HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Guide to
Additional Monitoring Requirements and Statements Encouraging Reporting of Adverse Reactions

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This guide does not purport to be an interpretation of law and/or regulations and is for guidance purposes only.

CONTENTS

1 SCOPE

This guide was developed to provide guidance to marketing authorisation holders (MAHs) and marketing authorisation applicants on the implementation and introduction of the new requirements into the product information for medicinal products authorised in Ireland. It also includes national recommendations for including information on the status of additional monitoring in materials to be distributed to healthcare professionals and patients.

2 INTRODUCTION

In accordance with the new European Union (EU) pharmacovigilance legislation, a new framework for enhanced risk proportionate post-authorisation data collection for medicinal products has been introduced. This includes the new concept of additional monitoring, which aims to further characterise the safety profile of newly authorised medicinal products or those requiring further safety data and also the inclusion of a standard text in the product information expressly asking healthcare professionals and patients to report suspected adverse reactions in accordance with their national spontaneous reporting system.

3 IMPLEMENTATION OF TEXT HIGHLIGHTING ADDITIONAL MONITORING REQUIREMENTS

3.1 Background

The purpose of additional monitoring is to promote the reporting of suspected adverse reactions and thereby contribute to the benefit/risk profile of a medicinal product. Medicinal products under additional monitoring are identified by an inverted black triangle which is a common symbol which is now used across all EU member states.

According to Article 23(1) of Regulation (EC) No. 726/2004, the following medicinal products are included in the list of products subject to additional monitoring:

- medicinal products authorised in the EU that contain a new active substance which, on 1 January 2011, was not contained in any medicinal product authorised in the EU;

- any biological medicinal product authorised after 1 January 2011;

- products for which a PASS was requested at the time of marketing authorisation (Article 9(4)(cb) of Regulation (EC) No. 726/2004 and Article 21(a)(b) of Directive 2001/83/EC);

- products authorised with specific obligations on the recording or suspected adverse drug reactions exceeding those referred to in Chapter 3 of Directive 83/2001/EC (Article 9(4)(cb) of Regulation (EC) No. 726/2004 and Article 21(a)(c) of Directive 2001/83/EC);

- products for which a PASS was requested following the grant of marketing authorisation (Article 10(a)(1) of Regulation (EC) No. 726/2004 and Article 22(a)(1) of Directive 2001/83/EC);

- products which were granted a conditional marketing authorisation (Article 14(7) of Regulation (EC) No. 726/2004));

- products authorised under exceptional circumstances (Article 14(8) of Regulation (EC) No. 726/2004) and Article 22 of Directive 2001/83/EC)).

Other products may also be included on the list of medicinal products subject to additional monitoring. This may be done at the request of the European Commission or a national competent authority, following consultation with the Pharmacovigilance Risk Assessment Committee (PRAC) (see Article 23(2) of Regulation (EC) No. 726/2004). The situations that could form the basis for a request for inclusion in the list are defined in Module X of the Guideline on good pharmacovigilance practices, available on the EMA website. Additional monitoring status may also be assigned to a medicinal product at any time during the product lifecycle if a new safety concern is identified.

The European list of products under additional monitoring is available on the European Medicines Agency (EMA) website and is reviewed every month by the PRAC. Medicinal products may be included or removed from this list either in the context of a regulatory procedure (e.g. marketing authorisation application, extension of indication, renewal) or outside of a regulatory procedure. MAHs should therefore maintain their awareness of the products included in the list.

3.2 Centrally authorised products

The EMA announced an updated product information template to label medicines subject to additional monitoring and an implementation plan for centrally -authorised products. For new marketing applications, applicants must implement the inverted black triangle, additional monitoring statement and the statements encouraging the reporting of suspected adverse reactions to comply with the revised QRD template and country specific information as stated in Appendix V of the QRD template. The documents are available on the EMA website.

For existing marketing authorisations, MAHs are encouraged to use the first upcoming regulatory procedure affecting product information annexes to implement the requirements. If no suitable regulatory procedure is identified, a Type IA_{IN} variation should be submitted. Any procedures implementing these changes are required to be completed no later than 31 December 2013.

3.3 Decentralised and mutual recognition products

The Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) has published guidance for MAHs in their Questions and Answers document on variations, available on the HMA website. The information appears under question 2.11a and specifically addresses how product information can be updated in line with the revised QRD template for MR/DC procedures and country specific information as stated in Appendix V.

3.4 Nationally-authorised products

For nationally-authorised products which are subject to additional monitoring, the HPRA will apply the same procedure as outlined in the CMD(h) guidance provided for products authorised through the decentralised and mutual recognition procedures. MAHs should use the first upcoming regulatory procedure to update the product information by complying with the revised QRD template and country specific information as stated in Appendix V. If no suitable regulatory procedure is identified, a Type IAIN variation should be submitted. All medicines subject to additional monitoring are required to have included the necessary wording in all product information by 31 December 2013 in accordance with Commission Regulation 198/2013. The text to be included should be identical to that outlined in the most recent version of the QRD template for MR/DC procedures published on the CMDh website.

Queries relating to the implementation of text highlighting additional monitoring requirements should be directed to the Customer Service team at info@hpra.ie.

4 STATEMENTS ENCOURAGING REPORTING OF ADVERSE REACTIONS

4.1 Background

For all medicinal products for human use, a standard text shall be included in the product information expressly asking healthcare professionals to report any suspected adverse reaction in accordance with the national spontaneous reporting system referred to in Article 107a(1) (Article 11 of Directive 2001/83/EC), and expressly asking patients to communicate any suspected adverse reaction to his/her doctor, pharmacist, healthcare professional or directly to the national spontaneous reporting system referred to in Article 107a(1). This wording must be implemented for all medicinal products irrespective of the additional monitoring status.

4.2 Centrally-authorised products

The EMA has updated the product information templates and published an implementation plan for this requirement in relation to centrally authorised products, available on the EMA website. The text to be included is outlined in the revised QRD template for centralised authorised products and country specific information as stated in Appendix V.

4.3 Decentralised and mutual recognition products

CMDh has published guidance for MAHs in their Questions and Answers document on variations, available on the HMA website. The information appears specifically under question 2.11(b) and specifically addresses how product information can be updated according to the QRD template for MR/DC procedures and country specific information as stated in Appendix V.

4.4 Nationally-authorised products

For nationally-authorised products that are not subject to additional monitoring, the HPRA will apply the same procedure and timelines as outlined in CMD(h) guidance provided for products authorised through the decentralised and mutual recognition procedures, i.e., it is recommended to implement the updates in line with the most recent version of the QRD template for MR/DC procedures and country specific information as stated in Appendix V as soon as possible, but no later than April 2015 for medicinal products with regulatory activity or April 2016 for medicinal products with no regulatory activity.

For products which have no separate package leaflet, the following abbreviated text should appear on the label:

> **Reporting of side effects:** If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed on this label. You can also report side effects directly (see details below). By reporting side effects you can help provide information on the safety of this medicine.
> Ireland: www.hpra.ie

The MAH may discuss their proposals on how to integrate this information within the label with the HPRA on a case-by-case basis as needed.

MAHs should use the first upcoming regulatory procedure to update the product information. Alternatively, a separate Type IA_{IN} notification should be submitted to make the required changes where there are no regulatory activities for a product.
Queries relating to the implementation of text encouraging reporting of adverse reactions should be directed to the Customer Service team at info@hpra.ie.

5 MATERIALS FOR DISTRIBUTION TO HEALTHCARE PROFESSIONALS AND PATIENTS

5.1 Background

In GVP Module X additional monitoring, document available on the EMA website, it is recommended that 'the MAH should include information on the status of additional

monitoring in any material to be distributed to healthcare professionals and patients and should make all efforts to encourage reporting of adverse reactions, as agreed with national competent authorities'. The HPRA recommends that this guidance is followed for educational and promotional materials.

5.2 Educational materials specified in the EU risk management plan (RMP) or as part of the conditions of marketing authorisation

Educational materials for healthcare professionals and patients may be specified in the EU-RMP or as part of the conditions for marketing authorisation for new or authorised medicinal products; it is a requirement that the Irish version of these materials must be submitted to the HPRA for review prior to issue. For medicines subject to additional monitoring, educational materials distributed to patients and healthcare professionals about a medicine should contain information on its additional monitoring status. The MAH should also make all efforts to encourage reporting of adverse reactions within all educational materials. The MAH may discuss their proposals on how to integrate this information within the materials with the HPRA on a case-by-case basis as needed taking account of the nature of the tools. For existing materials, the MAH should implement the changes as appropriate within 6 months of the publication of this guidance or at the next time the material is revised, whichever is sooner.

Please submit a completed HPRA 'Submission of risk minimisation and educational materials by marketing authorisation holders' form (available in the 'Publications and Forms' section of www.hpra.ie) along with the accompanying documents to medvigilance@hpra.ie for review by the Human Products Monitoring department.

5.3 Other educational materials not specified in the RMP and promotional materials

Taking into account the opportunity for increased engagement with healthcare professionals and patients and in order to ensure that a consistent message is provided, the HPRA recommends the inclusion of information on the additional monitoring status of the product on promotional materials. The symbol should appear once and be located adjacent to the most prominent display of the name of the product. The size of the symbol should be appropriate to the font size of the promotional materials. The MAH should also endeavour to include the explanation of the symbol in addition to wording to encourage reporting of adverse reactions on full advertisements for products subject to additional monitoring. On reminder advertisements at least the inverted black triangle symbol should be included. For existing promotional materials, the changes should be implemented within 6 months of the publication of this guidance or the next time the material is revised, whichever is sooner.

Queries should be sent to advertising@hpra.ie for the relevant section in the Compliance department.