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1. How are PSURs to be submitted as of 13 June 2016?

As of 13 June 2016 all PSURs are to be submitted to the PSUR Repository via the eSubmission-Gateway/Web-Client. Other paths of submission will no more be accepted. This is also valid for PSURs on active substances which are not included in the EURD list and, therefore, are not subject to PSUSA procedures.

Submission in individual Member States per CESP, on paper, etc. is no longer possible as of 13 June 2016.

For further information see:
PSUR Repository website
CMDh SOP on the processing of PSUR single assessment for nationally authorised products
Periodic safety update reports: questions and answers

The cover letter previously provided by the BfArM can no longer be used for submission as of 13 June 2016.

Instead, use the submission cover letter of the EMA (“Formatted table template - To be inserted in each procedural submission cover letter”); it contains all the formal criteria required for the PSUR submission.

For further information see:
Template table cover letter
Periodic safety update reports: questions and answers

To allow the regulatory activities and data analyses required in connection with PSURs to be carried out properly, pharmaceutical companies must ensure that the information on their medicinal products authorised in the EU is entered correctly and completely in the Article 57 database.

For further information see: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000336.jsp&mid=WC0b01ac058058f32a#section1

2. What is the PSUR Repository and what is the format for submission to the Repository?

The PSUR repository is a central database set up by the EMA for the submission and archiving of PSURs as well as for the management and archiving of all documents relating to PSUR assessment procedures (assessment reports, response documents, comments, Commission decisions, CMDh positions, etc.). The national licensing authorities and the European Commission have direct, secure access to the PSUR repository.

The electronic submission of PSURs is organised by the EMA via the eSubmission Gateway/Web Client. The preferred submission formats are the electronic Common Technical Document format (eCTD, obligatory for all centralised authorisation procedures) or the non-eCTD electronic submission format (NeeS). No other submission formats (e.g. pdf files) are accepted as of 13 June 2016.

Before submission of a PSUR to the PSUR repository the user needs to register completing the EMA registration form. For detailed information on registration visit the following link: how to register for the Web-Client.

For information on submission of PSURs via the eSubmission Gateway and the Web-Client to the
3. **In which format are PSURs to be compiled?**

PSURs are to be compiled in accordance with the specifications of the [Guideline on good pharmacovigilance practices (GVP) Module VII – Periodic safety update report](http://esubmission.ema.europa.eu/psur/psur_repository.html).

GVP Module VII (PSUR) shows considerable changes with regard to the extent and content of the PSURs as compared to Volume 9A. For instance, while there are no more summary bridging reports and addendum reports, it now contains a category for current efficacy data. Line listings are no longer to be compiled/submitted as a matter of routine, but can still be requested by the competent authority.

4. **Which medicinal products can be presented combined in one PSUR?**

PSUR Single Assessment (PSUSA) procedures are specific to the active substance and partly specific to indication or pharmaceutical form. The EURD list includes information on whether the procedure in question is subject to any restrictions, e.g., regarding indication or pharmaceutical form. In the case of no such restrictions, all medicinal products of a pharmaceutical company containing the same active substance/combination of substances may be combined in one PSUR, irrespective of indication, pharmaceutical form, type of authorisation, etc. If restrictions are specified they are to be observed accordingly.

Medicinal products containing a single active substance can be presented together with combination preparations in one PSUR only if the EURD list contains a corresponding entry (e.g. hydrochlorothiazide / telmisartan, telmisartan).

In the case of substances not included in the EURD list, all medicinal products containing the same substance or the same combination of substances can be presented in one PSUR. PSURs of combination preparations should be submitted separately and should only include medicinal products with identical substance combinations.

If a PSUR combines medicinal products with different indications and/or pharmaceutical forms or routes of administration (e.g. oral and topical), the data (e.g. patient exposure, adverse reactions, etc.) are to be presented separately for each indication / pharmaceutical form / route of administration according to the requirements of the GVP Module VII for PSURs.

5. **What is the EURD list?**

The list of the European Reference Dates and Frequency of PSUR Submission (EURD-List) specifies all those active substances and combinations of active substances for which the PSUR submission dates have been harmonised in the EU. These substances are subject to harmonised European assessment within the PSUSA procedure.

The following is specified:

- active substance/combination of active substances
- European Reference Date
- PSUR submission frequency
- Data Lock Point (DLP) and submission date for the next PSUR
- whether PSURs have to be submitted for medicinal products for which there is actually a waiver (e.g. generic medicinal products)
6. **Is the EURD list binding?**

Yes. If an active substance/combination of active substances is on the list, all pharmaceutical companies that have a valid marketing authorisation for this/these active substance/s have to submit a PSUR.

It is stated in the EURD list whether PSURs are also to be submitted for listed active substances in the case of marketing authorisations referred to in question 17 "For which medicinal products do no PSURs have to be submitted?"

7. **Does a PSUR have to be submitted for combination products if the specific combination is not included in the EURD list, but one or more of its substance components?**

No. Based on the information in the EURD list on individual components, no PSURs have to be submitted for assessment in a PSUSA procedure for combination products whose individual substances are included in the list.

However, the pharmaceutical companies need to check in such cases whether a PSUR must be submitted for PSUR assessment on a national level:

- no PSUR is required if the medicinal products are exempted from routine PSUR submission;
- if a specific condition that a PSUR is to be submitted is included in the notice of marketing authorisation, this has to be observed;
- if there is neither a waiver nor a specific condition in the notice of marketing authorisation, PSURs are submitted according to the standard submission cycle (generally every 3 years, see question 15 “Can reporting intervals be extended for substances not included in the EURD list?”).

8. **Is the DLP in the EURD list binding, even if this means that the period specified for the PSUR frequency is exceeded?**

Example: according to EURD list, the DLP is 2018, the specified PSUR frequency is 6 years, the last PSUR was submitted in 2010 – observing the DLP would lead to a frequency of 8 years.

Yes, the DLP is binding. The DLPs specified in the EURD list are intended to harmonise the
submission of PSURs. At present, many medicinal products with the same active substances have different DLPs. Therefore, the period between the last PSUR and the first PSUR in accordance with the EURD list can differ from or be longer than the frequency specified in the list. The period mentioned in the EURD list can thus only be harmonised starting with the second PSUR submission according to the EURD list. Make sure that the PSUR submitted according to the EURD list comprises the entire reporting period since the last DLP even if the PSUR frequency specified in the EURD list is exceeded.

9. Does harmonisation with the EURD list have to be notified?

Harmonisation of PSUR submission with the EURD list lies within the responsibility of pharmaceutical companies.

If a specific condition to submit PSURs has been imposed in the notice of marketing authorisation (in accordance with Section 28 sub-sections 3 or 3a AMG), notification of variation regarding harmonisation with the EURD list is required. For information on such variations please refer to Section 29 (1e) AMG and the EMA website: [http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2012/05/WC500127658.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2012/05/WC500127658.pdf).

If the notice of marketing authorisation does not impose a specific condition for the submission of PSURs, notification of variation is not required.

It is generally not necessary for pharmaceutical companies to inform the BfArM of harmonisation with the EURD list in cases where submission of PSURs is not imposed in the notice of marketing authorisation. The BfArM kindly requests companies not to submit such information and not to inquire about confirmation of DLPs. Please note that the licensing authority will normally not send out confirmations of DLPs for individual medicinal products.

10. What is the PSUR Single Assessment (PSUSA)?

PSUR Single Assessment, for short PSUSA, stands for the assessment of PSURs of active substances/combinations of active substances included in the EURD list, by the Pharmacovigilance Risk Assessment Committee (PRAC).

PSUSA procedures are administered by the EMA and include both substances with centralised marketing authorisations and those with purely national authorisations in the Member States.

PSUSA procedures are managed by the PRAC rapporteur responsible for the compilation of the Assessment Report. The other Member States are involved in the PSUSA procedure by commenting on the Assessment Report. The PSUSA procedure is finalised in the PRAC by a PRAC Recommendation. The latter is then discussed in the CHMP and the EC (substances with centralised authorisations) or the CMDh, and the EC where required (substances with purely national authorisations); it is finalised by the EC Decision or the CMDh Position.

11. **Do the variations resulting from a PSUSA procedure have to be implemented by all pharmaceutical companies?**

Yes. The risk relevant variations in the product information resulting from the Assessment represent the latest scientific findings and have to be implemented by all pharmaceutical companies for the active substance/combination of active substances referred to in the PSUSA procedure. This applies also in cases where no PSURs were submitted in the procedure for the products concerned due to an exemption permission (waiver, e.g. for generic medicinal products).

12. **Where are the variations in the product information texts, resulting from a PSUSA procedure, published?**

In the case of PSUSA procedures on active substances/combinations of active substances for which there exist purely national authorisations in the EU (including MRP/DCP authorisations), the required variations in the texts, including the scientific reasons for the variations, are published on the EMA website: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/psusa_search.jsp&mid=W0b01ac0580902b8d

The texts are available there in the languages of all EU Member States. In Germany the results are implemented by a notice of implementation.

In the case of PSUSA procedures on active substances/combinations of active substances for which there exists at least one centralised marketing authorisation in the EU beside national marketing authorisations, the required text variations are published on the website of the EC: http://ec.europa.eu/health/documents/community-register/html/refh_others.htm

The text variations and the scientific reasons are also available in all languages of the EU Member States. In Germany the results are implemented by a notice of implementation.

In the case of PSUSA procedures on active substances/combinations of active substances for which there exist only centralised marketing authorisations the required text variations are published on the EMA website under EPAR: [European public assessment reports](http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/psusa_search.jsp&mid=W0b01ac0580902b8d)

13. **How to submit variations in product information texts resulting from PSUSA procedures?**

Information on implementation is provided on the EMA website “Periodic safety update reports: questions and answers”: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000041.jsp&mid=W0b01ac0580023e7d


Further details result from the relevant documents on the CMDh website and the relevant notices of implementation.
14. **What does the PSUR submission depend on if the active substance is not on the EURD list?**

First, it has to be verified whether a condition to submit a PSUR has been imposed in the notice of marketing authorisation. If this is so, PSURs are to be submitted accordingly (see question 22 “How is a condition to submit a PSUR formulated in the notice of marketing authorisation?”). If this is not the case the following applies:

In the case of marketing authorisations that are exempted from the obligation to submit PSURs in accordance with Section 63 d) sub-section 4, no submissions must be made.

In all other cases, submissions are required according to the standard cycle pursuant to Section 63d sub-section 3 AMG, unless the pharmaceutical company has applied for prolonging the PSUR submission intervals (see question 15 “Can reporting intervals be extended for substances not on the EURD list?”).

A request for PSURs by the competent federal higher authority in individual cases pursuant to Section 63 d) sub-section 4 sentence 1 number 2 AMG remains unaffected by the afore-mentioned.

15. **Can reporting intervals be extended for substances not on the EURD list?**

Yes, extension on request is principally possible unless the notice of marketing authorisation contains a condition pursuant to Section 28 sub-section 3 or 3a AMG. Either procedural path may be followed:

1.) The pharmaceutical company contacts the BfArM per e-mail: PSUR@bfarm.de (Reference: Request for extension of the obligation to submit PSURs) presenting the following details: the INN of the active substance/combination of active substances for which the request is made; the last PSUR period; the proposed new PSUR frequency; the DLP proposed for extension; reasons for the proposal; a list of all medicinal products concerned by the PSUR based on the information available at the time, inclusive of the ATC code(s).

The BfArM reviews the proposal and communicates the result of the review. The DLP and PSUR frequency confirmed by the BfArM should then be notified by Variation IA IN.

2.) The pharmaceutical company will directly submit a Variation IB for extension of the PSUR period presenting the details as stated under 1.) The BfArM reviews the proposal and communicates the result of the review.

The request should be made three months prior to the next DLP at the latest. Requests with retrospective effect, i.e. submitted when the DLP is already exceeded, are rejected.

16. **Can several MAHs or pharmaceutical companies submit a joint PSUR?**

No, both the AMG and the GVP Module VII (PSUR) only provide for submission by the relevant MAH. Submission of a PSUR by different pharmaceutical companies is not possible even if they are subsidiaries of the MAH.
17. For which medicinal products do no PSURs have to be submitted?

Generally, PSURs have to be submitted for all authorised medicinal products whose active substances/combinations of active substances are included in the EURD list. Pharmaceutical companies are requested to regularly check the EURD list, the exemption rules and their notices of marketing authorisation with regard to the requirement to submit PSURs.

The following medicinal products are exempt from the routine submission of PSURs in accordance with Section 63 d) sub-section 4 AMG and Directive 2001/83/EC:

- generic medicinal products (marketing authorisations in accordance with Section 24b sub-sections 1 and 2 AMG)
- marketing authorisations in accordance with Section 22 sub-section 3 AMG (well-established use)
- homeopathic and traditional herbal registrations (Sections 38 and 39a AMG)
- standard authorisations

However, PSURs have to be submitted for these groups of medicinal products if they are required for the active substances involved according to the EURD list (see question 5 "What is the EURD list?"); if the BfArM requests PSURs in individual cases; or if a specific condition to submit PSURs is imposed in the notice of marketing authorisation (see question 22 "How is a condition to submit a PSUR formulated in the notice of marketing authorisation?").

In accordance with Section 63 d) sub-section 5 AMG, the regular reporting requirements mentioned therein do not apply to parallel imports.

If a marketing authorisation expires within the reporting period or within the interval between the end of the reporting period until the due date of the PSUR submission (70 or 90 days after the DLP), the requirement to submit PSURs no longer applies. This is also true if the medicinal products are still being sold off.

For clarification, the following table presents the terms used in Directive 2001/83/EC and the corresponding terms in the AMG:

<table>
<thead>
<tr>
<th>AMG</th>
<th>EURD List labelling / or according to (Directive 2001/83/EC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generic medicinal products (authorisations pursuant to Section 24b (2) AMG)</td>
<td>Generic application (Art. 10 (1), Art. 10 (2)</td>
</tr>
<tr>
<td>Authorisations pursuant to Section 22 (3) AMG</td>
<td>Bibliographical (or well-established use) applications (Art. 10a)</td>
</tr>
<tr>
<td>Homeopathic registrations (Section 38 AMG)</td>
<td>Registrations of homeopathic medicinal products (Art. 14)</td>
</tr>
<tr>
<td>Traditional herbal registrations (Section 39a AMG)</td>
<td>Registrations of traditional herbal medicinal products (Art. 16a)</td>
</tr>
<tr>
<td>Section 105 in conjunction with Section 109 AMG</td>
<td>Does not apply</td>
</tr>
<tr>
<td>Authorised medicinal products, if no pre-/clinical trials have been presented</td>
<td>Does not apply</td>
</tr>
<tr>
<td>Standard authorisations</td>
<td>Does not apply</td>
</tr>
<tr>
<td>Parallel import authorisations</td>
<td>Does not apply</td>
</tr>
<tr>
<td>Expired authorisations max. 70 or 90 days after DLP</td>
<td>Does not apply</td>
</tr>
</tbody>
</table>
18. Do PSURs have to be submitted for applications in accordance with Section 24 b) sub-section 2 sentence 6 AMG and for applications in accordance with Section 24 a AMG?

Applications in accordance with Section 24 b) sub-section 2 sentence 6 AMG (so-called “hybrid applications”) and in accordance with Section 24 a AMG (so-called “informed-consent-applications”) are not mentioned in Section 63 d) sub-section 4 AMG or in Art. 107 b) sub-section 3 of Directive 2001/83/EC and therefore hybrid applications remain subject to the submission requirement in accordance with Section 63 d) sub-section 1 AMG.

19. Do PSURs have to be submitted for medicinal products with (post-)marketing authorisations („Nachzulassung“) in accordance with Section 105 AMG?

Pharmaceutical legislation does not provide for a general exemption from the requirement to submit PSURs for this type of medicinal products. In accordance with the criteria laid down in Section 63 d) sub-section 4 AMG, no PSURs have to be submitted on a routine basis in the following constellations:

- Marketing authorisation in accordance with Section 105 AMG in conjunction with 109a AMG.
- A prolongation of the marketing authorisation in accordance with Section 105 AMG was granted in accordance with Section 22 sub-section 3 AMG. In most cases this is explicitly stated in the application forms.

In all other respects, post-marketing authorisations in accordance with Section 105 AMG are to be equated with marketing authorisations in accordance with Section 22 sub-section 3 AMG if no preclinical and/or clinical studies were submitted in the course of the prolongation procedure, but other scientific findings/monographs were referred to. If own preclinical and/or clinical studies were submitted in the course of the post-marketing authorisation process, the submission requirement in accordance with Section 63 d) sub-section 1 AMG remains valid.

Moreover, PSURs must be submitted
- if, in accordance with the EURD list for the active substances concerned, PSURs are also required for marketing authorisations pursuant to Article 10 a of Directive 2001/83/EC, or
- if the BfArM requests PSURs in individual cases in accordance with Section 63 d) sub-section 4 sentence 1 number 3 AMG

20. Do PSURs have to be submitted for licensed homeopathic medicinal products and anthroposophic medicinal products?

If homeopathic/anthroposophic medicinal products are licensed in accordance with Section 22 sub-section 3 AMG no PSURs have to be submitted (see question 17 “For which medicinal products do no PSURs have to be submitted?”). Homeopathic/anthroposophic marketing authorisations in accordance with Section 22 AMG that were granted on the basis of monographs, are equivalent to marketing authorisations in accordance with Section 22 sub-section 3 AMG.

If, in individual cases, studies in accordance with Section 22 sub-section 2 AMG were submitted in the course of the licensing of homeopathic/anthroposophic medicinal products, PSURs would have to be submitted.
21. **Does claiming of an exemption from the obligation to submit PSURs have to be brought to the authority's attention?**

The alignment of the PSUR submission with the new legal provisions lies in the responsibility of the pharmaceutical company. After review of the licensing dossier and according to the criteria stated in these FAQ (see question 19 "Do PSURs have to be submitted for medicinal products with (post-)marketing authorisations in accordance with Section 105 AMG?"), the pharmaceutical company also has to decide whether a medicinal product is exempted from the obligation to submit a PSUR in accordance with the derogation rule laid down in Section 63 d) sub-section 4 AMG.

It is not necessary for the pharmaceutical company to notify the BfArM that it is claiming an exemption (e.g. for generic medicinal products). Companies are kindly requested not to submit such information. The licensing authority will not send out confirmations of exemptions for individual medicinal products.

22. **How is a condition to submit a PSUR formulated in the notice of marketing authorisation?**

In accordance with Section 63d sub-section 4 sentence 1 AMG, PSURs must be submitted for medicinal products exempted from the routine submission requirement if such a condition was imposed in the notice of marketing authorisation in accordance with Section 28 sub-section 3 or 3a AMG.

The following standard wordings in the notice of marketing authorisation do not constitute a condition entailing the reporting obligation:

- request to adjust the PSUR cycle to the reference product
- approval of a 3 year cycle for submission of PSURs based on an application for deadline extension

23. **Will the HMA's PSUR Worksharing Project (WSP) be continued?**

Open WSP procedures will be carried out and completed. The list of active substances still awaiting processing is published on the website of the Heads of Medicines Agencies (HMA): [http://www.hma.eu/348.html](http://www.hma.eu/348.html). When the still outstanding procedures have been completed the WSP project will be terminated (presumably in the course of 2016).

24. **How are the costs for the processing of PSURs determined?**

For PSURs submitted in the framework of PSUSA procedures the fees are determined by the EMA. The fees are charged on the basis of the provisions in the Fee Regulation: [http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000632.jsp&mid=WC0b01ac058089678e](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000632.jsp&mid=WC0b01ac058089678e)

For PSURs which are not subject to a PSUSA procedure and which are processed on a purely national level by the BfArM, the fees are calculated on the basis of the current version of the AMG Kostenverordnung (cost regulation). The level of fees charged for assessment of a PSUR depends on the type of authorisation procedure of the smallest processing number (Eingangsnummer / ENR) valid at DLP (end of reporting period), and on the time the active substance or the same combination of substances was first authorised in Germany.
25. **Is an Assessment Report compiled in any case?**


In the case of PSURs that are not subject to a PSUSA procedure and that are assessed by the BfArM, the MAH will only receive Comments or an Assessment Report if regulatory measures are required. In such cases the Comments or the Assessment Report are transmitted exclusively electronically via e-mail. If the currently valid MAH has not received an Assessment Report by the time he receives the notice of fees and expenses for the PSUR, no regulatory measures are necessary.