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SME Office NEWSLETTER

Information for SMEs on the EU regulatory environment for medicines.
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IN THIS ISSUE

Guidance on pharmacovigilance for human medicines

PSUR repository

From 13 June 2016, all periodic safety update reports (PSURs) for human medicines authorised in the European Union (EU) must be submitted electronically to the PSUR repository (Link). The PSUR repository is a single platform for PSURs and related documents to be used by all regulatory authorities and pharmaceutical companies in the EU. Marketing authorisation holders must now use the repository as a single point for submissions and should no longer submit their PSURs to national competent authorities. The obligation applies to both centrally and nationally authorised medicinal products. PSUR submissions to the repository are made through the eSubmission Gateway/Web Client (Link). More information on how to submit a PSUR through the repository can be found in a questions & answers document (EMA/395434/2016).

New Eudravigilance system

The updated EU pharmacovigilance legislation brought significant changes to electronic reporting requirements for suspected adverse reactions. EMA has launched a project to deliver a new EudraVigilance system with enhanced functionalities in November 2017 (Link). A modular training programme will be provided in 2016 and 2017, and the first set of e-learning modules is available via the EudraVigilance training page (Link). Further information can be found in the training plan (EMA/835422/2016).

Eudravigilance registration

From 13 June 2016, changes are being implemented to the EudraVigilance registration system (EMA/410776/2016) including: a 'regulatory contact point' for marketing authorisation holders (EMA/398931/2016), mandatory password change functionality for first time users, editable fields and affiliate categories, new troubleshooting functionality, and separate adverse drug reaction (ADR) and XEVMPD user rights.

A document detailing the registration user management (EMA/404288/2016) and an updated questions & answers document on Eudravigilance registration (EMA/353007/2016) have also been published on the EMA website.

New Eudravigilance webpages

The EudraVigilance website (https://eudravigilance.ema.europa.eu) is being de-commissioned.

All public information about EudraVigilance can now be accessed on the EMA corporate website (Link). Registered users will continue to be able to access the EudraVigilance restricted area as usual. Further information can be found in this document (EMA/422535/2016).

Pharmacovigilance fees

The explanatory note on pharmacovigilance fees payable to EMA (Link) and related guidance (EMA/409768/2015; EMA/175299/2015 Rev.1) have been updated to introduce changes relating to calculations of chargeable units, fee determination and payment, and fee corrections for SME pharmacovigilance fees where applicable.

Support on queries

EMA has published a guidance document on the support offered by the EMA on EudraVigilance and Pharmacovigilance related queries (Link).

Non-clinical and clinical guidance

Four documents on clinical trials have been released for consultation by the European Commission until 31 August 2016 (Link): risk proportionate approaches in clinical trials (Link), summary of clinical trial results for laypersons (Link), definition of investigational medicinal products (IMPs) and use of Auxiliary Medicinal Products (AMPs) (Link), and ethical considerations for clinical trials on medicinal products conducted with minors (Link).

A guidance document on the use of patient-reported outcome (PRO) measures in oncology studies will come into effect on 1 November 2016 (EMA/CHMP/292464/2014). It is an appendix to the guideline on the evaluation of anticancer medicinal products in man (EMA/CHMP/205/95/Rev.4) and addresses how patient-reported outcome data should be integrated in oncology trials.

A revised guideline on the clinical investigation of medicinal products in the treatment of lipid disorders will come into effect on 1 January 2017 (EMA/CHMP/748108/2013, Rev. 3). It provides guidance for the evaluation of drugs in the treatment of lipid disorders and details the main regulatory requirements that are expected to be followed in the development of a lipid modifying medicinal product. It was aligned with other relevant EMA guidance (i.e. reflection paper on assessment of cardiovascular safety profile of medicinal products EMA/CHMP/50549/2015; guideline on the clinical investigation on medicinal products in the treatment of hypertension (see below); guideline on the clinical evaluation of medicinal products used in weight management (see below)).

A revised guideline on the clinical investigation of medicinal products in the treatment of hypertension will come into effect on 1 January 2017 (EMA/CHMP/29947/2013/Rev.4). The section on the collection of long-term safety data has been aligned with the other relevant EMA guidance (see above).

A revised guideline on the clinical evaluation of medicinal products used in weight management will come into effect on 1 January 2017 (EMA/CHMP/311805/2014). The update clarifies the recommended methods of assessing efficacy, selection of patients, strategy and design of clinical trials. The safety section was updated in light of other relevant EMA guidance (see above).

A revised guideline on the clinical development of medicinal products for the treatment of HIV infection will come into effect on 1 January 2017 (EMEA/CPMP/EWP/633/02 Rev. 3). It has been updated to include a recommendation to perform drug-drug interaction studies prior to marketing authorisation.

A draft guideline on the clinical investigation of medicinal products for the treatment of acute coronary syndrome (ACS) has been released for consultation until 31 October 2016 (EMA/CHMP/207892/2015). It will replace the 'Points to consider on the clinical investigation of new medicinal products for the treatment of acute coronary syndrome (ACS) without persistent ST segment elevation' (CPMP/EWP/570/98). The revision takes into consideration major developments in the field and provides updated guidance on ST and non-ST segment elevation myocardial infarction (STEMI and NSTEMI), as well as unstable angina (UA), sets

out updated definitions, risk stratification and endpoints.

A draft guideline on good pharmacogenomics practice has been released for consultation until 16 September 2016 (EMA/CHMP/268544/2016). It provides guidance on the choice of appropriate genomic methodologies during a product's development and life-cycle. Principles for a robust clinical genomic dataset are discussed and key scientific and technological aspects for the determination and interpretation of genomic biomarker data and their translation into clinical practice are highlighted.

A revised draft guideline on the clinical evaluation of direct acting antivirals (DAAs) for the treatment of chronic hepatitis has been released for consultation until 31 December 2016 (EMEA/CHMP/EWP/30039/2008 Rev 1). It has been revised to take into account the developments in the field of hepatitis C virus (HCV) therapy and in particular the approval of DAA for the treatment of chronic HCV infections within interferon-free combination regimens.

A questions & answers document on 'ICH guideline S3A - Note for guidance on toxicokinetics: the assessment of systemic exposure in toxicity studies' (EMA/CHMP/ICH/320985/2016) has been released for consultation until 31 August 2016.

Quality guidance

A guideline on process validation for the manufacture of biotechnology-derived active substances and data to be provided in a regulatory submission will come into effect on 1 November 2016 (EMA/CHMP/BWP/187338/2014). It addresses the data requirements for process characterisation and verification for the submission of a marketing authorisation application or variation.

A draft guideline on the requirements to the chemical and pharmaceutical quality documentation of investigational medicinal products (IMPs) in clinical trials has been released for consultation until 12 October 2016 (EMA/CHMP/QWP/834816/2015). It addresses the documentation requirements on the quality of IMPs and Auxiliary Medicinal Products containing chemically defined drug substances, synthetic peptides, synthetic oligonucleotides, herbal substances, herbal preparations and chemically defined radio-active/radio-labelled substances to be submitted to the competent authority for approval prior to beginning a clinical trial in humans.

A revised draft guideline on the requirements for quality documentation of biological investigational medicinal products (IMPs) in clinical trials has been released for consultation until 31 December 2016 (EMA/CHMP/BWP/534898/2008 rev. 1). It details the documentation requirements on the biological, chemical and pharmaceutical quality of IMPs containing biological/biotechnology derived substances and also gives examples of modifications which are typically considered as 'substantial'. The guidance applies to proteins and polypeptides, their derivatives, and products of which they are components and Auxiliary Medicinal Products containing these proteins and polypeptides as active substances.

A draft guideline on the sterilisation of a medicinal product active substance, excipient and primary container has been released for consultation until 13 October 2016 (EMA/CHMP/CVMP/QWP/BWP/850374/2015). It provides guidance on the choice of the sterilisation method, and the development and manufacturing data required to support the manufacture of the finished product. It applies to chemical and biological medicinal products for human and veterinary use and is not applicable for immunological veterinary medicinal products.

A revised guideline compiling product-specific guidance on the demonstration of bioequivalence for individual products authorised within the EU has been published on the EMA website (EMA/CHMP/736403/2014 Rev 3). It enables a consistent approach to the assessment of applications based on bioequivalence data, particularly generic applications, across all submission routes.

A questions & answers document on Quality of medicines (Link) has been updated (e.g. data required for sterilisation processes of primary packaging materials subsequently used in an aseptic manufacturing process; possibility for an active substance to be used in either powdered or granulated forms in a single marketing authorisation for a veterinary medicinal product containing 100% of the active substance).

Guidance for veterinary medicines

A draft guideline on user safety of topically administered veterinary medicinal products has been released for consultation until 31 December 2016 (EMA/CVMP/SWP/721059/2014). It provides advice on how user risk assessments should be conducted for such products.

A draft guideline on plant testing strategy for veterinary medicinal products has been released for consultation until 30 November 2016 (EMA/CVMP/ERA/689041/2015). This guideline replaces the reflection paper on testing strategy and risk assessment for plants (EMA/CVMP/ERA/147844/2011). The species sensitivity distribution approach presented in the reflection paper has been complemented with two additional options for higher tier testing: testing of metabolites or transformation products, and a plant toxicity test using manure mediated exposure.

A document setting out questions on extraneous agents of stem cell-based products for veterinary use to be addressed by the Ad Hoc Group on Veterinary Novel Therapies (ADVENT) has been released for consultation until 30 September 2016 (EMA/CVMP/ADVENT/174610/2016).

A document describing the defined daily doses for animals (DDDvet) and defined course doses for animals (DCDvet) for antimicrobial agents for use in cattle, pigs and broilers (poultry) has been published (EMA/224954/2016).

A report on the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) trial for collecting data on consumption of antimicrobial agents in pigs has been published (EMA/836856/2015). It describes the trial performed to test the proposed system for collecting data on antimicrobial consumption in pigs and its results. Experience from this trial will be used to prepare future guidance.

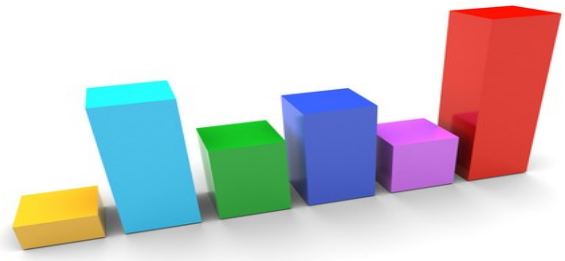
Veterinary Dictionary for Drug Related Affairs (VeDDRA)

A revised combined VeDDRA list of clinical terms for reporting suspected adverse reactions in animals and humans to veterinary medicinal products will enter into force on 1 October 2016 (EMA/CVMP/PhVWP/10418/2009-Rev.8). A list of changes to this list (EMA/CVMP/PhVWP/286361/2016) and a revised guidance on the use of VeDDRA terminology for reporting suspected adverse reactions in animals and humans (EMA/CVMP/PhVWP/288284/2007-Rev.9) have also been published.

PRIME

Statistics on PRIME

The outcome of the assessment of the first series of applications received into the PRIME scheme have been published on the EMA website. Information on PRIME will be published on a monthly basis, on the Wednesday following the plenary meeting of the CHMP and will be part of the annexes of the CHMP highlights (refer to "Recommendations on eligibility to PRIME scheme" under "Other updates").



Fee reductions for scientific advice requests for PRIME products

The explanatory note on general fees payable to EMA (Link) has been updated to introduce a 100% fee reduction for scientific advice for products eligible to the PRIME scheme for SMEs and applicants from the academic sector. The fee exemption is restricted to the development in the indication for which eligibility to the PRIME scheme has been accepted.

Regulatory and procedural guidance

New post-authorisation guidance

A new guidance on the procedural management of risk management plans (RMP) submissions has been published (Link) and provides information on the classification of RMP changes as well as procedural aspects of the RMP lifecycle. It simplifies the management of complex RMP updates as some RMP changes currently submitted as "groupings" (type IIs/IBs or IBs/IBs variations) will now be accepted as a single variation. Guidance on the classification of changes to the marketing authorisation post authorisation and for certain variation classification categories has also been published and includes a simplified approach for handling quality-related changes due to the introduction of a new manufacturing site for a finished product (Link).

New questions & answers documents are available on the EMA website:

- Questions & answers document on Article 13 referral procedures (EMA/265223/2016);
- Questions & answers document on Article 29 (4) referral procedures (EMA/457269/2016);
- Questions & answers document on Article 20 non-pharmacovigilance procedures (EMA/457260/2016);
- Questions & answers document on Article 31 non-pharmacovigilance referrals (EMA/457344/2016);
- Questions & answers document on Article 30 referral procedures (EMA/457319/2016).

The following guidance documents and templates were also updated:

- EMA post-authorisation procedural advice for users of the centralised procedure (on e.g. type IA variation, type IB variation, type II variation, extension application, renewal, annual re-assessment, PSURs, PAES, post authorisation measures, transfer of marketing authorisation applications, risk management plan) (EMEA-H-19984/03 Rev. 62).
- EMA pre-authorisation procedural advice for users of the centralised procedure (on e.g. submission of EU Risk Management Plan) (EMA/339324/2007).
- EMA procedural advice for users of the centralised procedure for generic/hybrid applications (on e.g. submission of EU Risk Management Plan) (EMEA/CHMP/225411/2006).
- Checklist for sponsors applying for the transfer of orphan medicinal product designation (EMA/41277/2007 Rev. 6) to update the corresponding orphan designation transfer form (Link).

Reports, workshops and meetings

SME Office

A report summarising the EMA experience with small and medium-sized enterprises (SMEs) since the launch, in December 2005, of the SME Regulation and the establishment of the Agency's SME Office has been published (EMA/155560/2016). The results of a survey conducted in 2015 to gather feedback on its SME initiative from stakeholders has also been published (EMA/242286/2016). New webpages on the Agency's support to SMEs are available on the EMA website (Link).

Guide to information on human medicines evaluated by EMA

A guide describing the information published by EMA on centrally and non-centrally authorised medicinal products for human use is available on the EMA website (EMA/515416/2015).

Interaction between EMA and Health Technology Assessment bodies

EMA and the European network for Health Technology Assessment (EUnetHTA) published a report on their joint work plan (Link) covering the period between November 2012 and December 2015. It highlights the value of EMA and EUnetHTA collaboration that fosters an approach to the generation of data on medicines, pre- and post-authorisation, that reconciles regulatory and HTA requirements into one clinical development programme. Further information is also available on the dedicated press release (Link).

Advanced therapy medicinal products

A report from a multi-stakeholder meeting held on 27 May 2016 detailing proposals to encourage the development and authorisation of advanced therapy medicinal products (ATMPs) in the EU has been published on the EMA website (EMA/345874/2016).

Selection of upcoming events

September 2016

- Second annual scientific workshop at EMA: applying regulatory science to neonates – 12 & 13 September 2016 (Link)

October 2016

- Workshop for micro, small and medium-sized enterprises: Focus on non-clinical aspects – 3 October 2016 (Link)
- Joint DIA/EFGCP/EMA better medicines for children conference 2016 on optimisation of drug development for the benefit of children – 10 & 11 October 2016 (Link)

Reports, presentations and/or videos of the following meetings have been published:

February 2016

- Workshop on the challenges for the approval of anti-cancer immunotherapeutic drugs (Link)

March 2016

- European Medicines Agency / International Federation for Animal Health Europe info day 2016 (Link)

April 2016

- Seventh industry stakeholder platform: operation of European Union pharmacovigilance legislation (Link)
- European Union (EU) workshop on ICH Q3D from a quality perspective (Link)
- Third industry stakeholder platform on the operation of the centralised procedure for human medicinal products (Link)
- European Medicines Agency—Industry Stakeholders Platform second meeting on paediatric medicines (Link)

May 2016

- Workshop on applying regulatory science to neonates: launch of the International Neonatal Consortium (INC) (Link)
- EMA public workshop on extrapolation of efficacy and safety in medicine development (Link)
- Multi-stakeholder advanced therapy medicinal products (ATMPs) expert meeting: exploring solutions to foster ATMPs' development and patient access in Europe (Link)

June 2016

- 2016 annual workshop of the European network of paediatric research (Enpr-EMA) (Link)

Registered SMEs

Currently, 1652 companies have SME status assigned by the Agency.

The names and profiles of these companies are published in the Agency's public SME Register.

If you would like to have your company details included in the SME Register, you must first apply for SME status at the Agency.

See the How to apply section of the SME Office pages on the Agency's website for information on how to do this.

About the SME Office

The SME Office was set up within the European Medicines Agency to address the particular needs of smaller companies.

The Office has dedicated personnel who can help SMEs by:

- responding to practical or procedural enquiries;
- setting up briefing meetings to discuss regulatory strategy;
- organising workshops and training sessions.

Need more information?

Visit the European Medicines Agency website:

http://www.ema.europa.eu

In particular, these sections may interest you:

SME Office
Pre-authorisation (human medicines)
Pre-authorisation (veterinary medicines)

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