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HPRA MEDICINAL PRODUCTS NEWSLETTER

ISSUE 53

In this Issue

Human Medicines

Pseudoephedrine - Implementation of Risk Minimisation Measures

Background

Pseudoephedrine is an active ingredient in non-prescription cough and cold medicines and acts as a decongestant. It is also a precursor material in the production of methamphetamines. The diversion of pseudoephedrine-containing medicines is a significant problem in countries such as the US and Australia and this has led to the implementation of restrictive measures to limit the access to non- prescription pseudoephedrine. EU Member States have also taken action, of note, the UK limits the pack size to 720mg with no greater than 720mg pseudoephedrine sold per transaction; the Czech Republic limits sale to one pack containing 720mg pseudoephedrine per person per week with a central register and Germany also introduced restrictions on the sale of these medicines limiting to 720mg pseudoephedrine per pack and imposing a prescription requirement for more than one pack per sale. Pseudoephedrine is a prescription only medicine in Sweden, Finland and Norway.

Proposals

HPRA proposed two risk minimisation measures surrounding the sale and supply of pseudoephedrine containing medicinal products in Ireland.

1. Impose a maximum quantity per pack of 720mg pseudoephedrine. Packs containing more than 720mg would not be marketed for pharmacy sale without a prescription.
2. Limit pharmacy sales of all pseudoephedrine containing medicines to one pack per transaction.

Action

In support of these proposals, HPRA sought the views of relevant experts and interested parties. Responses supported these proposals as reasonable and proportionate in achieving broader health benefits. The measures are justified and appropriate and will continue to allow appropriate patient access to pseudoephedrine containing medicines. The proposals are in line with the position in the UK and this is important to limit cross-border diversion.

HPRA proposed these measures to all marketing authorisation holders (MAH) of pseudoephedrine- containing medicines and the response was positive. The conditions have been added to the licenses of all relevant pseudoephedrine containing medicinal products. MAHs have provided timelines for run-down of stocks that do not meet the conditions outlined, where required. Pharmacies will be permitted to run down existing stocks that do not meet the conditions. There will be no recall of stock at this time.

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'QPPV Update: What's new in Pharmacovigilance' – New EMA publication

The EMA recently published the first issue of 'QPPV Update'. This publication replaces the 'Pharmacovigilance Programme Update' which provided information on the development of the Pharmacovigilance systems and services at EU level. The 'QPPV update' will provide Qualified Persons for Pharmacovigilance (QPPVs) and other people working in Pharmacovigilance with relevant updates on what is new in EU Pharmacovigilance. MAHs are encouraged to monitor these publications in order to maintain awareness of relevant EU Pharmacovigilance related activities and to support appropriate and timely updates to internal procedures and systems, as necessary.

Good Practice Guide on Medication Errors

The revised European Union (EU) legislation introduced a number of changes related to reporting, assessment and management of medication errors which affect the operation of pharmacovigilance systems in EU Member States. To support the implementation of the relevant legal provisions amongst stakeholders involved in recording, reporting, evaluation and prevention of medication errors, the European Medicines Agency (EMA) in collaboration with the EU regulatory network developed regulatory guidance for medication errors, taking into account the recommendations of a stakeholder workshop held in London in 2013, along with feedback from several consultations. This guidance was published in November 2015 and is split into two sections. The first part of the guide clarifies the key principles of recording, coding, reporting and assessment of medication errors associated with suspected adverse reaction(s) in everyday medical practice. Its main objective is to improve reporting and learning from medication errors for the benefit of public health.

Good practice guide on recording, coding, reporting and assessment of medication errors.

The second part of the guide clarifies the key principles of risk management planning in relation to medication errors and describes the main source and categories of medication errors and how the risk of such errors can be minimised throughout the product lifecycle.

Good practice guide on risk minimisation and prevention of medication errors.

For further information see the dedicated webpage on the EMA website at medication errors.

Article 57 database

The Article 57 database was established in line with the legal provision in Regulation (EC) No 726/2004, namely Article 57(2). According to this Article, Marketing Authorisation Holders (MAHs) are required to submit product related data to the European Medicines Agency (EMA). This data includes full contact information on the Qualified Person responsible for Pharmacovigilance (QPPV) and on the location of the Pharmacovigilance System Master File (PSMF). The MAH is also obliged to keep this information up to date.

Variations – Changes to QPPV and PSMF information

MAHs are obliged to inform competent authorities about changes to the QPPV including contact details and/or changes in the location of the PSMF. Previously, these changes were subject to a type 1AIN variation, however, as the Article 57 database is now considered fully functional for these purposes, such variations are no longer necessary. Since 1st February 2016, MAHs should provide changes to QPPV and PSMF information through the Article 57 database and ensure their entries are kept up to date. No final variation is required to notify an explicit cross reference to the Article 57 database as the source of QPPV and PSMF information.

For further information, see the European Commission's press release and detailed guidance on the EMA's 'Guidance documents' webpage.

Communication of referral procedures using Article 57 database

MAHs are reminded that the QPPV email addresses included in the Article 57 database are used by the EMA as the main point of contact for companies during a pharmacovigilance referral procedure, with QPPVs for the medicinal products concerned notified electronically via Eudralink, further highlighting the importance of ensuring that the QPPV information in the Article 57 database is kept up to date.

For further information, see issue 1 of the EMA's publication 'QPPV update – What's new in Pharmacovigilance'

Parallel Importation - Update to Variation categories

Following a review by the HPRA of the categories and classifications of variations to parallel import product licences Type II variations have been removed as a category and the number of Type IB and Type IA variations have been reduced. The HPRA Guide to Parallel Imports of Human Medicines has been updated to reflect these changes and also to expand the list of changes for which a variation is not required. Furthermore the guide now specifies how frequently Parallel Importers should be reviewing their product information against the originator. HPRA hosted webinar which was broadcast on March 10th 2016 and presented these changes to the industry. The presentations and recording of the webinar are available on the HPRA website at https://www.hpra.ie/homepage/medicines/regulatory-information/medicines-authorisation/parallel-importation.

Further queries may be directed to customer services at customerservices@hpra.ie

Implementation of ICH Q3D on Elemental Impurities

Marketing Authorisation Holders (MAHs) are reminded that from **June 2016**, all **new applications** submitted for a marketing authorisation should comply with the new ICH Guideline on Elemental Impurities (Q3D).

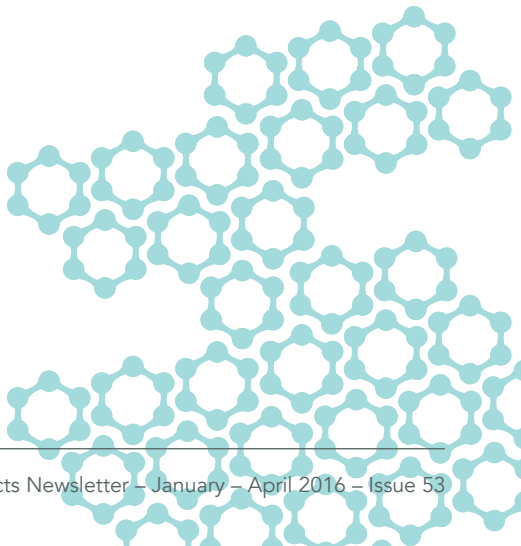
For products that are already authorised, this compliance with the guideline applies from **December 2017**. During the implementation period (from June 2016 until December 2017) MAHs should:

1. Perform a risk assessment covering all potential sources of elemental impurities in the finished product
2. Evaluate the effectiveness of the control strategy for ensuring that any elemental impurity is within the permitted daily exposures given in the guideline.

It is foreseen that the parts of the risk assessment may be common across some products (e.g.: contribution from manufacturing equipment) while other parts (e.g.: use of an elemental catalyst) will be product specific. The new guideline describes the principles of a risk based approach that companies can follow to ensure the adequate control of elemental impurities.

A variation to the marketing authorisation is not required where the risk assessment shows that no additional controls are necessary for the product to comply with the requirements of the guideline.

Where the risk assessment shows that further controls are necessary to control elemental impurities then a variation is necessary. The variation should be categorised according to the variation guidelines for the change being proposed and, in addition to the documentation required by the variation, a summary of the risk assessment should be provided. The summary should give information on the elements considered in the assessment, the risk tools that were utilised and the findings and conclusion of the assessment. Specific results are not required in the summary but should be available upon request.



Veterinary Sciences

QP declaration for intermediate sites

The HPRA wishes to advise MA holders that all manufacturing sites involved in the manufacture of the active substance, including those involved in complete or partial manufacture (e.g. synthesis of intermediates, micronisation), are required to be listed on the QP declaration. The QP declaration should be based on an audit of the active substance manufacturers. It is established good practice that the audit should be conducted at the manufacturing site i.e. an on-site audit.

Appointments to the Advisory Committee for Veterinary Medicines

The Department of Health has advised the HPRA of the following appointments to the ACVM for the period 1 January 2016 to 31 December 2020:

Mr Pat Brangan (Chairperson), Mr Ciaran Mellet, Ms Eugenie Canavan, Dr Ruadhri Breathnach, Dr Martin Danaher, Dr Nola Leonard, Dr Helena Kelly, Mr Warren Schofield, Dr Christina Tlustos, Dr Bryan Markey and Mr Robert Shiel.

Staff Changes and updates

Ms. Orla Barry, Scientific Officer
Dr. Anne McNaughton, Scientific Officer – Veterinary Pharmacovigilance, left the Veterinary Sciences Department to take up new positions within the HPRA's Human Products Authorisation & Registration Department. Dr. Anne was replaced by Dr. Michael McDonald who took up his appointment on 22 February.

Ms. Mary O'Grady, Pharmaceutical Assessment Manager, was elected as the veterinary vice-chair of the joint CHMP/CVMP Quality Working Party, at the meeting of the CVMP in March.

We wish all well in their new roles.

The up-to-date organogram of personnel in the Veterinary Sciences Department is available on the HPRA website at the following link:

https://www.hpra.ie/homepage/about-us/our-structure/management-committee/management-teams

Compliance

Applications for Controlled Drugs Waste Export Licenses

To date, all organisations applying for an export licence, from the Department of Health, relating to the exportation of controlled drugs waste have submitted a spreadsheet containing the calculations of controlled drug waste quantities. This spreadsheet was then reviewed in full by the HPRA. Once reviewed, the applicant then submitted its request for an import licence to the relevant authority of the country of destination.

As of 1 June 2016, calculations of controlled drugs waste will no longer be reviewed in full by the HPRA prior to the organisation requesting the associated import licence from the destination country's authority. It is anticipated that this change will facilitate a more expedient process for organisations wishing to export controlled drugs waste. The spreadsheet containing the controlled drug waste calculations and the associated import licence should be submitted to the HPRA with the application for an export licence.

It is of utmost importance, therefore, that applicants perform their own quality checks of controlled drug waste calculations provided to the HPRA (for example, including but not limited to the use of correct controlled drug 'salt to base' conversion factors). The HPRA will conduct spot checks of controlled drug waste calculations submitted by organisations and, where necessary, if an error is identified, the application for a controlled drug export licence may be returned to the applicant for amendment and resubmission.

Additionally, spreadsheets containing details of the calculations should continue to be retained as part of the organisation's records and may be examined during an inspection.

Any queries should be sent to controlleddrugs@hpra.ie.

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