Recommendations on the procedure for coordinating additional risk minimisation measures with the State Medicines Control Agency of Lithuania

1. GENERAL INFORMATION

'Risk minimisation measure' (RMM) is defined as a tool to prevent or reduce the occurrence of adverse reactions associated with the exposure to a medicinal product, or to reduce their severity or impact on the patient should an adverse reaction occur.

Routine RMM: summary product characteristics (SmPC), package leaflet (PL), labelling, pack size, classification of the medicinal product (prescription/OTC medication)

Additional RMM (aRMM): guides (brochures) for risk minimisation for patients or healthcare professionals , healthcare professional checklist for risk minimisation, risk awareness dialogue form/aid, Patient card, Patient diary for risk minimisation.

Information about RMM can be found in the GVP Module XVI Risk minimisation measures (Rev 3) (https://www.ema.europa.eu/en/human-regulatory-overview/post-authorisation/pharmacovigilance-post-authorisation/good-pharmacovigilance-practices-gvp)

aRMM must be printed and distributed in accordance with a distribution plan only after it has been approved by the State Medicines Control Agency (SMCA).

2. SUBMISSION OF ADDITIONAL RISK MINIMISATION MEASURES:

If agreed during the marketing authorisation application, aRMMs must be submited at least 2 months prior to the launch of the medicinal product to facilitate assessment by SMCA.

If aRMM are imposed on a medicinal product that has already been authorised for the Lithuanian market, the proposed aRMM must be submitted to the SMCA no later than 2 months after the obligation to prepare aRMM (European Commission decision, CHMP opinion, other). The same deadline applies when previously approved aRMM must be revised/updated following the outcome of a regulatory procedure.

The following information/documents should be submitted to SMCA via the e-mail RMinM@vvkt.lt:

- **In case of newly prepared aRMM or significantly updated aRMP:**

A. General information:

- Rationale for and objectives of the aRMM;
- For a new marketing authorisation, estimation date of introduction of the product to the market;
- The contact details of the marketing authorisation holder and/or, if applicable, another organisation to which it has subcontracted the submission (with the names and e-mail addresses of the contact persons);
- Completed checklist.

B. Reference documents:

- The regulatory procedure which has led to the need of the aRMM with supportive documents (e.g. European Commission decision, CHMP opinion, approved/updated RMP);
- The most recently approved summary of product characteristics (SmPC) and patient information leaflet (PIL);
- Risk management plan (RMP), reflecting the relevant aRMM.

C. Additional risk minimisation measures:

- Draft aRMM in text format (word) in the Lithuanian language;
- In case of a modification of aRMM: track-changed documents in text format (word);
- Complete script of the video material, if applicable;
- Screenshots of the MAH‘s website where aRMM will be published online, as well as the URL (direct link) that will be used for this purpose.

D. Cover letter intended for HCPs in Lithuania.

E. Dissemination plan - indicating target HCPs, their specialisation, as well as other target groups (organisations, associations, patients, etc.), which aRMM and methods of their distribution (by post, by e-mail, by representatives of the MAH, on demand), time point when dissemination is anticipated to start and timeframes of (re)dissemination.

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

- **In case of aRMM is submitted after editorial changes, update of contacts, etc.:**

A. Reason for updating aRMM.
B. Track-changed aRMM in text format (word).

3. CONTENT

- The content of any aRMM should be fully aligned with the currently authorised product information for the medicinal product, i.e. the summary product characteristics (SmPC), the package leaflet (PL);
- Additional information rather than replicate SmPC and PL information should be provided in aRMM;
- Content should specifically address important safety concern;
- aRMM should not include or be combined with promotional elements either direct or indirect (e.g. suggestive images and pictures). Images are allowed only if illustrating the content of the material, such as possible injection application sites, technique, etc;
- The invented name of the medicinal product is not considered a promotional element, but should be used as rarely as possible;
- The marketing authorisation holder`s and/or the product`s logo should generally be avoided; however, if suggested to appear for a given reason, it/they should appear only once in each aRMM material and not be larger than the heading font size;
- The date of approval should be provided on the first and/or the last page;
- Before dissemination the final layout of the aRMM must be submitted for final approval;

- aRMM for healthcare professionals may, in exceptional cases, be approved solely in the English language. This shall be always assessed and approved by SMCA with a view to the specific circumstances of the case in question.

Important points

The cover letter for HCPs. It should contain the following information:

- Version of aRMM;
- Purpose of aRMM;
- Indication of the medicinal product;
- In case of an update, changes to previous version should be specified;
- For medicinal products subject to additional monitoring: « black inverted triangle » ▼ and explaining sentence should be present in the cover letter and also in all components of aRMM;
- A list of all components of the aRMM and instructions with regards to which component is intended to which recipient group;
- Contacts of where and how HCPs can request new and/or paper material;
- Link to Vapris and MAH website where aRMM is placed;
- A paragraph how to report ADRs.

The cover letter, together with the aRMM, must be sent to HCPs in paper version or electronically.

The template of cover letter for HCP is attached.

Each aRMM must specify:

- Date and version number;
- The « black inverted triangle » ▼symbol, and an abridged explaining sentence, if applicable;
- Encouragement to read the SmPC (for HCPs) and PIL (for patients);
- A paragraph how to report ADRs.

GVP Module XVI Risk minimisation measures (Rev 3) https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-good-pharmacovigilance-practices-gvp-module-xvi-risk-minimisation-measures-rev-3_en.pdf should be followed for aRMM preparation.

4. TIMEFRAMES

The SMCA has 15 calendar days to send information about eligibility of aRMM. However, if the information is missing or incorect (e.g. dissemination plan is not provided, not full information provided in aRMM according to RMP), the MAH is given the opportunity to rectify this within 10 working days. The SMCA has 10 calendar days to evaluate the updated aRMM or other information.

If the aRMM is approved by the SMCA, the MAH must submit the approved material within 20 calendar days to the SMCA, with the final layout in PDF format.

The final version of aRMM in PDF format, without the cover letter, will be published on Vapris. Make sure that the material does not contain any personal data.

5. DISSEMINATION

The aRMM for patients should be disseminated in paper version. The cover letter must be sent to HCP (requirements for cover letter for HCPs see above 'important points'). If patient card is placed inside the package or affixed to the outer side of the package, the MAH should send the patient card to SMCA in order to publish it on Vapris.

HCPs should not be required to print any of aRMM for the patients, therefore the MAH should proactively provide these materials to HCP as a hard copy.

In case the patient card is placed inside the package or affixed to the outer side of the package, the cover letter and example of patient card should be send to HCPs. This can be done electronically.

The aRMM designated for HCPs should be disseminated electronically and/or in paper version by the MAHs. The cover letter must be sent to HCP (requirements for cover letter for HCPs see above 'important points').

The final version of aRMM in PDF format, without the cover letter, will be published on Vapris. However, this is not regarded the only way of dissemination.

Significant updates of aRMM require re-distribution to the entire target group.

Evidence of dissemination of aRMM, approximate number of recipients, and other information may be requested at any time by SMCA.

6. TEMPLATES

How to report ADRs – information for HCPs:

Svarbu pranešti apie įtariamas nepageidaujamas reakcijas, pastebėtas po vaistinio preparato registracijos, nes tai leidžia nuolat stebėti vaistinio preparato naudos ir rizikos santykį. Sveikatos priežiūros ar farmacijos specialisto pranešimas apie įtariamą nepageidaujamą reakciją gali būti teikiamas šiais būdais:

- tiesiogiai užpildant pranešimo formą internetu Valstybinės vaistų kontrolės tarnybos prie Lietuvos Respublikos sveikatos apsaugos ministerijos Vaistinių preparatų informacinėje sistemoje https://vapris.vvkt.lt/vvkt-web/public/nrv/SPECIALIST_PUBLIC;
- užpildant Sveikatos priežiūros ar farmacijos specialisto pranešimo apie įtariamą nepageidaujamą reakciją formą, kuri skelbiama https://vvkt.lrv.lt/lt, ir atsiunčiant elektroniniu paštu (adresu NepageidaujamaR@vvkt.lt).

How to report ADRs – information for patients:

Jeigu pasireiškė šalutinis poveikis, įskaitant pakuotės lapelyje nenurodytą, pasakykite gydytojui, vaistininkui arba slaugytojui. Apie šalutinį poveikį taip pat galite pranešti Valstybinei vaistų kontrolės tarnybai prie Lietuvos Respublikos sveikatos apsaugos ministerijos šiais būdais:

- tiesiogiai užpildant formą internetu Valstybinės vaistų kontrolės tarnybos prie Lietuvos Respublikos sveikatos apsaugos ministerijos Vaistinių preparatų informacinėje sistemoje https://vapris.vvkt.lt/vvkt-web/public/nrv/PATIENT_PUBLIC;

- užpildant paciento pranešimo apie įtariamą nepageidaujamą reakciją formą, kuri skelbiama https://vvkt.lrv.lt/lt, ir atsiunčiant elektroniniu paštu (adresu NepageidaujamaR@vvkt.lt);
- nemokamu telefonu 0 800 73 568.

In case aRMM concerning a medicinal product under additional monitoring, this fact shall be distinctly shown on the title page, including the text as bellow:

for HCPs:

▼ Vykdoma papildoma šio vaistinio preparato stebėsena. Tai padės greitai nustatyti naują saugumo informaciją. Sveikatos priežiūros specialistai turi pranešti apie bet kokias įtariamas nepageidaujamas reakcijas.

for patients:

▼ Vykdoma papildoma šio vaisto stebėsena. Tai padės greitai nustatyti naują saugumo informaciją. Mums galite padėti pranešdami apie bet kokį Jums pasireiškiantį šalutinį poveikį

Cover letter for HCP

<data>

Gerbiamas (-a) sveikatos priežiūros specialiste,

<Kompanijos pavadinimas> suderinusi su Valstybine vaistų kontrolės tarnyba prie Lietuvos Respublikos sveikatos apsaugos ministerijos, norėtų Jums pateikti papildomą rizikos mažinimo priemonę vaistiniam (-s) preparatui (-ams) *<vaistinio preparato pavadinimas>* (*<veiklioji medžiaga>), <indikacija>.*

Papildomas rizikos mažinimo priemones sudaro: *<išvardinti pateikiamas aRMM ir nurodyti kam jos skirtos (pvz, pacientams, sveikatos priežiūros specialistams). Prie kiekvienos aRMM nurodyti versijos numerį>*

Šių papildomų rizikos mažinimo priemonių tikslas *<parašyti konkretų tikslą>.*

<aRMM atnaujinimo atveju reikia nurodyti pakeitimus>.

<Jei aRMM skirta pacientams, turi būti šis sakinys: „Kiekvieną pacientą, kurį pradedate gydyti šiuo vaistiniu preparatu, supažindinkite su mokomąja medžiaga ir/arba paciento kortele ir duokite pateiktą mokomąją medžiagą ir/arba paciento kortelę. Pasakykite pacientui apie būtinybę nešiotis paciento kortelę su savimi ir pateikti sveikatos priežiūros specialistui kiekvieno apsilankymo metu“.

Jei paciento kortelė platinama su vaistinio preparato pakuote, nurodykite, kur tiksliai bus paciento kortelė (pakuotės viduje, prikabinta prie išorinės pakuotės ir t.t.)>.

Šias papildomas rizikos mažinimo priemones galima rasti *<nuoroda į VAPRIS ir registruotojo svetainę, kurioje patalpinta aRMM >.*

Norint gauti naujas ir (arba) popieriniu formatu papildomas rizikos mažinimo priemones, kreipkitės šiais kontaktais *<nurodyti kontaktus>.*

<Jei vaistiniam preparatui yra taikoma papildoma stebėsena, turi būti nurodytas juodas apverstas trikampis ▼ *ir paaiškinamasis sakinys>.*

Svarbu pranešti apie įtariamas nepageidaujamas reakcijas, pastebėtas po vaistinio preparato registracijos, nes tai leidžia nuolat stebėti vaistinio preparato naudos ir rizikos santykį. Sveikatos priežiūros ar farmacijos specialisto pranešimas apie įtariamą nepageidaujamą reakciją gali būti teikiamas šiais būdais:

- tiesiogiai užpildant pranešimo formą internetu Valstybinės vaistų kontrolės tarnybos prie Lietuvos Respublikos sveikatos apsaugos ministerijos Vaistinių preparatų informacinėje sistemoje https://vapris.vvkt.lt/vvkt-web/public/nrv/SPECIALIST_PUBLIC;
- užpildant Sveikatos priežiūros ar farmacijos specialisto pranešimo apie įtariamą nepageidaujamą reakciją formą, kuri skelbiama https://vvkt.lrv.lt/lt, ir atsiunčiant elektroniniu paštu (adresu NepageidaujamaR@vvkt.lt).

<Kompanija gali nurodyti savo kontaktus, kuriais sveikatos priežiūros specialistas gali pranešti apie ĮNR>.