5 February 2016
EMA/505633/2011, Rev. 2[1]
Inspections & Human Medicines Pharmacovigilance Division

Legal notice on the implementation of Article 57(2) of Regulation (EC) No. 726/2004

"Electronic submission of information on medicinal products for human use by marketing authorisation holders to the European Medicines Agency"

This legal notice has been prepared and updated by the European Medicines Agency (hereafter "the Agency") to implement the requirements for the electronic submission of information on medicinal products for human use authorised in the Union as provided for in Article 57(2) of Regulation (EC) No 726/2004. For this purpose, marketing authorisation holders are required to:

(a) electronically submit any information on medicinal products for human use authorised in the Union as set out in this legal notice;

(b) electronically complete and notify any amendments to previously submitted information on medicinal products for human use authorised in the Union as set out in this legal notice.

1. Format for the electronic submission of information on medicinal products for human use

1(a) Marketing authorisation holders shall use the updated eXtended EudraVigilance Medicinal Product Report Message (XEVPRM) published on 5 March 2012 as amended on 31 January 2014 as the format to electronically submit to the Agency information on all medicinal products for human use authorised in the Union.

1(b) Updated detailed guidance on the use of the format as referred to in paragraph 1(a) of this legal notice has been published by the Agency.

1(c) The format as referred to in paragraph 1(a) of this legal notice and the detailed guidance as referred to in paragraph 1(b) of this legal notice shall take account of the work on international harmonisation carried out in the area of pharmacovigilance and shall, where necessary, be revised to take account of technical and scientific progress.

[1] Changes are highlighted in red.

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2. Timelines

2(a) Since 2 July 2012, marketing authorisation holders have been required to electronically submit to the Agency information on all medicinal products for human use authorised in the Union using the format as referred to in paragraph 1(a) of this legal notice. This has been independent of the type of the authorisation procedure (e.g. national procedures).

2(b) Information on medicinal products for which a new marketing authorisations in the Union was obtained after 2 July 2012 shall be submitted by marketing authorisation holders electronically to the Agency no later than 15 calendar days from the date of authorisation.

2(c) As of 16 June 2014 and by no later than 31 December 2014, marketing authorisation holders were required to electronically update, complete, improve the quality of the information on medicinal products for human use as referred to under paragraph 3 and 4 of this legal notice and to submit to the Agency information on all medicinal products for which the terms of the marketing authorisations in the Union was amended following variation, transfer, renewal, suspension, revocation or withdrawal of the marketing authorisation.

2(d) Following the submission as referred to in paragraph 2(c) of this legal notice, marketing authorisation holders shall electronically notify to the Agency information on any amendments to the terms of the marketing authorisations following variation, transfer, renewal, suspension, revocation or withdrawal no later than 30 calendar days from the date of which the amendments have been authorised.

As of 1 February 2016 changes in qualified person responsible for pharmacovigilance (QPPV), including contact details (telephone and fax numbers, postal address and email address) and changes to the pharmacovigilance system master file (PSMF) location (street, city, postcode, country) shall be updated through the Article 57 database only, without the need to submit a type IAIN variation to the Agency or the national competent authority (as applicable). Changes to the QPPV and/or PSMF shall be notified to the Agency via the Article 57 database immediately and no later than 30 calendar days from the date the change applies. No variation to include in the marketing authorisation dossier a cross reference to Article 57 as the source of QPPV and PSMF information is required.

2(e) The format as referred to in paragraph 1(a) of this legal notice and the processes described in the detailed guidance as referred to in paragraph 1(b) of this legal notice shall be used for the notification as referred to in paragraph 2(a) to 2(d) of this legal notice.

3. Information on medicinal products for human use

Using the electronic format as referred to in paragraph 1(a) of this legal notice and following the detailed guidance as referred to in paragraph 1(b) of this legal notice, marketing authorisation holders shall provide the following information on medicinal products authorised for human use:

i. a description of the (invented) name of the medicinal product;

ii. a description of the pharmacodynamic properties, which shall include:

    a. the ATC code(s) for the medicinal product;

iii. details of the marketing authorisation holder, which shall include:

a. name and address of the marketing authorisation holder,

b. a description of the status of the marketing authorisation holder i.e. micro-, small- and medium-sized-enterprise (SME);

iv. details of the marketing authorisation and the status, which shall include:

a. marketing authorisation procedure,

b. legal basis of the marketing authorisation,

c. country of marketing authorisation,

d. marketing authorisation number as described in the detailed guidance as referred to in paragraph 1(b) of this legal notice,

e. authorisation/renewal date and the date of the lifting of the suspension, where applicable,

f. marketing authorisation status,

g. mutual-recognition/(de)centralised or national authorisation procedure number,

h. orphan drug designation,

i. date of withdrawal/revocation/suspension of the medicinal product authorisation, where applicable;

v. a description of the medicinal product type as described in the detailed guidance as referred to in paragraph 1(b) of this legal notice;

vi. a description of the therapeutic indications, which shall include:

a. therapeutic indication(s) coded in the Medical Dictionary for Regulatory Activities (MedDRA),

b. declaration that the medicinal product is "authorised for the treatment in children";

vii. details of the qualitative and quantitative composition of the medicinal product, which shall include:

a. a description of the active substance(s) and adjuvant(s), where applicable,

b. a description of the strength (amount) of the active substance(s) (including adjuvants);

viii. a description of the excipients;

ix. a description of the medical device(s) for combined advanced therapy medicinal product in accordance with Regulation (EC) No 1394/2007, as applicable;

x. the authorised and administrable pharmaceutical form(s);

xi. a description of the posology and method of administration, which shall include route(s) of administration;

xii. an electronic copy of the latest approved summary of product characteristics (SmPC) including version date, document reference number(s) and document language(s).

The specific requirements to submit amendments to the terms of marketing authorisation following variation, renewal, transfer, suspension, revocation or withdrawal are described in paragraph 5 of this legal notice.

4. Pharmacovigilance information

To facilitate the technical implementation of Article 57(2) of Regulation (EC) No 726/2004, certain pharmacovigilance information has to be provided by the marketing authorisation holders. In particular, information on the qualified person responsible for pharmacovigilance (QPPV) is required to ensure controlled access to EudraVigilance. To this end and for practical reasons, the following information in relation to medicinal products authorised for human use should be provided by marketing authorisation holders by using the electronic format as referred to in paragraph 1(a) and following the detailed guidance as referred to in paragraph 1(b) of this legal notice:

i. name, address and contact details of the qualified person responsible for pharmacovigilance (QPPV);

ii. contact e-mail for pharmacovigilance enquiries;

iii. contact phone number for pharmacovigilance enquiries.

Only the contact information for pharmacovigilance enquires (e-mail and phone number) will be made public by the Agency.

In line with Article 4 (4) of Commission Implementing Regulation (EU) No 520/2012, marketing authorisation holders shall notify immediately the Agency of any change to the contact details and name of the qualified person responsible for pharmacovigilance (QPPV) or any change in the location of the pharmacovigilance system master file (PSMF).

The following information in relation to medicinal products authorised for human use should be provided by marketing authorisation holders to indicate the location of the PSMF by using the electronic format as referred to in paragraph 1(a) and following the detailed guidance as referred to in paragraph 1(b) of this legal notice:

i. Street;

ii. City;

iii. Postcode;

iv. Country.

The Agency shall update the Eudravigilance database referred to in Article 24(1) of Regulation (EC) No 726/2004.

5. Maintenance of information on medicinal products for human use

Using the electronic format as referred to in paragraph 1(a) of this legal notice, following principles outlined in the detailed guidance as referred to in paragraph 1(b) of this legal notice and according to the processes and circumstances referred to in paragraphs 2(c) and 2(d) of this legal notice, marketing

authorisation holders shall electronically notify to the Agency any amendments to the terms of the marketing authorisation of medicinal products authorised for human use that shall include:

i. notification of extensions of marketing authorisations as defined in paragraph 1 and 2 of Annex I of Regulation (EC) 1234/2008;

ii. notification of variations to the terms of marketing authorisations as set out in Regulation (EC) 1234/2008 that is affecting the XEVPRM structured information referred to in paragraph 3 of this legal notice;

iii. notification of any amendments to the pharmacovigilance information referred to in paragraph 4 of this legal notice which shall include:

    a. the name and the contact details of the qualified person responsible for pharmacovigilance (QPPV) in accordance with Article 4(4) of Commission Implementing Regulation (EU) no 520/2012,

    b. the contact e-mail and phone number for pharmacovigilance enquiries,

    c. the location of the pharmacovigilance system master file (PSMF);

iv. notifications of transfers of marketing authorisations in accordance with Commission Regulation (EC) No 2141/96;

v. notifications of any suspension/lifting of the suspension, revocation or withdrawal of a marketing authorisation granted in the Union including the following circumstances:

    a. the marketing authorisation was not renewed by the relevant competent authority,

    b. an application was not submitted for renewal by the marketing authorisation holder or,

    c. the marketing authorisation expired due to sunset clause;

vi. notifications of renewal of the marketing authorisation;

vii. notification of any variations that lead to a significant revision of the content of the below sections of the summary of product characteristics (SmPC) by submitting the electronic copy of the latest approved SmPC:

    a. section 4.2 Posology and method of administration (other than route of administration),

    b. section 4.3 Contraindications,

    c. section 4.4 Special warnings and precautions for use,

    d. section 4.5 Interaction with other medicinal products and other forms of interaction,

    e. section 4.6 Fertility, pregnancy and lactation,

    f. section 4.8 Undesirable effects,

    g. section 4.9 Overdose.

6. Quality and integrity of information

6(a) Marketing authorisation holders shall ensure that information on all medicinal products for human use authorised in the Union, which is submitted electronically to the Agency using the format and content as referred to in paragraph 1, 3 and 4 of this legal notice is accurate and up to date.

6(b) The Agency will perform an overall review of the quality and integrity of the medicinal product information submitted. Where there is a need for corrections or the provision of additional information, the marketing authorisation holder shall respond to requests of the Agency no later than 15 calendar days following receipt of such request.

For further information, please refer to the Agency's or EudraVigilance website or submit an enquiry via the EMA Service Desk portal (https://servicedesk.ema.europa.eu).

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