01 **Issue 1 - 2017**
April 2017

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

What's new in Pharmacovigilance?

QPPV UPDATE

Published by the European Medicines Agency

An agency of the European Union

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QPPV Update

This is the first issue of QPPV Update in 2017. It provides Qualified Persons responsible for Pharmacovigilance (QPPVs) and all other people working in pharmacovigilance with an update on EU Pharmacovigilance.

We would welcome your feedback as well as any suggestions on topics you think would be of interest to colleagues. Your feedback should be sent to Jolanta.Palepsaitiene@ema.europa.eu.

Need more information?

Further information about the work of the European Medicines Agency is available on our website

For topics on implementation of the new Pharmacovigilance legislation – see here

Links to the National Competent Authorities can be found here

Pharmacovigilance in the product lifecycle

Patient Registries Initiative

What's new?

The EMA's Patient Registries Initiative aims to make better use of existing registries and facilitate the establishment of high-quality new registries. At a workshop hosted in October 2016 following the pilot phase of the initiative, stakeholders including registry owners, patients, marketing authorisation holders, reimbursement agencies, and regulators shared their experiences and made recommendations to improve collaboration and integration of registry data in the approval process. A report and a video recording of the workshop are available on EMA website.

As a follow-up, EMA is updating the mandate and strategy of the Registries Initiative and has restructured its registries Cross-Committee Task Force. Two disease-area workshops will be hosted in 2017. Each will provide guidance on disease-specific core data sets, common protocols, governance and registry interoperability that will serve as models for other disease areas.

How can you be involved?

To help stakeholders to identify and communicate with relevant registries, EMA has invited European patient registry holders to be included in an inventory of registries that will be hosted on the ENCePP platform (http://www.encepp.eu/).

The revised mandate and strategy of the Initiative will be posted on the EMA website by the end of April. Comments on these or to the workshop recommendations are welcomed and should be sent to EMAregistries@ema.europa.eu.

PSUR Roadmap

What's new?

EMA has published the explanatory note to the Good Pharmacovigilance Practice (GVP) Module VII and the questions & answers (Q&A) guidance for assessors, developed in close collaboration with the Pharmacovigilance Risk Assessment Committee (PRAC) and the Co-ordination Group for Mutual Recognition and Decentralised Procedures - human (CMDh).

PRAC and CMDh members first discussed the outline of a common understanding of the optimal use of the periodic safety update single assessment (PSUSA) in a workshop in January 2016. This later led to the drafting of the two above mentioned documents to address the challenges encountered during the two years of running the PSUR single assessment process. Following endorsement by both the Committee and the Coordination Group in October 2016, a consultation with industry associations was initiated and discussed at the pharmacovigilance industry platform meeting held at the EMA on 3 February 2017.

The final explanatory note incorporating the proposals discussed and agreed with the industry stakeholders, together with the assessors Q&A guidance were endorsed by PRAC and CMDh in March 2017.

What do you need to know?

The explanatory note is available to marketing authorisation holders (MAHs) for the preparation of PSURs subject to the single assessment, complementing GVP Module VII. It should be read in conjunction with the GVP Module VII; where appropriate, references to ICH E2C (R2) are made as well. The explanatory note will serve as the basis for the update of GVP Module VII and will eventually be incorporated into it, while the Q&A for assessors will continue to be updated as further experience is gained with the PSUSA process.

Together, these documents continue to foster the optimisation of the PSUR content. Providing the adequate level and quality of information within a PSUR and throughout the assessment procedure is key to substantiating the MAH's conclusions and any actions taken or proposed. This helps the Members States and PRAC to optimise the benefit/risk balance, which in the end contributes to improving the PSUSA outcomes and ensuring adequate product information is provided to the patients.

Please consult the Agency's page Periodic safety update reports: questions and answers to access the documents directly.

Pharmacovigilance processes

1000th study recorded in EU PAS Register

What's new?

In February 2017 the 1000th study was registered in the European Union (EU) electronic Register of Post-Authorisation Studies (EU PAS Register). Further information on this major EU PAS register milestone can be found here.

What do you need to know?

The EU pharmacovigilance legislation requires the Agency to make public the protocols and abstracts of results of non-interventional post-authorisation safety studies (PASS) imposed as an obligation of a marketing authorisation in this register.

Marketing authorisation holders should submit information for publication in the EU PAS Register on:

- non-interventional PASS imposed as an obligation of a marketing authorisation;
- any PASS required in a risk management plan to further investigate safety concerns or to evaluate the effectiveness of risk minimisation activities, in line with GVP Modules V and VIII;
- any PASS initiated, managed or financed voluntarily;
- post-authorisation efficacy studies that are not clinical trials;
- any other PAS.

Medical Literature monitoring

What's new?

The Agency runs stakeholder surveys twice a year to assess stakeholder satisfaction with EMA's Medical Literature Monitoring (MLM) service. Following the survey in March 2016, it was clear that, while the service was improving, there was still room for further improvement, and that detailed industry feedback regarding specific improvements could help to drive these enhancements.

A workshop with industry was held in September 2016, from which over 20 specific, detailed, recommendations for enhancements emerged. Nine of these recommendations have already been implemented or will be very shortly and a further eight are in scheduled to be completed by Q1 2018.

In parallel, the MLM service underwent an independent audit, which started in January 2016. The report was received in December 2016. The audit also produced a number of recommendations for enhancements or risk mitigation. These recommendations have either been closed or will be by May 2017.

What do you need to know?

In order to give stakeholders an overview of which enhancements will be happening when and to allow MAHs to manage the changes efficiently, EMA will shortly be publishing a roadmap for future enhancements to the MLM service on the MLM webpage, incorporating the full audit report and the most recent survey results & workshop output.

All affected MAHs will be informed about the publication of the roadmap by email.

Pharmacovigilance processes

Regulatory contact point in the EudraVigilance registration system for non-pharmacovigilance referral procedures

What's new?

EMA is changing the way it communicates with MAHs involved in non-pharmacovigilance referral procedures under Article 31 of Directive 2001/83/EC.

Since 10 April 2017, the Agency has been using the regulatory contact point email address provided in the EudraVigilance registration system as the main contact point for the concerned products throughout the procedure. All correspondence from the Agency related to the start of a non-pharmacovigilance referral procedure, as well as all subsequent documents provided to the MAHs during the procedure, will be sent electronically to the regulatory contact point email address (via Eudralink).

What do you need to know?

MAHs need to ensure that the regulatory contact point listed in the EudraVigilance registration system is up to date.

Whenever possible and provided an email address for the regulatory contact point is available, MAHs will be informed on the Wednesday before the CHMP meeting of new non-pharmacovigilance Article 31 procedures that the CHMP will consider the following week. This communication will be provided for information only. Note that notifications for referrals can be received at any time, including during the CHMP meeting, and it may not always be possible to provide MAHs with advance information on the Wednesday before the CHMP plenary meeting. Following the CHMP meeting, all concerned MAHs will receive further information from the EMA, including the details of the EMA procedure manager and procedure assistant.

EU Network projects on Pharmacovigilance

PROTECT: impact on regulatory practice

What's new?

An article on Advancing regulatory science, advancing regulatory practice* has been recently published. This article reviews four examples of PROTECT results and discusses the different impact on regulatory practice and public health the results have already had or may have in the future.

For more information on the PROTECT project please visit http://www.imi-protect.eu/

*Kurz X., Pharmacoepidemiol Drug Saf. 2017 Feb 21. doi:10.1002/pds.4184

Pharmacovigilance IT Systems

EudraVigilance

What stakeholders need to know:

- The fieldwork of the independent audit of the EudraVigilance functionalities agreed by PRAC and the EMA Management Board in December 2013 took place in February 2017.
  It is planned that PRAC will issue its recommendation on the basis of the independent audit report on 3 May 2017.
  If EMA Management Board confirm that full functionality of the EudraVigilance system has been achieved and that the functional specifications adopted by the Board in December 2013 have been met, an announcement is expected on 22 May 2017.

- As part of the go live of the new EudraVigilance system in November 2017, MAHs should consult the Change Management Plan published at the dedicated webpage. In addition, the Agency will publish in the second quarter of 2017 a checklist to assist stakeholders in following the most important steps in preparation of the changes that will come with the launch of the new EudraVigilance system in November 2017.

- The release of the new EudraVigilance TEST environment (XCOMP) is scheduled for June 2017, which will allow national competent authorities (NCAs) and MAHs to start the testing of the Individual Case Safety Reports (ICSRs) in the new ISO/ICH E2B (R3) format as well as the message exchange (NCA re-routing and MAH ISCR download functionalities). All stakeholders are invited to ask their users to check the validity of their user-IDs and passwords and to contact the EudraVigilance Registration team if user credentials need to be updated or if new users need to be registered. Further instructions for the EudraVigilance and EVDAS user registration will be communicated to MAHs in April.

- The remaining set of planned e-learning modules was published in January 2017. Additional e-learning modules as well as user manuals will be released in the second quarter of 2017 including the calendar for the stakeholder support webinars, which will start in July 2017.
  Face-to-face training courses on the new EudraVigilance system will be launched in June 2017. The courses calendar, programme and course registration information are available on the dedicated EudraVigilance training webpage. In April the course calendar for the third and fourth quarter of 2017 will be released.
  For more information on the training strategy, please refer to EudraVigilance training plan.

Pharmacovigilance dialogue

Reports from meetings and events

- A report from the Workshop on identifying opportunities for big data in medicine development and regulatory science, which was held on 14 and 15 November 2016, has now been published. The objective of this workshop was to increase understanding of how big data will impact on our understanding of disease and facilitate medicines development, so that the regulatory community can identify opportunities and address challenges in its use for medicines decision-making. Videos and presentations from the workshop are available on EMA website.
- A report from the workshop on measuring the impact of pharmacovigilance activities was published on 27 March 2017. The workshop concluded with six key recommendations which are further detailed in the report. Videos and presentations from the workshop are available on EMA website.

Upcoming EMA meetings

- Industry platform meeting* - 2 June 2017.
- 11th Stakeholders forum on the pharmacovigilance legislation – 21 September 2017.
- Industry platform meeting* - Q4 2017 (date to be confirmed).

Training

- For EudraVigilance training courses, please visit the EudraVigilance training page.

*Meetings are organised for representatives of trade associations.

Pharmacovigilance guidance

Recently published guidance

- The final Scientific Guidance on Post-Authorisation Efficacy Studies has been published and will come into effect on the 1 June 2017.
  This guidance outlines situations where post-authorisation efficacy studies (PAES) may be imposed in the context of the Delegated Regulation (EU) No 357/2014 and may therefore be required for initial marketing authorisations or for an extension to an existing marketing authorisation. This guidance specifically highlights situations where PAES may be considered (including when not imposed), general methodological study design considerations for PAES and principles that should be applied to the conduct of PAES. MAHs should be aware that PAES should be carried out when there is a well-reasoned and clinically relevant scientific uncertainty, the resolution of which is essential for the therapeutic efficacy and benefit-risk of the medicinal product, thereby impacting the licensing status and/or product labelling.
- Vaccine project ADVANCE has published the ADVANCE Code of Conduct, which was developed to support the planning, initiation, design, conduct and reporting of observational studies in the field of vaccines. This is the first module of the Best practice guidance for vaccine benefit-risk studies, which includes governance models, quality recommendations and communication recommendations. The development of this Code of Conduct was co-led by EMA within the ADVANCE project. The ADVANCE Code of Conduct will be subject to periodic revisions and the authors welcome comments and proposals for improvement. Revised versions will be published on the ADVANCE website (http://www.advance-vaccines.eu/).

Pharmacovigilance guidance

Recently published guidance

- Following the public consultation, EMA has published Revision 2 of the Guideline on good pharmacovigilance practices: Module V – Risk-management systems and Revision 2 of the Guidance on the format of risk-management plans in the European Union. The documents provide updated guidance on what the RMPs should focus on: major identified or potential risks and missing information at initial marketing authorisation application or throughout the life span of the medicinal product.
  The transitional arrangements published with the guidance detail how and when the RMP submitted for assessment should be drafted using the updated template. It also explains the principles of risk management in the updated GVP Module V that the RMP is based on. The refocusing of the RMP document is expected to impact the safety specification of the products, with the aim of creating and maintaining risk-proportionate RMPs. The updated template will also facilitate the publication of RMP summaries on the EMA website, which is expected to resume for all initial RMP submissions and post-marketing updates. All MAHs should take into account the updated guidance when preparing upcoming RMP submissions.
- GVP Module II - Pharmacovigilance System Master File (Rev.2) has been released, after an administrative update.
- GVP Module XVI – Risk minimisation measures (Rev.2) has been released, including amendments in line with the public consultation for GVP Module V – Risk management systems.

Updated guidance to be released as final in 2017

- GVP - Annex I - Definitions (Rev 4) is anticipated to be released in Q3 2017.
- GVP Module XV – Safety communication (Rev 1) and related templates in Annex II is expected in Q3 2017.
- GVP Module IX – Signal management (Rev 1) and revised guidance on statistical methods (addendum I), following the public consultation in 2016, will be released as final in Q3 2017.
- GVP Module VI – Management and reporting of adverse reactions to medicinal products (Rev 2), following the public consultation in 2016, will be released as final in Q3 2017.

Guidance under revision or development

- The pharmacovigilance guideline for paediatric medicines is being revised to become a chapter of GVP.
- The pharmacovigilance guideline regarding use of medicines in pregnancy is under development to become a chapter of GVP.
- The pharmacovigilance guideline for medicines used by older populations is under development to become a chapter of GVP and is planned to be released for public consultation in 2017.
- GVP Module VI Addendum I on ICSR Duplicate Management is under development.
- GVP Module VII – Periodic Safety Update Reports (Rev 2) drafting is ongoing.

European Medicines Agency
30 Churchill Place • Canary Wharf • London E14 5EU • United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union