INSTRUCTIONS FOR MARKETING AUTHORISATION HOLDERS FOR PREPARATION AND SUBMISSION OF ADDITIONAL RISK MINIMISATION MATERIAL (aRMM) FOR EVALUATION AND APPROVAL IN LUXEMBOURG

1. INTRODUCTION AND GENERAL REQUIREMENTS

For each new medicinal product for which a marketing authorisation is granted, a risk management plan (RMP) is established. In this RMP, the marketing authorisation holder (MAH) describes in detail the actions necessary to identify, characterise and avoid risks when using the medicinal product.
Usually, the risks of most medicinal products are sufficiently limited using routing risk minimisation measures (rRMM), defined for all medicinal products in the Summary of Product Characteristics (SmPC), the patient information leaflet (PIL), the labelling, the package size and/or the legal status of the product.
However, additional risk minimisation measures (aRMM) may be necessary to manage some important risks and/or strengthen the positive benefit-risk balance of a medicinal product. aRMM can be categorised into the following categories: Educational materials; Direct healthcare professional communications (DHPCs)[1]; Pregnancy prevention programmes (PPPs); Controlled access programmes. aRMM should be completely separated from promotional activities.

This document provides instructions for the submission of **Educational Materials,** commonly defined as **Risk Minimization Activities (RMA)** for a medicinal product. RMAs are specified as a requirement in the RMP or Annex II of the Conditions of Marketing Authorisation of the product. Prior to distribution, these materials, intended for healthcare professionals (HCPs) and/or patients, must be assessed at national level by the Division of Pharmacy and Medicines (DPM) of the Directorate of Health in Luxembourg.

2. SUBMISSION

For newly authorized medicinal products, submissions must be made at least three months prior to their launch to facilitate assessment by DPM. Any subsequent revisions need to be sent for evaluation in a timely manner after their central approval, so that updated materials are implemented shortly after agreement.

In order to validate the distribution of educational materials/RMA, the following information/documents should be submitted to DPM via the e-mailbox pharmacovigilance@ms.etat.lu or via Eudralink, in case of large files.

[1] For the submission of DHPCs, please refer to document DPM-COM-2021-002 "INSTRUCTIONS FOR MARKETING AUTHORISATION HOLDERS FOR DISTRIBUTION OF DIRECT HEALTHCARE PROFESSIONAL COMMUNICATIONs (DHPC) IN LUXEMBOURG"

A. In the e-mail or in an attached cover letter addressed to DPM :
   - Rationale for and objectives of the RMAs;
   - Brief description of the tools/materials proposed;
   - For a new marketing authorisation, estimation date of introduction of the product to the market.

B. Reference documents :
   - A copy of the Marketing Authorisation and/or the positive opinion of the CHMP and any annexes (whichever applies);
   - The most recently approved summary of product characteristics (SmPC) and patient information leaflet (PIL);
   - Annexes of the RMP describing RMAs;
   - Other supporting data accompanying the submission.

C. Cover letter intended for HCPs in Luxembourg.

D. Cover letter submitted to the Competent Authority of the country of origin of the medicinal product, if applicable.

E. Intention for approval or final approval of the RMA material (cover letter included) by the Competent Authority of the country of origin of the medicinal product, if applicable.

F. Copy of the RMA material for validation (guide, poster, checklist, forms, patient card, etc.):

   - Documents in mock-up format (pdf), to guarantee their good readability and, where applicable, relevant visual aids;
   - In case of a modification of the materials : track-changed documents in text format (word);
   - Complete script of the video material, if applicable;
   - Translation compliance declaration, if applicable;
   - If documents are uploaded to a specific website, access procedures must be specified (domain name if it is a dedicated website or section of the institutional site where documents are presented).

G. Dissemination plan - indicating target HCPs, their specialization, as well as other target groups (organizations, associations, patients, etc.), approximate number of recipients in Luxembourg, which materials and methods of their distribution (by post, by e-mail, by representatives of the MAH, on demand), quantity of the materials sent per HCP, time point when dissemination is anticipated to start and frequency of further disseminations.

H. The terms of cessation or withdrawal of previous versions of RMAs in case of a request for approval of amendment.

I. Follow-up activities – details of the plan for evaluation the effectiveness of the RMAs (process and outcomes including milestones), where applicable.

3. CONTENT AND DISTRIBUTION

RMA material should have a clearly defined scope and objective and add value beyond the SmPC and PL. Content should specifically address important safety concern to prevent that important key messages are lost. No promotional illustrations or information is allowed. The final layout in electronic version of the educational material must be submitted to the DPM before dissemination.

Important points:

A. The **cover letter** for **HCPs** should be available at least in French. A translation in German is strongly recommended. It should contain the following information:
   - Title and introduction mentioning that the material is part of the RMP implemented in Luxembourg;
   - Version of the RMA;
   - Indication of the medicinal product;
   - Purpose of the RMA;
   - In case of update, changes to previous version should be specified.
   - For medicinal products subject to additional monitoring: « black inverted triangle » ▼ and abridged explaining sentence should be present in the cover letter but also in all components of the RMA.
   - A list of all components of the RMA and instructions with regards to which component is intended to which recipient group.
   - An encouragement to discard previous/outdated versions of the RMA, if applicable.
   - A statement of where and how HCPs can request new material.
   - A paragraph with contact details for adverse drug reactions (ADRs) notification as stated in the latest version of Annex V of QRD template.

B. **Educational material** intended for **HCP**s should be available at least in French. A translation in German is strongly recommended but not mandatory.
   - All components of the RMAs must have a date and version number.
   - Indication of the medicinal product (optional or a summary, in case this is too long to fit the material)
   - The « black inverted triangle » ▼, and an abridged explaining sentence, if applicable;
   - No logos of the MAH or local representatives of the MAH should appear on the material.
   - Encouragement to read the SmPC;
   - A paragraph with contact details for adverse drug reactions (ADRs) notification as stated in the latest version of Annex V of QRD template.

C. **Educational material** intended for **patients** should be available in both French and German.
   - All components of the educational materials must have a date and version number.
   - The « black inverted triangle » ▼, and an abridged explaining sentence if applicable
   - Encouragement to read the PIL;
   - Contact details for adverse drug reactions (ADRs) notification as stated in the latest version of Annex V of QRD template (not mandatory for Patient card).

D. **Dissemination plan**

- The **cover letter** intended for **HCPs** must be sent to the relevant recipients in printed version or by e-mail (if consent previously obtained from the HCPs for this method of contact).
- Printed copies of **educational materials** intended for **patients** may be required to be distributed/sent to appropriate recipients, even when they are available online for future use.
- The first approved version of the RMA materials must always be sent as a paper version (at least one copy) to the entire defined target group, and actively distributed. Redistribution of the approved RMA materials is recommended on annual basis for new HCPs in the target group. The redistribution to the entire target group may be every three years. Updates of the educational material require distribution to the entire target group as well.
- Distribution upon request can be decided if the target group has already been informed about the content of the material. For example, when amending previously approved and distributed material.
- The effective date of distribution is communicated to DPM as well as possible feedback, such as results of the follow-up activities to measure the efficacy of the RMA dissemination.

- A copy of the final printed educational materials is to be sent to DPM at the same time as it is sent to other relevant recipients. Address of the DPM:

  Direction de la Santé
  Division de la Pharmacie et des Médicaments - Pharmacovigilance
  2a, rue Thomas Edison
  L-1445 Strassen

4. REFERENCES

- Good Pharmacovigilance Practices
  Module V: Risk management systems (Revision 2)
  Module XVI: Risk minimization measures: selection of tools and effectiveness indicators (Revision 2)
  Module XVI Addendum I – Educational materials