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HPRA MEDICINAL PRODUCTS NEWSLETTER

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Human Medicines

European Medicines Agency (EMA) Signal Management Pilot

On 22 November 2017, the EMA launched the new EudraVigilance system and enabled manufacturing authorisation holders (MAHs) access to the system. The revised GVP module IX on signal management has also been effective since 22 November 2017 and provides updated guidance on regulatory requirements and monitoring and reporting processes for signals.

Stakeholders will be aware that the EMA Signal Management Pilot began on 22nd February 2018, for all MAHs of active substances included in the list published on the EMA website.

All other MAHs also have access to EudraVigilance data and can integrate the data into their own signal management processes. However, during the pilot period they will have no obligation to continuously monitor EudraVigilance and inform the regulatory authorities of validated signals. After one year, the EMA will base the next phase of implementation on experience gained through the pilot.

The EMA is supporting MAHs involved in this project through targeted e-learning, face-to-face training, webinars and information days. Further information on signal management and available training and supports is available on the EMA website.

Revised EudraVigilance questions and answers document

The EMA published an update to its questions and answers document on the EudraVigilance System on 28 March 2018, which is available on the EMA website.

This document addresses questions received from stakeholders as a part of the launch of the new EudraVigilance system, which went live on 22 November 2017. It also includes questions received through the agency's service desk and through the EudraVigilance technical and pharmacovigilance support webinars organised by the EMA. Some of the topics where guidance has been updated includes the registration process, use of the download functionality, access levels, ICH E2B(R3), amendments, nullification reports, and Medical Literature Monitoring (MLM) by the EMA.

HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Kevin O'Malley House, Earlsfort Centre, Earlsfort Terrace, Dublin 2, Ireland
T: +353 1 676 4971 E: info@hpra.ie **www.hpra.ie**

Revised EudraVigilance questions and answers document cont'd

The EMA has also highlighted some key 'Do's and Don'ts' for Marketing Authorisation Holders (MAH), including:

- Don't send ICSRs back to EudraVigilance that were submitted by other MAHs or by NCAs (even if you disagree with the other sender's assessment).
- Don't send MLM ICSRs back to EudraVigilance.
- ICSRs downloaded from EudraVigilance should only be resubmitted if you have received NEW information from the primary source that qualifies for the submission of a follow-up report.
- Don't send acknowledgements for ICSRs you have downloaded from EudraVigilance.
- Don't send nullifications for ICSRs that were sent to EudraVigilance by other sender organisations.
- Don't use "Regulatory" for the data element E2B(R3) C.1.8.2, as the source of an C.1.8 Worldwide Unique Case Identification for an MAH. Both C.1.8.1 (Worldwide Unique Case Identification Number) and C.1.8.2 (First Sender of This Case) should always be populated and should never be changed in any subsequent re-transmission.
- When a regulator is the initial sender, C.1.8.2 should be flagged as 1=Regulator. When an entity other than a regulator is the initial sender, C.1.8.2 should be flagged as 2=Other.
- Do always include a valid organisation registered either as a Gateway Trader or Web-Trader in EudraVigilance.
- Do always consider a '2 day processing window' in the Export Transformation Loading (ETL) process for ICSRs in EVDAS.
- Do run the active substance grouping report before retrieving data from EVDAS.
- Do send an email to duplicates@ema.europa.eu when reviewing cases obtained from EudraVigilance and there is a suspicion that two or more cases are duplicates of one another.

Please continue to monitor the EMA's website for further updates.

Excipients in the labelling and package leaflet of medicinal products for human use

The European Commission has recently published a revised guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. The updated annex to the European Commission guideline was published in October 2017 and is effective as of its date of publication.

For new marketing authorisation applications, implementation of the information as per the latest revision of the guideline annex should be followed.

For already authorised medicines, MAHs should use the first regulatory opportunity to implement the wording in compliance with the revised annex.

For medicines with no foreseeable regulatory submissions, MAHs holders should submit a type IB variation within 3 years after the publication of the revised annex.

MAHs should note that for sodium-containing formulations of effervescent, dispersible and soluble medicines, the implementation timeline of the addition of the new statements in relation to 'cardiovascular events' is one year following publication of the updated annex (i.e. by October 2018) as per the PRAC signal recommendation in relation to these products. This recommendation applies only to products containing ≥ 17mmol of sodium (391mg) in the maximum daily dose for which the labelled posology allows the product to be taken on a daily basis for > 1 month or repeated use for more than 2 days every week. Further information on implementation of this update is available in the minutes of the February 2018 CMDh meeting.

Veterinary Medicines

QR Codes in the labelling and packaging of veterinary medicinal products

In December 2017, the EMA adopted a general principles document in relation to the use of quick response (QR) codes for veterinary medicinal products (EMA/364980/2017). All information provided through a QR code for use by Irish users must be approved by the HPRA. Applicants must ensure that the additional information provided through a QR code does not contain promotional elements (e.g. information not directly relevant to the use of the veterinary medicinal product, hyperlinks to other websites, etc.). Where agreed with the HPRA, a link to the website of the marketing authorisation holder may be included.

Example of a QR code which is linked to the EMA general principles document:

HPRA Veterinary Medicines Information Day 2018 - update

Arrangements for the Veterinary Medicines Information Day on Wednesday 13 June 2018 are progressing. The meeting will take place in the Hilton Hotel Dublin Airport, Malahide Rd, Northern Cross, Dublin D17 Y924. There is a shuttle bus between Dublin Airport and the Hotel (http://www3.hilton.com/resources/media/hi/DUBAPHI/en_US/pdf/en_DUBAPHI_AirportShuttleSchedule_Aug17.pdf) so as to facilitate those travelling. There is a fee of €5 for a return trip, payable on board.

The purpose of this information day is to:

1. Update marketing authorisation holders and other stakeholders with respect to:
   - Brexit developments and HPRA preparations;
   - Developments on the new draft European Regulation on veterinary medicines.
2. Facilitate discussions between stakeholders on on-going and future regulatory developments.
3. Outline initiatives being developed in relation to communications and pharmacovigilance.
4. Allow an opportunity for stakeholders to network with HPRA personnel responsible for the authorisation and monitoring of veterinary medicines.

The draft programme is available on the HPRA website. The fee for this event is €210, but there are reductions in fees for groups of three or more persons from the same organisation, as well as for not-for-profit organisations.

For more information on this event, please contact events@hpra.ie. Registration for this event is available on the HPRA website.

Compliance

Safety features and wholesale distribution authorisation (WDA) holders

WDA holders are reminded that the Commission Delegated Regulation (EU) 2016/161 regarding safety features will apply from 9 February 2019.

At this point in time, wholesalers should have already reviewed the Commission Delegated Regulation against their processes, suppliers, customers and types of products they distribute to determine what products need to be verified, or verified and decommissioned, prior to onward distribution.

In order to meet legal obligations, wholesalers need to install software systems to create a connection to the national repository / hub. The Irish Medicines Verification Organisation (IMVO) manages this national hub and will provide wholesalers with the software development kit and the support they may need to create an interface between their IT systems and the hub. The IMVO have an onboarding process for wholesalers. Further information regarding the onboarding process for wholesalers is available by contacting the IMVO. http://www.imvo.ie/

Further information on Safety Features is available from the links below:

https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2016_161/reg_2016_161_en.pdf

https://ec.europa.eu/health/home_en

http://www.hpra.ie/homepage/medicines/special-topics/falsified-medicines-legislation

Notification of GDP inspections

At present, GDP inspections performed by the HPRA are announced to companies, typically 6 weeks in advance of the inspection date. Prior announcement of the inspection helps to ensure that companies have the required resources available for the inspection. Despite advance notifications, the scheduling of inspections has become increasingly difficult as an increasing number of companies are requesting the rescheduling or cancellation of inspections at short notice. This results in significant difficulties for the HPRA inspection scheduling team. The rescheduling of inspections reduces the capacity of the inspection team as other inspections cannot be scheduled at short notice to fill the schedule gap created.

To address these challenges, the inspection notification period for GDP inspections will be increased. While individual cases may vary, the date of most routine inspections will be notified by email at least 8 weeks in advance of the inspection. This will be followed by a more detailed inspection notification containing documentation requests closer to the inspection date. In giving a longer notification period, the HPRA expects that companies will have an increased ability to plan and manage their resources accordingly, such that there should be no requirement to reschedule.

It is noted that the rescheduling of some inspections are requested due to absence of key personnel. When notified early, the HPRA will try to accommodate changes to the schedule where at all possible, but companies are reminded that measures should be in place for delegation of duties of key personnel during periods of absence. It is expected that a deputy responsible person has adequate knowledge and oversight of the systems in place such that they can effectively deputise for the responsible person. This includes management of inspections.

The HPRA reserves the right to perform unannounced inspections.

The HPRA are delighted to announce the registration for the International Conference of Drug Regulatory Authorities (ICDRA) 2018 is now open!

Please visit the dedicated ICDRA website for further information www.icdra2018.ie

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