data (section 10 of the PSUR).
* Literature (section 11 of the PSUR).
* Other periodic reports (section 12 of the PSUR).
* Medication errors

*Reference Member State assessment comment:*

* + 1. <Lack of efficacy in controlled clinical trials>

This section should summarise data from clinical trials indicating lack of efficacy, or lack of efficacy relative to established therapy(ies).

*Reference Member State assessment comment:*

* + 1. <Late-breaking information>

In this section the assessor should comment on any potentially important safety, efficacy and effectiveness findings that arose after the data lock point of the PSUR.

*Reference Member State assessment comment:*

1. Signal and risk evaluation
   1. Summary of safety concerns

In this section, the “baseline” important safety concerns (i.e. at the start of the reporting period) should be presented by including the summary table in line with section 16.1 of the PSUR.

* 1. Signal evaluation

• Tabular overview of signals: new, ongoing or closed during the reporting interval <dd.mm.yyyy to dd.mm.yyyy>.

| Signal term | Date detected | Status (new, ongoing or closed) | Data closed (for closed signals) | Source or trigger of signal | Reason summary | Method of signal evaluation | Outcome, if closed |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Stroke | MMM/YYYY | New | MMM/YYYY | Spontaneous | Brief summary of key data and rational for further evaluation | Review cases, epidemiological study |  |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |

For explanatory notes, please refer to GVP Module VII on PSURs section VII.B.5.15 and appendix 2.

The P-RMS should comment on the signals classified by the MAH(s) as new, ongoing and closed during the reporting interval.

The P-RMS should critically assess the evidence presented in support of the MAH(s) conclusions on the safety signals. It should be made clear where the P-RMS does not agree with the outcome of the MAH’s signal evaluation and/or considers further actions are needed. The P-RMS should also consider whether other signals should have been evaluated by the MAH(s) (e.g. further to review of Eudravigilance data).

*Reference Member State assessment comment:*

* 1. Evaluation of risks and new information

This sub-section should assess the critical appraisal provided by the MAH of new information relevant to previously recognised risks that is not already included in sub-section 2.2 (“Signal evaluation”). The aim is to provide new information (e.g. information arising from studies to further characterise an important potential risk) and not to present all the information related to the list of safety concerns.

Where new risks are identified, there should be consideration of whether these might be classified as ‘important’ or ‘other’ risks and whether any action (e.g. update of product information) is warranted.

*Reference Member State assessment comment:*

* 1. Characterisation of risks

This section should reflect a characterisation of the important identified and/or potential risks for the product based on cumulative data (i.e. not solely based on information received during the reporting period) and also describe important missing information associated with the use of the product.

*Based on information arising from the evaluation period (e.g. successful risk minimisation measures in place), the MAH may propose changes to the list of safety concerns. When an important risk or missing information is re-classified or removed, a justification should be provided in this section as well as a proposal to update the RMP accordingly.*

If no changes are identified, it is sufficient to state that the safety concerns remain unchanged (e.g. if the information on the risks has only been updated with most recent data with no consequence on the known safety profile).

*Reference Member State assessment comment:*

1. Benefit evaluation

This section can include a brief summary of the MAH(s) benefit evaluation submitted by the MAH(s) in section 17 of the PSUR.

Further elaboration on the benefits may be required in case the benefit-risk balance is considered changed during the assessment of the PSUR (e.g. recommendation for restriction of indication or revocation. In that case, the RMS should discuss here the important baseline efficacy and effectiveness information, the newly identified information on efficacy and effectiveness in order to characterise the benefits.

1. Benefit-risk balance

The main objective of a PSUR is to present a comprehensive, concise and critical analysis of the benefit/risk balance of the medicinal product taking into account new or emerging information in the context of cumulative experience with the use of the medicine, its place in therapeutics and whether this information affects the overall benefit/risk balance of the product. The PSUR is therefore a tool for post-authorisation evaluation at defined time points in the lifecycle of a product.

This section should represent the views of the RMS on the benefit-risk balance of the medicinal product, taking into account data presented in the PSUR and the arguments put forward by the MAH(s) in the section “Integrated Benefit-risk Analysis for Approved Indications” of the submitted PSUR(s).

Separate benefit-risk evaluations should be provided for each indication of the medicinal products authorised in more than one indication.

If no new safety concerns or change in benefits have been identified in the PSUR assessment, this section should be concise (i.e. to indicate that the benefit-risk balance remains unchanged).

In case a full appraisal of the benefit-risk is warranted based on important safety concerns and/or change of benefits during the reporting interval period, the benefit/risk evaluation should be presented in a structured manner (i.e. Beneficial effects and uncertainty in the knowledge about the beneficial effects, Unfavourable effects and Uncertainty in the knowledge about the unfavourable effects, followed by the balance in line with other assessment report templates).

General guidance on how to describe the benefit-risk assessment:

• Do not repeat results extensively, these are described in detail elsewhere. Just mention the conclusions, i.e., which are the key favourable/unfavourable effects that have been observed. Avoid that this section becomes the “summary of the summary”. For products approved for more than one indication, benefit-risk profiles should be evaluated and presented for each indication individually. If there are important differences in the benefit-risk balance among populations within an indication, benefit-risk evaluation should be presented by population, if possible.

• The key benefits and risks considered in the evaluation should be specified since not all benefits and risks contribute importantly to the overall benefit-risk evaluation. The information presented in the previous benefit and risk sections should be carried forward for integration in the benefit-risk evaluation.

• The strengths, weaknesses, and uncertainties of the evidence should be considered when formulating the benefit-risk evaluation. Describe how uncertainties in the benefits and risks impact the evaluation.

• Discuss the need for further studies or need for restrictions to product availability or usage, or any other conditions or measures aiming to improve the benefit-risk balance and reasoning for these measures.

• Conclude on the overall “benefit-risk balance” for the active substance and if necessary, for different indications.

• Discuss the need for changes to the frequency of PSUR submission.

• Consider if the substance is under the additional monitoring list and if any changes are warranted on that respect.

1. <P-RMS Request for supplementary information>

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

Considering the TT (15 days for P-RMS after receipt of comments to final AR), only questions critical to the assessment of the benefit/risk balance should be considered. Other questions should be included in the recommendations to be addressed in future PSURs.

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

*Reference Member State assessment comment:*

1. <Comments from Member States>

*Reference Member State assessment comment:*

**EU PSUR Work Sharing**

**Summary Assessment Report**

**<Product Name> (name of active substance)**

**XX/H/0000** (MRP/DCP procedure number)

|  |  |
| --- | --- |
| P-RMS |  |
| CMS included in this procedure | AT, BE, BG, CY, CZ, DK, EE, EL, ES, FI, FR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MT, NL, NO, PL, PT, RO, SK, SL, SE, UK  *Delete as appropriate* |
| Invented name of the medicinal product(s) in the P-RMS |  |
| INN (or common name) of the active substance(s) |  |
| Pharmaco-therapeutic group (ATC Code) |  |
| Indications authorised in the P-RMS for the product |  |
| Pharmaceutical form(s) and strength(s) |  |

**PSUR Period**

The period covered by this work sharing assessment was xxx to xxx.

**Final Conclusion**

Covering the following:

* In this section, the P-RMS should summarise the assessment conclusions and relevant comments highlighted in the AR. Further to the receipt of MAH and Member States comments, this section should be updated reflecting the received comments and providing the final position.
  + 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 main safety data that became available, including through signal evaluation, during the reporting interval and cumulatively.
  + This section should discuss whether the safety profile remains in accordance with the expected or whether risks have changed. If needed, discuss whether updates of the product information are necessary as well as risk minimisation activity to address specific safety concern(s).
  + The overall conclusion should be whether the Benefit Risk balance remains unchanged.
  + Change in PSUR frequency: Any proposals for changes of the PSUR frequency should be discussed based on data/information presented in the PSUR. Proposals for any changes should be clearly justified.
  + Although an RMP cannot be submitted with the PSUR, the assessor may provide comments, based on the data submitted with the PSUR, 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.

In the light of the information provided in the reviewed PSUR, the P-RMS/ CMDh considers there were no new major findings affecting the overall safety profile of <xxxxxxxxx> and the benefit-risk profile of the medicinal product(s) is unchanged.

<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.>

**Recommendations:**

* **Amendments to the Product Information**

During the assessment of the information in the PSUR the following issue was considered: (give a short summary of issue)

It has been agreed that the following amendments to the Product Information are required:

**Summary of Product Characteristics**

*In case of product-specific changes, these should be presented clearly and separately per product, formulation, indication, as applicable.*

[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]

* **Agreed topics for close monitoring and review in the next PSUR are:**

The following adverse events should be closely monitored and reflected in section 15 of the PSUR by the MAHs having marketing authorisation for products containing <substance>:

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

*The P-RMS should follow a risk based approach to limit the number of follow-up requests to the subsequent 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.*

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