Summary DIS-aRMM study

Dissemination of additional risk minimisation measures for patients and healthcare professionals in EU/EEA countries (DIS-aRMM study)

1. Project information

1.1 DIS-aRMM

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- HMA-EMA Catalogue of RWD Studies registration number: EUPAS1000000524 https://catalogues.ema.europa.eu/node/4425/administrative-details
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1.2 Key words

Risk minimisation, additional risk minimisation measures (aRMM) materials, dissemination, European Union, mixed-methods study

1.3 Disclaimer

This study was commissioned by the European Medicines Agency under framework contract SC01/EMA/2020/46/TDA/L4.01. This document expresses the opinion of the authors of the paper, and may not be understood or quoted as being made on behalf of or reflecting the position of the European Medicines Agency or one of its committees or working parties. This study has been registered in the HMA-EMA Catalogues of Real-World Data Sources and Studies: EUPAS1000000524.

2. Study

2.1 Rationale and background

Additional risk minimisation measures (aRMM) tools can be required for medicinal products when routine risk minimisation measures (RMM) insufficiently manage the risks these products can have. For these measures to be effective, aRMM materials should reach the intended users and be used as intended. However, current literature includes limited information on the distribution processes of aRMM materials. From a regulatory perspective, there is limited insight into current practice of the distribution of aRMM, as well as on the roles and responsibilities of stakeholders involved in dissemination processes at the national level. This study therefore focused on the physical dissemination of aRMM materials for seven substances and their medicinal products in six European Union Member States.

2.2 Research question and objectives

The overall objective was to gain an in-depth understanding of current practice for the dissemination of aRMM materials for patients and healthcare professionals (HCPs) in clinical practice, including the challenges encountered by stakeholders involved in the dissemination process and their preferences for aRMM tools and modes of delivery. A secondary objective was to provide recommendations for regulatory decision-making to regulators on aRMM based on patients' and HCPs' preferences and needs.

2.3 Study design

The study used a mixed-method approach, combining qualitative and quantitative methods. It included the following steps: 1) desk research, 2) online interviews with marketing authorisation holders (MAHs), 3) an online focus group with representatives of national competent authorities

(NCAs), 4) online surveys and focus groups with HCPs, patient organisations and patients, and 5) a webinar with stakeholders from all EU/EEA member states to discuss the results of the study. The webinar included stakeholders from countries not participating in the study.

2.4 Setting

This study included six countries with different healthcare systems: Finland, Hungary, Italy, Lithuania, the Netherlands, and Romania. The study focused on the following medicinal products and their associated aRMM materials: Aubagio® (teriflunomide), Eylea® (aflibercept), Lemtrada® (alemtuzumab), Lixiana® (edoxaban), Xeljanz® (tofacitinib), oral retinoids containing medicinal products, and valproate containing medicinal products.

2.5 Subjects and study size

The desk research retrieved 39 articles. Individual interviews were conducted with seven different MAHs. In addition, one MAH provided written responses for each of the three different products the MAH has in its portfolio. Representatives of all six NCAs participated in the focus group. In the questionnaire analyses, 27 patient organisations, 397 patients and 669 professionals were included. In total, 25 patients and 52 HCPs participated in the focus groups or interviews. Forty-one stakeholders from different EU/EEA member states participated in the webinar.

2.6 Variables and data sources

Relevant outcomes were: 1) **process** including the frequency of how aRMM materials are disseminated and the roles and responsibilities of key stakeholders (prescriber, pharmacist, MAH, NCA) in the dissemination process; 2) **access** to aRMM materials for patients and HCPs; 3) key **challenges** of disseminating aRMM; 4) **preferences** for aRMM tools for patients and HCPs and 5) **usefulness** of the materials. Data sources were scientific and grey literature, interviews with MAHs, focus groups with NCAs, focus groups/interviews with patients and HCPs, online questionnaires for patient organisations, patients and HCPs and a webinar for all stakeholders.

2.7 Results

Process

A considerable part of the prescribers (23.4-56.5%; range for the products under study) and the pharmacists (38.2-56.3%) indicated not to be aware of the existence of aRMM materials for the included medicinal products, and, if they were aware, still part of the HCPs indicated that they did not have received the aRMM materials. For the aRMM materials of most medicinal products less than half of the patients indicated that they have received it. In addition, for all medicinal products (except Lemtrada® (alemtuzumab)), per aRMM material 44.1-91.4% of the patients indicated that the aRMM material is not discussed with them. However, patients appear to be informed about the risks by HCPs, mainly verbally. Other stakeholders, like professional organisations and patient organisations currently appear to play only a limited role in the dissemination process of aRMM materials.

Access

Access to aRMM materials appears to be a practical challenge for HCPs. It is often unclear where to find the (latest version of) aRMM materials and maintaining physical stocks of aRMM materials is often unrealistic. In addition, except for the Netherlands (pharmacists), Hungary (pharmacists) and Romania (prescribers and pharmacists), most HCPs do not receive automated alerts within their electronic prescribing/pharmacy dispensing systems reminding them that aRMM materials are available or should be provided to patients. The wording and format of aRMM materials also appear to limit their accessibility, and as such are a challenge. The materials were perceived by HCPs as “legal documents” that are lengthy and difficult to understand, particularly for patients.

Challenges
Main challenges with regard to the dissemination of aRMM include lack of reliable insight into whether aRMM materials actually reach HCPs and patients, the fact that dissemination methods are not standardised and differ between countries, information overload for HCPs, HCPs confusing aRMM materials with spam or commercial material, the wording and format of aRMM materials, and lack of clarity about who is responsible for disseminating aRMM materials to patients. Additionally, HCPs identified specific challenges for their profession being lack of training on the materials and delayed receipt of aRMM materials, as well as remembering that aRMM materials exist for a product/remembering to distribute them, and having insufficient consultation time as challenges.

Preferences
HCPs and patients showed a preference for hybrid dissemination models, combining paper-based and digital access. They also highlighted preferences for more visual and accessible (i.e. concise, simple and written in understandable language) formats of aRMM materials. Next, HCPs preferred aRMM materials to be clearly distinguishable from promotional content and to come from a trusted sender (e.g. a professional organisation) or be integrated directly into software.

Usefulness
The findings showed that both HCPs and patients recognise the value aRMM materials can have. Participants acknowledged that, in principle, these materials can play an important role in supporting medication safety. However, their current design, dissemination, and integration into clinical workflows seem to limit their usefulness.

2.8 Discussion and conclusion
This study gained in-depth understanding of the current practice of disseminating aRMM materials to both HCPs and patients. The findings showed that both HCPs and patients recognise the value aRMM materials can have. However, in practice, the dissemination process at different levels does not function adequately. Therefore, four recommendations to improve this process were formulated:
R1: Develop a European guideline describing the steps of the dissemination process in concrete operational steps, including a clear role description, especially for HCPs, indicating who is responsible at each stage. This guideline should be adaptable at the country level.
R2: Consider the involvement of additional stakeholders in the aRMM dissemination process, such as nurses, informal caregivers, professional associations, and patient organisations. In this context, the roles of these stakeholders within a given setting (e.g. country) should be taken into account.
R3. Make the process as simple and accessible as possible. Concrete suggestions are a central repository including all aRMM materials, embedding aRMM materials in electronic systems of HCPs, include aRMM materials in or on the package.
R4: Tailor aRMM materials more closely to the needs of end users (both HCPs and patients). Concrete suggestions are a European logo on the aRMM materials, making the aRMM materials more accessible for patients, both in language, length, and in visibility, and make the aRMM materials available in a hybrid way.

This study focused on seven substances and their medicinal products and was performed in six European countries. Given the consistency of the findings regarding issues such as a lack of structure in the process and limited accessibility, it is likely that the results are also relevant to other medicinal products and EU/EEA countries. The study included different quantitative and qualitative research methods, desk research, and a webinar with participants from additional EU/EEA Member States. Webinar participants recognized and largely confirmed the study findings, which were also consistent with desk research which was not limited to the participating countries. This triangulation across

multiple methods and countries increases confidence that the findings are applicable beyond the specific study sample.

3. Tenderer & investigators

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