EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 November 2022
EMA/867258 /2022
Human Division

Highlights from the 17th EMA Industry Platform meeting on the operation of EU pharmacovigilance legislation – 7 November 2022

The following records announcements and action points from the 17th Pharmacovigilance Industry Platform meeting.

Welcome and matters arising

- S. Straus and G. Genov welcomed the participants to the EMA Industry Platform, which in this year falls on the 10-year anniversary of the EU new pharmacovigilance legislation.
- An A.O.B topic related to the international transfer of personal (health) data in ICSRs originating from EudraVigilance was announced.

Periodic safety update report (PSUR): Adherence to PRAC recommendations for NAPs

- Industry, represented by Medicines for Europe jointly with EFPIA and AESGP, followed on last year's meeting and shared their overall positive experience with the NAP PSUR procedures delivering timely on the EU/EEA labelling safety updates and relevant RMM. Industry stakeholders proposed that an improved communication could be achieved by notifying all concerned MAHs (e.g., via direct communication by EMA to all MAHs, not only those involved in the original procedure) on the PSUSA outcomes. Industry highlighted that the wording recommendations in Section 6 of the PSUR Assessment Report (AR) may benefit from further clarity and considerations especially in relation to the MAHs not involved in the original PSUSA procedure.
- In order to achieve a streamlined process and implementation, industry stakeholders suggested considerations around: single eCTD submission (versus country specific), that the adopted product information could be published on the respective NCAs websites, the use of user testing for the patient safety labelling updates and the importance of a timely communication of any late changes to the EURD list, as well as of a clear communication of any changes in the final assessment recommended/introduced by PRAC together with its scientific or regulatory rationale.

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- Industry presented a topic on educational materials for generics, a topic also followed on from last year's meeting, and they stressed that the implementation of the educational materials for generics can be delayed (by several months) after implementation by the originator MAH, because the full text which has been changed for the educational materials of the originator is not made public to the generic MAH. A recent relevant example included the educational material of a generic fingolimod.
- The regulators clarified that, in terms of the suggested patient label user testing, the PRAC regularly ensures the utility of recommended texts with patients and healthcare professional representatives as nominated by the European Commission and highlighted the committee's close collaboration with EMA Patients' and Consumers' working party and the Healthcare Professional Working Party. The regulators clarified also that the PSUSA outcomes and common agreed product information texts are publicly available in the CMDh/HMA MRI PI for MRP/DCP products although it is acknowledged that some delays or omissions may occur. The industry was reminded that relevant information on key elements for e.g., educational materials/questionnaires can be found in the assessment reports for the MRP/DCP products.

- **Actions:**

  1. EMA to explore feasibility of single eCTD submission for PSURs as opposed to country specific.
  2. Regulators to ensure that clear scientific rationale for changes and actions (including late changes to the EURD list) are always included in the PRAC AR.

Good Pharmacovigilance Practices (EU-GVP) - Update

- The regulators thanked the industry stakeholders for their input to the development of the EU pharmacovigilance good practice guidelines (EU-GVP) during the last 10 years and their comments on the recent draft updates of some EU-GVP documents, specifically GVP Module XVI on risk minimisation measures (RMM) and its addendum II, which are planned to be published in 2023 in their final post-consultation versions. They emphasised that these draft updated guidelines on the RMM tools and methods for RMM effectiveness evaluation should already be followed by industry. Regarding addendum III on the RMM tool of pregnancy prevention programme, the regulators acknowledged the comments received via public consultation, including those raising some complex issues from the perspective of several different parties, which will be addressed in the course of 2023. The estimated finalisation of GVP M XVI Addendum III is planned for 2023/24 (more likely 2024), likewise for the GVP Chapter P III on pregnancy and breastfeeding. Plans for revising GVP Module M VIII on post-authorisation safety studies (PASS) and GVP Module V on risk management plans (RMP) were announced to be started in 2022/3 and to be released for public consultation in (2023 or) 2024.
- The regulators provided an update on the development of the reflection paper on digital support to aRMM and their effectiveness evaluation and acknowledged industry interest and nominations in the newly created multi-stakeholder group.
- Finally, the regulators updated on the newly published guidance on the *Anonymisation of Protected Personal Data and assessment of Commercially Confidential Information during the preparation of RMPs (main body and annexes 4 and 6)*[1], an important contribution to EMA transparency

[1] https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guidance-anonymisation-protected-personal-data-assessment-commercially-confidential-information_en.pdf

commitment with further plans to expand on RMP publication and a reflection on the utility of the document.

https://www.ema.europa.eu/en/documents/presentation/presentation-good-pharmacovigilance-practices-eu-gvp-update-pbahri-ema_en.pdf

Update on PRAC Impact Strategy (Rev. 2) and impact research projects

- The regulators focused on the scope of revision 2 of the PRAC Impact Strategy published in April 2022 to integrate achievements since the last revision in 2017 and adjustments to the process for prioritising and regulatory follow-up on impact research. An overview of ongoing and completed impact studies is now provided under Research Projects on EMA's Big data/RWE webpage, including information on the study title, objective(s), timelines and link to the EU PAS® Register where the protocol, final study report and publication(s) are made available.
- Reflecting on the past 5 years since the launch of the strategy, the regulators highlighted the shift to measuring patient-oriented outcomes of risk minimisation driven by changes in knowledge and behaviour, considering lessons learnt as compared to the initial focus of the strategy on developing guidance and training on methods for impact research.

https://www.ema.europa.eu/en/documents/presentation/presentation-update-prac-impact-strategy-rev-2-impact-research-projects-tgoedecke-ema_en.pdf

Access of the off-patent sector to aRMMs & follow-up questionnaires of the reference products

- As a follow-up from the last meeting, the industry stakeholders, on behalf of Medicines for Europe, highlighted the need for making more RMP documents publicly available (the RMPs are the most requested documents from the Agency). As per GVP Module V, generic medicinal products need to align their RMPs, including aRMMs and follow-up questionnaires with the original products including any changes made into the RMP. Industry welcomed the publication of COVID-19 vaccines RMPs and are aware of more RMPs to be published.
- The regulators clarified that as of July 2022 CHMP Opinion, the EMA transparency initiative includes the publishing of RMPs (including Annex 4 containing the full follow-up questionnaires) for the following CAPs: COVID-19 products, products containing a new active substance, and products with high interest; and as the MRP/DCP products are concerned, the CMDh website could be considered as an additional resource[2] with the list of RMP safety concerns published and the template for the PAR specifically including a section on RMP[3]. The PARs for MRP/DCP products can be found in the MRI PI[4].
- **Action**: EMA to consider flagging as "new" on the EPAR webpage when an RMP is becoming publicly available.

[2] Heads of Medicines Agencies: RMP (hma.eu)
[3] CMDh_223_2005_Rev03_2014_02.doc (live.com)
[4] MRI - Home (cts-mrp.eu)

- **Post-meeting note**: RMP documents published from July 2022 onwards are flagged with a red "new" next to the document link.

PSUR (periodic safety update reports) frequencies for active substances with DLP 2025 based on a risk-based approach

- The regulators, representing the PRAC Granularity and Periodicity Advisory Group (GPAG), informed on upcoming updates with regards to the establishment of PSUR frequencies for active substances with data lock points (DLP) in 2025, encompassing a set of approximately 1,000 entries for which PSUR assessments were initially deferred since the PSUR assessment of other active substances was prioritised at the time of the EURD List creation. EMA has developed a statistical tool to support the determination of frequencies on a risk-based approach, in line with GVP Module VII. The statistical tool uses readily available data (e.g., age of product, number of ICSRs, number of referrals, number of signals evaluated) to determine a PSUR frequency. The tool has been applied to the full set of deferred entries. All impacted entries will receive a new DLP and a new frequency for the first PSUR assessment. GPAG and PRAC are currently evaluating different scenarios to implement these updates in the EURD List. The implementation of these changes is planned in different phases in 2023, pending outcome of ongoing discussions.

- **Action**: EMA to inform timely via publication of the updated EURD list taking into consideration that the changes will only take effect 6 months after publication.

https://www.ema.europa.eu/en/documents/presentation/presentation-psur-frequencies-active-substances-dlp-2025-based-risk-based-approach-mlopez-fauqued_en.pdf

PASS update

- As a follow-up from the last meeting, the industry stakeholders, on behalf of EFPIA jointly with Medicines for Europe, provided preliminary responses from a large industry survey encompassing about 550 studies. Overall, the feedback has been very positive with industry stakeholders endorsing the usefulness of the PASSes and noting good cooperation with the PRAC. The stakeholders highlighted some areas for Category 3 studies which could possibly be improved (e.g., alignment of PRAC comments with the comments from individual MSs, timing of the scientific advice, or feedback from the PRAC compared to other regulators, number of rounds of assessments and related changes to the protocols, drug utilization studies). The utility of interim reports was highlighted with most companies satisfied.
- Industry stakeholders were reminded of a relevant guidance document published on EMA webpage dedicated to category 3 studies (PAMs). In addition, the regulators clarified that although informal dialogue might take place with the Agency and PRAC Rapporteurs, each protocol needs to be endorsed by PRAC and/or discussed at the plenary. It is acknowledged that depending on the complexity of the study, certain situations might require several rounds of assessment. Overall, the feedback from industry will be considered, upon the provision of the final survey report (see Action 2 below).

- **Actions:**

  1. Improvement of the EU PAS® Register to with regards to the download options.

- **Post-meeting note:** EU PAS® Register is currently being rebuilt in an improved format and technology. A survey collecting feedback and requirements was run early this year and the current agreed future content of EU PAS can be found here. A better download function is part of the improvements envisaged by the technology upgrade.

  2. Industry to specify / further detail any unclarity about the Category 3 study process in the final survey report.

International transfer of personal (health) data in ICSRs originating from EudraVigilance

- At the end of August this year, EMA was notified that case narratives accessed from EudraVigilance under Level 2B access of the EudraVigilance Access Policy were downloaded by certain marketing authorisation holders (MAHs) and transferred in full, without further redaction of personal data, to third countries. Reference is made to the submissions of ICSRs by MAHs to the Center for Biologics Evaluation and Research (CBER) – FDA in the U.S., which resulted in the publication of such unredacted case narratives on the VAERS website and the WONDER database.
- In this context, the regulators reminded about the following key data protection principles:
  - The need to adhere to the principles set out in the EudraVigilance Access Policy, which provides two access levels for MAHs:
    - Level 2A - to fulfil their pharmacovigilance obligations
    - Level 2B – including case narratives - to validate signals and to support a review of ICSR data warranted in the context of a pharmacovigilance assessment procedure (GVP Modules VII and IX). Level 2B is subject to a confidentiality undertaking (annex C of the policy) which clearly states the need for MAH authorised users to "*ensure that personal data reported can no longer be attributed to a specific data subject*" (when there is a legal requirement for the MAH to report suspected adverse reactions for the medicinal products for which they hold a marketing authorisation in the EEA to a medicines regulatory authority in a third country).
  - The need for MAHs as data controllers to comply with the rules on the international transfer of personal data in the context of pharmacovigilance as set out in CHAPTER V of Regulation (EU) 2016/679 (GDPR).
- As recently highlighted by the EDPS, the regulators stressed the importance for MAHs to assess (namely by carrying out a transfer impact assessment) whether the laws and practices of the third country of destination applicable to the processing of the personal data by the "data importer" in a third country could prevent the data transfer, considering the specific circumstances of the transfer, or if additional ("supplementary") safeguards will be required.
- **Action:** EMA will actively contact all QPPVs registered in EV to remind about their data protection obligations and provide further information on the data fields reportable to FDA CBER and Centers for Disease Control and Prevention (CDC) in compliance with Union data protection legislation.

https://www.ema.europa.eu/en/documents/presentation/presentation-international-transfer-personal-health-data-icsrs-originating-eudravigilance-sbrosch_en.pdf

Conclusions and next steps

Regulators and Industry stakeholders recognised the benefit and importance of continued dialogue acknowledging the progress achieved since the pharmacovigilance platforms were set up, further to the new pharmacovigilance regulation implementation. It was confirmed that these will be continued in 2023 with possible dates to be shared shortly.

Future topics as proposed by industry associations:

- Update on the pilot of MAH EudraVigilance Signal detection
- Risk minimisation measures / additional risk minimisation measures e.g., DHPC, PPP