



State Agency of Medicines of the Republic of Latvia

Information for marketing authorisation holders

27 May 2016

Submission of educational materials laid down in the risk management plan to the State Agency of Medicines and their agreement

Legislation

- [Regulation \(EC\) No 726/2004 of the European Union and of the Council of 31 March 2004 laying down the Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency \(hereinafter - Regulation No. 726/2004\)](#)
- [Commission Implementing Regulation \(EU\) No 520/2012 of 19 June 2012 on the performance of the pharmacovigilance activities provided for in Regulation \(EC\) No 726/2004 of the European Parliament and of the Council and Directive 2001/83/EC of the European Parliament and of the Council](#)
- [Pharmaceutical Law](#)
- [22 January 2013 Cabinet of Ministers Regulation No. 47 “Procedure for Pharmacovigilance” \(hereinafter - Regulation No. 47\)](#)
- [8 March 2005 Cabinet of Ministers Regulation No. 175 “Regulations for Manufacture and Storage of Prescription Forms, as well as Writing Out and Storage of Prescriptions” \(hereinafter - Regulation No. 175\)](#)
- [Guideline on good pharmacovigilance practices](#), Module V “Risk management systems”; Module XVI “Risk minimisation measures: selection of tools and effectiveness indicators”; Addendum I of Module XVI “Educational Materials”

Education materials (EM) and educational programs are additional risk minimisation measures with the objective of preventing and minimising serious adverse reactions associated with the use of medicinal products, the degree of severity of such reactions and their impact on the patient health, specifically emphasising the information provided in the summary of Product Characteristics (SPC) and Package Leaflet (PL). These educational materials shall ensure a positive risk/benefit balance for the use of medicinal products in patients. EM have a specific target audience.

When submitting the EM developed by the marketing authorisation holder (MAH) to the State Agency of Medicines (hereinafter – SAM), SAM invites marketing authorisation holders to comply with the following requirements laid down in normative acts:

1. The marketing authorisation holder shall regularly update the risk management system and monitor pharmacovigilance data to determine whether there are new risks or whether risks have changed or whether there are changes to the risk-benefit balance of medicinal products. The marketing authorisation holder shall submit the established risk minimisation measures to the State Agency of Medicines for approval (Regulation No. 47, Article 15.8).
2. The marketing authorisation holder shall ensure the availability of the developed materials for risk minimisation measures approved by the State Agency of Medicines to the doctors entitled to prescribe the appropriate medicinal product (Regulation No. 175, Article 34⁴).
3. The marketing authorisation holder shall ensure that the provided information is objective, it shall not be misleading (Regulation No. 47, Article 19; Regulation No. 726/2004, Chapter 3, Article 24(5)).

When developing EM, please take into account the following:

Content

- The wording of the EM should be directed towards specific safety issues included in the risk management plan. The text should not be unjustly supplemented with information directly unrelated to the relevant safety issue or with information that is adequately reflected in the SPC and PL of the relevant medicinal product. The content of the EM should be completely compliant with the approved product information (SPC and PL) in effect in Latvia. Furthermore, EM should include directions to seek further information in the SPC and PL.
- The implementation of educational programs should not be associated with measures promoting prescription, use or marketing of medicinal products.
- EM of centrally authorised medicinal products or EM required as a result of European Union (EU) assessment procedures should include the key elements of the relevant materials approved by the Committee for Medicinal Products for Human Use (CHMP), Coordination Group for Mutual Recognition and Decentralised Procedures-Human (CMDh) or Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) or by the European Commission.
- The cover page should indicate, if the medicinal product is a biological medicinal product.
- EM should be kept as brief as possible. If the EM is more extensive, it should include an introduction summarising the key messages and a list of contents, if necessary.

- The target audience of EM may be healthcare professionals or patients; the indication is required. The EM should include an additional heading at the top of the first page of each EM:
 - In materials intended for doctors, pharmacists and other healthcare professionals (in Latvian) – “Svarīga informācija veselības aprūpes speciālistiem par zāļu riska mazināšanu” (*“Important information regarding medicinal product risk minimisation for healthcare professionals”*);
 - In materials intended for patients (provided to the patients by the relevant healthcare professional) (in Latvian) – “Svarīga informācija pacientam par zāļu riska mazināšanu” (*“Important information regarding medicinal product risk minimisation for patients”*).
- If the medicinal product is under additional monitoring, the symbol ▼ should be added in the EM right after the heading together with the standard explanatory text (in Latvian):
 - In materials intended for doctors, pharmacists and other healthcare professionals – “Šīm zālēm tiek piemērota papildu uzraudzība. Tādējādi būs iespējams ātri identificēt jaunāko informāciju par šo zāļu drošumu. Veselības aprūpes speciālisti tiek lūgti ziņot par jebkādam iespējamām nevēlamām blakusparādībām” (*“This medicinal product is subject to additional surveillance. This will allow to quickly identify new information regarding the safety of this medicinal product. Healthcare professionals are asked to report any possible adverse reactions”*);
 - In materials intended for patients – “Šīm zālēm tiek piemērota papildu uzraudzība. Tādējādi būs iespējams ātri identificēt jaunāko informāciju par šo zāļu drošumu. Jūs varat palīdzēt, ziņojot par jebkādam novērotajām blakusparādībām.” (*“This medicinal product is subject to additional surveillance. This will allow to quickly identify new information regarding the safety of this medicinal product. You can help by reporting any observed adverse reactions”*).
- EM should indicate that it is necessary to report any adverse reactions and include the company's address for reporting in Latvian. In addition, the materials should include the standard text in Latvian regarding national requirements for adverse reaction reporting:
 - In materials for doctors, pharmacists and other healthcare professionals: “Atgādinām, ka saskaņā ar zāļu blakusparādību ziņošanas noteikumiem Latvijā ārstniecības personām un farmaceitiem jāziņo par novērotām iespējamām zāļu blaknēm Zāļu valsts aģentūrai (ZVA), sūtot ziņojumu (veidlapa ”Ziņojums par zāļu blakusparādībām”) pa faksu: 67078428 vai pa pastu, adrese: Jersikas iela 15, Rīga, LV-1003. Ziņojumus iespējams nosūtīt arī elektroniski ZVA mājaslapā www.zva.gov.lv. Papildinformācijas nepieciešamības gadījumā jāsazinās ar ZVA pa tālr.: 67078438” (*“We remind you that in accordance with the regulation regarding reporting of adverse drug reactions in Latvia healthcare providers and pharmacists shall report observed suspected adverse reactions to the State Agency of Medicines (SAM) by submitting a report (“Adverse Drug Reaction Report” form) via fax (67078428) or mail (address: Jersikas Street 15, Riga, LV-1003). The reports may also be submitted electronically on SAM website www.zva.gov.lv. For additional information please contact SAM via phone: +371 67078438.”*);
 - In materials for patients: ”Jūs varat ziņot par blakusparādībām tieši Zāļu valsts aģentūrai. Pacients ziņojumu par zāļu blakusparādībām var iesniegt divos

veidos – elektroniski un papīra formātā. Elektroniskā iesniegšana tiek nodrošināta interneta vietnē www.zva.gov.lv, klikšķinot izvēlni „Pacienta ziņojuma e-veidlapa”. Papīra formātā veidlapu iegūsi, lejuplādējot ziņojuma veidlapu. Parakstīta papīra formāta veidlapa jāšūta ZVA pa pastu vai faksu. ZVA adrese: Jersikas iela 15, Rīga, LV-1003, tālrunis informācijai: 67078400, fakss: 67078428.” (*“You can report adverse reactions directly to the State Agency of Medicines (SAM). Patients can submit adverse reaction reports either electronically or in paper format. Electronic submission is ensured on SAM website www.zva.gov.lv by clicking on the menu “Patient report e-form.” You can obtain the paper format form by downloading the report form. A signed paper format report form should be sent to SAM via mail or fax. SAM address: Jersikas Street 15, Riga, LV-1003; phone for additional information: +371 67078400; fax: +371 67078428.”*);

- If the relevant medicinal product is a biological medicinal product (biomedicines or biosimilars), the text in the materials for healthcare professionals, as well as patients should be supplemented with the following text in Latvian: “Šīs zāles ir bioloģiskas izcelsmes, tāpēc, ziņojot par blaknēm, jānorāda zāļu oriģinālnosaukums un sērijas numurs” (*“This medicinal product is a biological medicinal product, therefore, the original name and serial number of the product should be indicated upon reporting adverse reactions.”*).
- EM should be limited to the approved key messages. Additional information such as efficacy data, comparative data with other medicines or statements regarding the good tolerance or the lack of adverse reaction reports should not be included. On some occasions efficacy data may be included in the EM, if the MAH can justify the need for this.
- Whenever possible, MAHs should come to a mutual agreement to prepare common/identical EM for their medicinal products containing the same active substance. The EM of generic medicinal products should be in accordance with the EM of the original medicinal product, if not regulated/required otherwise.
- If the relevant medicinal product is not distributed in Latvia, the EM should not be disseminated, but it should be discussed with SAM in any case. Please note that as soon as a medicinal product enters circulation in Latvia (even, if prescribed to separate patients), it is the responsibility of the MAH to provide updated safety information to the relevant target audience.
- The EM should include the company's contact information, as well as the contact information of the MAH's national level contact regarding pharmacovigilance issues in Latvia (phone number and address), so that healthcare professionals could communicate in the state language.
- The contact information of patients and healthcare professionals obtained by MAH within the educational program must not be used for purposes of advertising medicinal products.
- When developing the materials for risk minimisation measures the MAH should comply with the lexical, grammatical and stylistic standards of the literary language and terminology in order to ensure the effectiveness and high quality of the risk minimisation communication. Compliance with these requirements will shorten the time for approval of the documents.

Format

- The first page of the EM should include the original name of the medicinal product and the name of the active substance(s) and/or therapeutic group in brackets. If the educational materials are prepared for several medicinal products with several MAHs, the materials should indicate only the active substance or therapeutic group, and the original names of the medicinal products should be provided in the addendum. In order for the information to be clearly presented, bullet points should be used whenever necessary.
- The number of the version of the materials should be indicated (a unique version identifier is preferable). The date <month> <year> of the last revision of the text should be indicated on the first and last page. If the materials are an updated version of previously approved EM, the text of the previous version with changes highlighted should be submitted.
- EM regarding medicinal product safety issues should not contain advertisement elements, for example, the colours, images, slogans or statements of the product brand that promote prescription, supply, marketing or use of the medicinal product. If the MAH and/or the logo of medicinal product is indicated in the EM, it should not appear more than once in a single EM, preferably on the first or last page and no larger than the title of the document.
- The footnotes should not be included in the materials.
- The EM can refer to the websites of SAM and the European Medicines Agency or to the website specifically designed by the MAH, if it contains a publicly available summary of product characteristics and package leaflet.
- References to other websites with the direction “for additional information” are not acceptable, except cases when it is agreed by SAM, for example, reference to a specific antibody test or video containing instructions for patients on the use of a medical device.
- References to other medicinal products are not permitted.
- All of the educational materials for healthcare professionals (healthcare providers or pharmacists) and patients included in the set of documents should be submitted to SAM in Latvian attaching the original document in English.
- In the interests of the public health and in order to prevent misleading of patients, MAHs of medicinal products containing the same active substance should submit educational materials for patients that are as similar as possible in form, content, colour and format.

Publication of educational materials on a special MAH website

The marketing authorisation holder may publish its educational materials on a website specifically designed and appropriate for this purpose, if the MAH complies with the following requirements:

- SAM has approved the mode of distribution.
- SAM has been informed about the address of the website.
- The website contains a reference or standard text indicating that the content of the website corresponds to the EM agreed by SAM.
- The specifically designed website may not contain references to other documents or websites that are not agreed by SAM.
- All of the elements and information on the website should be in Latvian.
- The specifically designed website should not contain references to other medicinal products that are not authorised in Latvia.

- The website may contain references to documents such as SPC, PL or risk management plan.

Procedure for submission and agreement of documents

1. Submission of EM draft to SAM

Only electronically by sending the EM to the following e-mail address: em_dhpc@zva.gov.lv. *The use of the checklist (Addendum No. 1) is recommended upon the preparation of the EM document package.*

The following documents should be submitted:

- Cover letter indicating:
 - Documented justification (indicating specific documents providing justification) for preparing and submitting EM,
 - List of documents included in the EM package (indicating the precise title and number of pages),
 - Target audience and distribution plan for the EM in Latvia,
 - Indicate, if the format and content, as well as the target audience and distribution plan of the EM was discussed with, for example, scientific associations, professional associations or healthcare professionals (doctors or pharmacists),
 - If specific distribution requirements have been applied, please also indicate how the MAH shall ensure this in Latvia (for example, a requirement to ensure cooler bags, etc.),
 - Contact information (at least the e-mail address, phone number) of the EM submitter (MAH or authorised person);
- Draft EM in Latvian in MS WORD format;
- Copies of documents justifying the necessity for EM (for example, a European Commission decision, marketing authorisation conditions or risk minimisation measures laid down in the MAH risk management plan);
- EM in English;
- Updated version of the SPC and PL.

2. EM agreement

The MAH should continue the discussion regarding the Latvian version of EM draft documents, their content and format, as well as the distribution plan and target audience via e-mail communication or via phone or during SAM client service hours, previously coordinating the time of visit with the competent expert:

- During the agreement process of educational materials SAM may ask the MAH to consult with terminologists, linguists, medical and pharmaceutical professional associations, as well as separate specialists in order to clarify or verify:
 - ✓ Compliance of terminology
 - ✓ Comprehensibility and perceptibility of the information,
 - ✓ Whether the information is compliant with the medical and laboratorial possibilities available in Latvia
- The SAM expert may ask the MAH to submit additional information or materials, if necessary.

If the SAM expert has no further objections to the content, format, distribution plan and target audience of the materials submitted in the package of documents, the expert shall ask to submit the approved Latvian versions of all of the documents included in the EM package without track-changes for final proofreading. If the expert accepts the approved version upon completing the final proofreading, the expert shall send an e-mail inviting to submit the final version EM to SAM.

3. Submission of the final EM version to SAM

The final version should be submitted:

- preferably electronically to the e-mail address em_dhpc@zva.gov.lv (the cover letter should be signed with a secure electronic signature) or
- in paper format.

The following documents should be submitted:

- 1) The cover letter of the final version indicating:
 - ✓ Additional standard text: Izglītojošo materiālu gala versiju <MAH> iesniedz pēc izglītojošo materiālu uzmetuma apspriešanas un saskaņošanas ar ZVA ekspertu” (“<MAH> submits the final version of educational materials after discussing and approving the draft educational materials with a SAM expert”) (it should be indicated in the cover letter, if during the approval process the materials were discussed with other organisations or persons);
 - ✓ List of documents included in the package of educational materials, version number;
 - ✓ SAM approved list of EM target audiences and distribution plan in Latvia.
- 2) Full package of documents of the SAM approved final EM version.

In case of uncertainties, please contact the senior experts of the SAM Efficacy and Safety Division. Phone: +371 67078442, e-mail: Inese.Studere@zva.gov.lv; Gunta.Pauksena@zva.gov.lv.

4. Confirmation of SAM agreement of EM

SAM will inform the submitter of educational materials in writing regarding the agreement of educational materials by sending out a letter.

5. Publication of information on SAM website regarding agreement of EM

In accordance with Article 34⁴ of the 8 March 2005 Cabinet of Ministers Regulation No. 175 “Regulations for Manufacture and Storage of Prescription Forms, as well as Writing Out and Storage of Prescriptions” the information regarding list of medicinal products, for which the marketing authorisation holder has established risk minimisation measures that have been approved by the State Agency of Medicines, shall be published on SAM website www.zva.gov.lv in the section “Zāļu riskmazināšanas izglītojošo materiālu saraksts” (“List of risk minimisation educational materials for medicines.”).