Bundesamt für
Sicherheit im
Gesundheitswesen
BASG

FAQ Pharmacovigilance

Periodic Safety Update Reports (PSUR)

For which medicinal products are PSURs to be submitted?

1. For all purely national approvals.
2. For all active substances/active substance combinations that are obligated to submit a PSUR according to the EURD list. These products are treated in the PSUSA process.

Only generics, bibliographic ("well established use") approvals and registrations as traditional herbal, pharmacy-owned and homeopathic medicinal specialties are exempt from the submission of a PSUR. However, regular, updated safety reports must also be submitted for these products if 2. applies or if:

- such an obligation has been imposed as a condition or requirement for the granting of an authorization or registration; or
- a submission is ordered by the Federal Office for Safety in Health Care because of concerns related to pharmacovigilance data or because of concerns about the lack of regular updated drug safety reports for an active substance after authorization or registration.

Authorization holders of homeopathic medicinal products for human use are advised that from January 1st, 2020 [ie from the data lock point: September 30th, 2019] no further PSUR submissions will be necessary, unless these are ordered by the BASG on a case-by-case basis.

Are additions to the EURD list possible?

Yes - if one of the following justifications can be given - in the interest of public health - to avoid multiple assessments for authorizations in more than one country of the European Union - for the international harmonization of the PSUR template.

Requests for amendments should be sent by email using the dedicated “template” (available on the EMA website) .

Do PSURs have to be submitted for herbal medicinal products?

Only traditional herbal medicinal specialties registered according to AMG §12 are exempt from the PSUR template.

If the herbal active ingredient or the combination of active ingredients is on the EURD list, the obligation to submit a PSUR results in accordance with the information contained therein.

If the active substance or the combination of active substances of the herbal medicinal product is not mentioned on the EURD list, the PSUR is required according to the submission cycle, with the exception of traditional herbal medicinal products registered according to AMG §12.

Do generics also have to carry out any safety measures (such as conducting cumulative reviews on certain suspected side effects) that have been prescribed for marketing authorization holders of originator preparations? Are reports to be submitted to the BASG?

Irrespective of the type of authorisation, according to AMG §75i(1) all authorization holders are obliged to monitor pharmacovigilance data to determine whether there are new risks, whether existing risks have changed or whether the risk-benefit balance of pharmacovigilance has changed medicinal products has changed in order to be able to take appropriate measures if necessary. The implementation of measures such as "close monitoring" or evaluations such as "cumulative reviews" are part of this obligation.

Although generic or Section 10a marketing authorization holders are not required to routinely submit an updated report, a PSUR submission may be required due to concerns related to pharmacovigilance data, particularly where those concerns result in a change in benefit -Risk ratio could result (cf. AMG §75m).

What is the submission rhythm of PSURs?

The BASG must specify in the notification of approval how often PSURs are to be submitted.

The submission date is calculated according to the prescribed frequency from the legal force of the notification of admission.

If the submission frequency for PSURs has not been specified in the notification of approval (applicable to medicinal products that were approved before the federal law came into force in the version of Federal Law Gazette I No. 110/2012), PSURs must be submitted according to the following specifications:- if the medicinal product has not yet has been placed on the market: At least every 6 months after approval - if the medicinal product has been placed on the market: At least every 6 months during the first two years after the first placing on the market, once a year in the following two years and thereafter at three-year intervals - At any time immediately upon request by the BASG.

If the active substance is on the EURD list, the specifications defined there are mandatory for all authorization holders.

The above requirements apply until a different frequency or other submission dates have been specified in a change to the approval.

How to report/apply for the PSUR cycle change?

For medicinal products whose active ingredient/active ingredient combination is on the EURD list, the frequency and submission date are calculated according to the data lock point (DLP) specified in the list. It is not necessary to report the adjustment of the PSUR template to the DLP of the EURD list, unless there is an existing condition for another PSUR cycle (e.g. due to the approval notice or due to an existing risk management plan in which the PSUR submission cycle is mandatory).

The marketing authorization holder is obliged to check the EURD list monthly for any changes.

For active substances that are not on the EURD list, an application for a change can be submitted to the Pharmacovigilance department using form F_B23 PSUR cycle change according to §24(4) AMG.

What happens to a medicinal product (generic, hybrid, bibliographical approval) that contains an active ingredient/combination of active ingredients that is not on the EURD list?

In principle, a PSUR for an active substance or an active substance combination that is not on the EURD list must be submitted at national level (not in a PSUSA). If it turns out that the active substance / the combination of active substances is authorized in more than one EU country and it is a full authorization / hybrid authorisation, the EMA should be informed by email .

How should I submit the PSUR?

Electronic PSUR submission via the “PSUR Repository” has been mandatory since June 13, 2016. The PSUR Repository provides a secure electronic submission point for Marketing Authorization Holders and serves as a database for PSURs, PSUR opinions, comments and results.
Both PSURs for PSUSA procedures ("EU single assessment") and PSURs for national PSUR submissions (for "non-EU single assessments") can only be submitted via the PSUR repository. CESP submissions, CD-ROMs, etc. are considered undelivered.

For detailed information and help with electronic filing, the PSUR Repository website, numerous webinars and the "MAH user guide" are available.

What are the requirements for the content and format of a PSUR?

The required design of the PSUR is described in the Guideline on good pharmacovigilance practices (GVP) Module VII - periodic safety update report.

PSUR submission and eCTD

Companies that have not yet submitted documents via eCTD but via NeeS should prepare them as follows before submitting the next PSUR:

- Creation of a "baseline" in the eCTD with the sequence 0000, which should contain at least the documents from module 3.
- Then submit the PSUR via the PSUR repository. In the eCTD, the next higher sequence (0001 in this case) is then assigned to the PSUR.

It should be noted that - once switched to eCTD - NeeS can no longer be used and that from 01/01/2019 NeeS will no longer be available at all!
The conversion should be made at the earliest opportunity, not just at the end of the year.
See BASG website for more information.

PSUR
charging See Fees Ordinance

PSUR Repository

What is a PSUR repository (= online data storage)?

The PSUR Repository is a common repository for all PSURs, PSUR Assessments Reports (ARs) from the competent regulatory authorities, for their comments and final results.
National authorities have secure access to the repository. More information about the PSUR repository can be found here .

What is changing in PSUR submission?

From June 13, 2016, it is mandatory for all marketing authorization holders within the EU to submit PSURs for medicinal products for human use via the PSUR Repository. All companies are asked to use this repository and no longer submit PSURs directly to the national authorities.
This repository is mandatory for central and nationally authorized medicinal products, regardless of whether they follow the EU Single Assessment or the national assessment procedure. The PSUR repository is intended exclusively for human medicinal products.

What happens if the PSUR is not submitted through the PSUR Repository after June 13, 2016?

PSURs that are not uploaded through the PSUR Repository will be considered unsubmitted and will not be reviewed. Thus, the marketing authorization holder does not fulfill his legal obligation to submit PSURs.

How to submit a PSUR?

All PSURs are submitted via the EMA PSUR Repository and uploaded via eSubmission Access/ Web Client .
In order to be able to submit the PSURs using the eSubmission access/ web client, all users must register themselves in advance. The PSURs can only be submitted as electronic Common Technical Documents (eCTDs) or as non-eCTDs (Nees). All other electronic formats cannot be uploaded to the PSUR repository and will therefore be rejected.

Information on the repository, registration instructions and multimedia instructions for marketing authorization holders on how to submit the PSURs correctly, as well as instructions on the compliant electronic formats of the submission documents can be found on the EMA PSUR Repository website .

What are the requirements to submit a PSUR through the PSUR Repository?

Before submitting via the PSUR repository, the marketing authorization holder must ensure that all information on their medicinal products is correctly entered in the Article 57 database. This is a legally binding requirement of EU drug legislation.

The PSUR repository is connected to the Article 57 database. If a product does not appear correctly in this database, it will not appear in the PSUR repository either.
Further details on the submission of information on medicinal products in the Article 57 database can be found on the EMA website .

Who can I contact if I have questions about the PSUR repository?

Any questions and feedback regarding the PSUR Repository or the eSumbission Access/ Web Client can be directed to EMA via the EMA Service Desk Portal .

Questions and answers from the AGES interview on May 30, 2016

Which cover letter should be used for submitting PSURs to the PSUR repository? What must be considered with the cover letter?

For PSUSA procedures: While a cover letter is currently provided by EMA to be used for PSUSA submissions, an update from EMA is planned for the near future.

In point 7, PSUR Single Assessment should be clicked.

Purely national procedures (non-EU single assessments) : The cover letter mentioned above should also be used for these procedures.
The additional indication of the GZ (basic number) for products approved in Austria is desired. The GZ should be noted in Annex I under "Authorization Number of product in the member state" in addition to the approval number.

Point 7 of the cover letter should indicate which document is involved, eg PSUR Single Assessment, Worksharing and many others can be selected.

A single cover letter for all countries where the product is approved is sufficient.

As soon as there is new information, it will be published on this page.

More information about the PSUR repository can be found here .

Please note the new instructions "MAH PSUR repository User Guidance document".

Can delivery files be used again?

The delivery file describes the metadata of a PSUR submission (e.g. the products concerned).

Since the PSUSA number is also part of this description and changes in the format of the delivery file are to be expected, **reuse is not recommended.**

Could the EMA provide information on how many MAHs are involved in an incipient PSUSA procedure?

This is currently not planned. Only information stating the chargeable units for the respective authorization holder is sent out.

Pharmacovigilance data for the extension process

Which pharmacovigilance data must be submitted for the extension procedure?

Irrespective of the recommendations of the "CMDh BEST PRACTICE GUIDE ON THE PROCESSING OF RENEWALS IN THE MUTUAL RECOGNITION AND DECENTRALISED PROCEDURES" , the following documents must be submitted for a renewal procedure in Austria:
AT=RMS: An "Addendum to the clinical overview" must be submitted.
AT=CMS: For the time being, an “addendum to the clinical overview” only needs to be submitted

when required by the reference member state.

National approval:
The submission of an "Addendum to the clinical overview" is required regardless of whether it is a "generic", "well established use", "traditional herbal" or "homeopathic approval".

The period of the "Addendum to the clinical overview" covers the period from the approval date of the product to the submission date of the extension procedure.

Even if the **pharmacy's own approvals** are exempt from the PSUR submission, the submission of pharmacovigilance data for the extension procedure may be necessary in the case of safety-relevant aspects.

Access to PSUR procedures for consultants - 09/15/2016

Questions and answers from the AGES interview on September 15, 2016

Who can see PSUR procedures in the Authorization and Lifecycle of Proprietary Drugs eService?

PSUR procedures are visible to affected marketing authorization holders after the procedure has been created in the eService. A one-time registration is required
to use the eService .

How do consultants get permission to see PSUR procedures in the Drug Proprietary Authorization and Lifecycle eService?

Access to PSUR procedures for consultants is possible after notification by email from the marketing authorization holder.

Please note that the consultant must be registered for the eService. Registration is available here .

Questions and Answers - 06/12/2018

Questions and answers from the BASG - conversation from 12.06.2018

Can a MAH of a generic drug for which he does not have to submit PSURs still get the assessment report for a PSUSA procedure?

Nein, doch das Outcome des PSUSA Verfahrens wird auf der EMA Homepage publiziert:
Information on the outcome of centrally authorised medicinal products is made available in the European Public Assessment Report (EPAR) page of the relevant medicine.
Information regarding the variation of NAPs that are part of a CAP/NAP procedure is available in the Community Register for nationally authorised products.
Information on the outcome of the EU single assessment of PSURs involving nationally authorised medicinal products only is made available on the EMA web page under 'Home/Find medicine/Human medicines/Periodic safety update report single assessments' until the EU web' portal is fully functional.

Is a longer PSUR period than 3 years possible for approved homeopathic medicinal products?

According to AMG, the 3-year cycle is currently the longest possible PSUR period.

Risk Management Plans (RMP)

For which medicinal products must RMPs be submitted?

In principle, a risk management plan for the medicinal product in question must be included with every application for authorisation. This also applies to related applications for approval (Section 10 AMG as amended)

The submission of an RMP for traditional herbal medicinal products and homeopathic products that are registered according to AMG §11 is not required.

The submission of an RMP or RMP update is required:

1. if the application represents a significant change to the existing authorisation, e.g.:

- new dosage
- new application/dosage form
- new manufacturing process (for biotechnologically manufactured substances)
- pediatric indication / other significant change in indication.

2. at the request of the BASG if there are concerns about the risk-benefit ratio,

- as part of the approval extension (renewal) if a risk management plan (RMP) has already been drawn up for the product.

When is an update of the RMP required?

In principle, updates of the RMP are always required in the life cycle of the medicinal product whenever significant new risks become apparent. If there are significant changes in the risk/benefit ratio or information that affects the safety specification, pharmacovigilance plan or risk minimization plan becomes available, an update of the RMP should be made immediately.

Please note that changes to the RMP must be submitted both in change mode and in the final version.

What are the requirements for the content and format of an RMP?

The risk management system must be proportionate to the identified and potential risks of the medicinal product and the need for post-authorisation/registration safety data.

The requirements for RMPs are set out in Module V of Good Vigilance Practice (GVP). An RMP template can be found in the relevant Marketing Authorization Holder Guidance :

Guidance on the format of the risk management plan (RMP) in the EU – in integrated format (Rev. 2)

What information related to the RMP is made public?

- A summary of the RMP to be prepared by the applicant/MAH in accordance with the provisions of the GMP.
- Information on risk-minimizing measures that are a condition for admission (e.g. register, PASS, patient brochures, questionnaires).

The RMP documents intended for publication must also be submitted as Word documents. The summaries of the RMPs for centrally authorized medicinal products are published on the EMA website. The summaries of the RMPs for nationally authorized medicinal products are published on the national BASG website in the medicinal product register.

How are risk management plans (RMPs) to be submitted for already approved medicinal products or updates to existing RMPs?

Both the addition of an RMP to an existing authorization and the submission of updates to existing RMPs correspond to a change in the authorization dossier (Section 1.8.2).
For this reason, these business cases must be submitted as formal changes/variations. For details see:
https://www.hma.eu/fileadmin/FILES/Human_Medicines/CMD_h_/Questions_Answers/CMDh_257_2012_Rev23_2020_12_clean_QA_on_PhV.pdf

Pharmacovigilance System

When is a "description of the pharmacovigilance system" to be submitted?

When submitting an application for authorization (or registration), a summary of the pharmacovigilance system (PSMF summary) must be submitted. A PHV system must be operated, which is described in the pharmacovigilance master file and whose summary is represented by the PSMF summary.

- Generally for all new registrations
- When submitting an application for approval for sales in parallel imports (AMG §10c Para.3 Z 13 idgF), a PHV system, PSMF and the submission of a PSMF summary are required.
- When submitting an application for a traditional-plant registration, a PSMF summary for new national registrations is also required.
- Pharmacy registrations

Exception:

- Registered Homeopathics

PSMF= Pharmacovigilance system master file
PHV=Pharmakovigilanz

Implementation of PHV issues / DHPC and educational material

We have received a request to incorporate safety-relevant wording into the technical information and instructions for use, which is already included in our texts. How should we proceed?

In this case, please write an email.

Are the marketing authorization holders always informed by the BASG if safety-relevant wording is to be included in the information for healthcare professionals and the information for use?

If, for example, within the framework of a PRAC referral, a PRAC signal recommendation or a PSUSA, it was decided to include new safety-relevant information in the information for healthcare professionals and instructions for use, marketing authorization holders of nationally (and decentrally, if AT=RMS) authorized medicinal products usually receive a request for an adjustment the lyrics. However, this does not relieve the marketing authorization holders from their obligation to regularly screen the relevant sources.

We have received a request to incorporate PRAC signal recommendations into the information for healthcare professionals and the information for use. The specified deadline for submission cannot be met. How should we proceed?

In this case, please apply for an extension of the deadline in good time by email. The application must be made in a timely manner so that the MAH can submit it in good time if it is rejected.

We have received a request to incorporate PRAC signal recommendations into the information for healthcare professionals and the information for use. However, due to another change, the texts of the corresponding products are currently under medical examination. How should we proceed?

In this case, please include a note in the accompanying cover letter and on the form that the texts are already being processed as part of another variation.

How to submit DHPC Letter and Educational Materials?

In principle, submissions are made by e-mail to the following e-mail addresses: dhpc-em@basg.gv.at .
Necessary documents are: German translation and English original version, planned distribution group, planned schedule.

Would it be possible, as is already common practice in other countries, to make educational materials from the individual MAHs available on the BASG homepage (possibly with access only for specialist groups)?

There are currently no plans to publish the educational material on the BASG website.

Is a joint design or distribution of DHPC or educational material, which refers to an active substance (across companies) or to class labelling, controlled and coordinated by the BASG?

The cooperation between the affected companies is supported by the BASG. Unfortunately, coordination by the BASG is not possible.

What are the requirements for the distribution group? The companies will certainly define different distribution groups / address lists for the same active ingredient. How can it be ensured that all affected doctors are reached?

The distribution group is only to be proposed to the Federal Office in the form of groups (as also specified for the EMA). E.g. general practitioners, internists...

The responsible MAH must ensure that an up-to-date address list is used.

Does a marketing authorization holder who had not marketed his product at the time of an active substance-related (several MAH relevant) DHPC mailing and therefore did not participate in the mailing, have to forward the DHPC if he still markets the product later?

In principle, it is necessary to make the relevant materials available for marketing. In this case, it is necessary to contact the BASG in good time.

The "Blue Hand" has already been implemented in Germany. Can we expect the same for Austria?

In Austria, the "Blue Hand" is currently not implemented and used

What would be acceptable distribution methods for the training materials for the BASG? Only by post, or also via emails, homepages?

In principle, distribution is possible via all of these routes. How the DHPC / Educational Materials can be distributed is a case-by-case decision. Therefore, the desired distribution method should be specified when submitting the application.

side effects

Reporting channels for suspected side effects

In terms of effective pharmacovigilance, it is essential that reports of suspected side effects are received by the competent authority.

Accordingly, § 75g AMG stipulates that **healthcare professionals** must report suspected side effects to the BASG immediately. According to § 75h AMG, **patients can and should also report suspected side effects to the BASG.**

Another way of reporting suspected side effects is to report them to the **marketing authorization holder** . According to § 75j AMG, a marketing authorization holder may not refuse to accept and examine reports from healthcare professionals and patients.
Marketing authorization holders are required to electronically submit information on all suspected adverse reactions to the Eudravigilance database. This ensures that the competent authorities are also aware of reports of suspected side effects that the marketing authorization holder receives. Furthermore, the authorization holder undertakes to provide regular information about the reports pursuant to Sections 75g and 75h AMG via the Eudravigilance database.

Other ways of reporting a suspected side effect are not provided for in the AMG.

The reporting channels for suspected side effects described above ensure that these reports of suspected side effects are evaluated for causality, and that the benefit-risk ratio of all approved medicinal products is continuously monitored in close cooperation with the EU network of authorities, and thus a continuous evaluation is carried out, which is in the current version the technical information is reflected.

Is there a way for patients or their relatives to submit a side effect report?

Yes. Patients or their relatives have the option of reporting suspected side effects of medicinal products to the Federal Office for Safety in Health Care as follows:

- using an electronic reporting form
- using a paper form

medication errors

Medication errors are unintentional errors in the prescribing, dispensing, administration or monitoring of a drug under the supervision of a healthcare professional or by a patient/consumer. They represent the most common preventable cause of adverse drug reactions (ADRs) in medical practice: an estimated 19-56% of all ADRs in hospitalized patients result from avoidable medication errors1.

According to statistics from the World Health Organization (WHO) , around 18% of all European Union (EU) citizens say they have experienced a serious medical error in hospital and 11% have been prescribed the wrong medication.

Since July 2012, the new EU pharmacovigilance legislation requires that all medication error-based ADRs in the EU area are reported to EudraVigilance , the EU database for ADRs.

The legal requirements for competent national authorities, the EMA and marketing authorization holders regarding data collection, data management and reporting of possible adverse effects (serious and non-serious) of medicines authorized in the EU are contained in the "Guideline on Good Pharmacovigilance Practices" (GVP): Module VI - Collection, management and submission of reports of suspected adverse reactions to medicinal products (Rev 2) " .

The EMA provides extensive information on medication errors and organized a regulatory workshop on medication errors in February 2013.

The Committee for Medicinal Products for Human Use (CHMP) of the EMA has published a position paper (EMA/274183/2012) on the topic of medication errors in the context of benefit risk balance and risk minimization .

1 'Creation of a better medication safety culture in Europe: Building up safe medication practices', Council of Europe Expert Group on Safe Medication Practices (2006).

Does an authorization holder have to carry out a test phase with the BASG for the conversion to electronic reporting in the E2B(R3) format?

no Tests are only carried out with the EMA, no longer with the national authority. Further information can be found on the EMA website under the keyword "EudraVigilance".

How does the authorization holder transmit the literature publications on the reported case reports from the literature?

A copy of the original publication of the domestic literature cases should be sent by email to evlit@ema.europa.eu. On request, the literature must also be sent to the BASG.

Wie meldet man "Emerging Safety Issues“?

Events or observations that do not fall within the scope of spontaneous reporting or do not meet the reporting obligation, but may affect the benefit-risk of a medicinal product and/or have an impact on public health, are reported as soon as possible, at least within 3 working days GVP Module IX rev. 1 and AMG §75m if they become known as "emerging safety issues" to the EMA by email or also by email to the national authority in which an approval exists.

When reporting an emerging safety issue, the marketing authorization holder should describe the problem, the source(s) of the information, any actions planned or taken with timelines and any relevant documentation available at the time of the first report. Any further information relevant to the issue should be communicated to the Agency and the relevant national competent authorities as soon as they become available.

Examples of such events are:

- significant safety issues identified in ongoing or newly completed studies, e.g. B. an unexpectedly increased rate of fatal or life-threatening side effects
- significant safety issues identified through spontaneous reports or publications in the scientific literature, which may lead to consideration of a contraindication, restriction of use of the drug or its withdrawal from the market
- Important safety-related regulatory measures outside the EU, e.g. B. a restriction on the use of the drug or its suspension

What are the pharmacovigilance obligations of the parallel import marketing authorization holder?

According to § 10c Para. 3 Z 13 AMG, the holder of a license for distribution in parallel imports must also have a pharmacovigilance system and, if necessary, a risk management system.

Although the holder of a license for sales in parallel imports is not obliged to submit a periodic assessment report (PSUR), he has to do according to § 94h Abs.9 AMG

- suspected side effects, or
- suspected adverse reactions in humans, or
- improper use, or
- the lack of the expected effectiveness, or
- insufficient waiting times, or
- frequently observed misuse and serious abuse, or
- Quality defects, or
- to record any suspected transmission of pathogens through the medicinal product that has occurred in a third country and to report it to the Federal Office for Safety in Health Care and the agency.

Furthermore, he **must inform the Federal Office for Safety in Health Care of all observations and data that may be of importance for the safety of medicinal products.**

Pursuant to Section 75q (6) AMG, the holder of a license for sales in parallel imports must also record quality defects that have occurred domestically and have been brought to his attention in accordance with Section 2 or have otherwise become aware of and report them to the Federal Office for Safety im health care system immediately, but no later than 15 days after becoming aware of it. The holder of a permit for distribution in parallel imports must document the original wording of the relevant notification made to him and keep it for five years and transmit it to the Federal Office for Safety in Health Care on request without delay.

If a notification according to § 75g (notification by members of the health professions) concerns a medicinal product that was brought to Austria on the basis of a license for distribution in parallel imports, the Federal Office for Safety in Health Care must inform the holder of the license for distribution in parallel imports without delay, but no later than 15 days after becoming aware. The information must be provided in anonymous form.

Query notice
pharm-vigilanz@basg.gv.at

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