HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Guide for
Marketing Authorisation Holders on Direct Healthcare Professional Communications

~~1 INTRODUCTION~~

1 ~~A~~ SCOPE

This document provides guidance to marketing authorisation holders (MAHs) on the submission of Direct Healthcare Professional ~~Communication (DHPC) aims~~Communications (DHPCs) and communication plans to the HPRA for national approval and should be read in conjunction with GVP Module XV – Safety Communications (Rev 1).

This guidance applies to DHPCs that are the subject of a regulatory request in order to promote the safe and effective use of a marketed medicine~~. It is delivered directly to~~ and to inform healthcare professionals ~~by marketing authorisation holders (MAHs)~~ of important new safety information and the need to take certain actions or ~~by competent authorities such as the Health Products Regulatory Authority (HPRA). However, a DHPC~~adapt their practices in relation to a medicinal product.

DHPCs should not include any material that might ~~constitute advertising or~~ be considered promotional~~ or~~, commercial~~.~~ or which constitutes advertising.

~~This document provides specific guidance on submitting DHPCs to the HPRA, and should be read in conjunction with GVP Module XV – Safety Communications.~~

~~OBLIGATIONS OF MARKETING AUTHORISATION HOLDERS AND NATIONAL COMPETENT AUTHORITIES~~

~~A marketing authorisation holder must ensure that it has an appropriate system of pharmacovigilance and risk management for marketed medicines and must take appropriate action when necessary.~~

2 LEGAL BASIS

The communication of safety information to patients and healthcare professionals is essential to achieve the objectives of pharmacovigilance. The pharmacovigilance legislation includes a number of provisions to strengthen safety communication and its coordination:

- Directive 2010/84/EU amending Directive 2001/83/EC,
- ~~,~~Regulation (EU) No. 1235/2010 amending Regulation (EC) No. 726/2004, and

- Commission Implementing Regulation (EU) No. 520/2012 on the Performance of Pharmacovigilance Activities Provided for in Regulation (EC) No. 726/2004 and Directive 2001/83/EC~~)~~.

MAHs must ensure that they have an appropriate system of pharmacovigilance and risk management for marketed medicines and must take appropriate action when necessary. GVP Module XV – Safety Communications ~~provides~~ (Rev 1) provides guidance to MAHs on how to communicate and coordinate communication of safety information in the EU~~. Accurate and timely communication of emerging data for risk is integral to pharmacovigilance. DHPCs are an important communication tool that can aid education and risk management for healthcare professionals.~~

~~In~~ as well as guidance on DHPCs. ~~GVP Annex II – Templates~~GVP Annex II – Templates DHPC (Rev 1) provides the ~~event of communication from an MAH to healthcare professionals, the content and timeline for distribution should be agreed with the HPRA (and with other competent authorities as necessary). The supporting risk assessment should be clearly presented and the issues highlighted in the DHPC template (in GVP Module XV) should be fully addressed.~~

~~All draft~~ templates to be used for DHPCs and associated communication plans~~ are referred to the Pharmacovigilance Risk Assessment Committee (PRAC) as indicated in GVP Module XV. PRAC recommendations are~~.

~~provided to the Committee for Medicinal Products for Human Use (CHMP) and the Co-ordination Group for Mutual Recognition and Decentralised Procedures (CMDh), as relevant.~~

~~3 KEY PRINCIPLES FOR COMMUNICATION OF SAFETY INFORMATION~~

3 WHEN TO USE A DHPC

GVP Module XV – Safety Communications (Rev 1) describes the key principles for communication, co-ordination and content of safety communications including DHPCs. ~~These include~~

A DHCP should be disseminated in the following~~:~~ situations when there is a need to take immediate action or change current practice:

- ~~Healthcare professionals should be notified of significant, new or emerging information in a timely manner and the reason for initiating the communication should be detailed;~~

- ~~Information on risks should be presented in the context of the benefits of the medicine and should include appropriate information on the seriousness, severity, risk factors, time to onset and reversibility of adverse reactions. Information on competing risks, such as the risk of non-treatment, should be included where appropriate and possible. Appropriate quantitative measures should be used when describing and comparing risks;~~

- ~~The uncertainties related to a safety concern should be addressed and updated as further evidence becomes available;~~

~~- A DHPC should not usually be distributed before the corresponding regulatory procedure has been completed;~~

~~- The DHPC should include the content of any information communicated directly to the general public;~~

~~If time allows, the text should be reviewed by representatives of the target audience;~~

~~- Agreement is needed between the marketing authorisation holder and competent authorities (and other partners as appropriate) on the content and format of the information with consideration of the supportive evidence, recipients, and distribution timetable.~~

~~3 WHEN TO USE A DHPC~~

~~Situations where the use of a DHPC should be considered as part of the risk-management process include:~~

- Suspension, withdrawal, or revocation of a marketing authorisation with recall of the medicine from the market for safety reasons;

- Important changes to the use of a medicine due to restriction of an indication, a new contraindication or a change in the recommended dose due to safety reasons;

- A restriction in availability or discontinuation of a medicine with potential detrimental effects on patient care.

Other situations where dissemination of a DHPC should be considered as part of the risk management process include:

- New major warnings or precautions for use in the product information;

- A change in the balance of benefits and risks for a medicine (e.g. new data identifying a previously unknown risk or a change in the frequency of a previously known risk; substantiated knowledge that the medicinal product is not as effective as previously considered);

- New recommendations for treating or preventing adverse reactions or to avoid misuse or medication errors with the medicinal product;

- Ongoing assessment of an important potential risk, for which data available at a particular point in time are insufficient to take regulatory action (in this case, the DHPC should encourage close monitoring of the safety concern in clinical practice and encourage reporting, and possibly provide information on how to minimise the potential risk).

4 SUBMISSION OF DHPCS TO THE HPRA FOR NATIONAL APPROVAL

An MAH may be requested to disseminate a DHPC in any situation where it is considered necessary for the continued safe and effective use of a medicinal product.

For centrally authorised medicinal products and for medicinal products subject to an EU procedure, the MAH should first submit the draft DHPC and communication plan to the EMA, which will coordinate the review process by its scientific committees (i.e. PRAC and CHMP) and CMDh.

For medicinal products authorised through the mutual recognition or decentralised procedure, the MAH should first submit the draft DHPC and communication plan to the Reference Member State, which will co-ordinate the process with the MAH, while keeping the concerned Member States involved.

However, all DHPCs requested during a regulatory procedure (e.g. PSUR, signal, referral procedure, etc.) must be submitted to the HPRA, irrespective of route of authorisation, in accordance with timelines agreed during that procedure. Although core messages may already have been agreed, the final content of the DHPC, proposed DHPC recipient groups and the timeline for distribution nationally must be agreed and approved by the HPRA prior to national dissemination by the MAH. A copy of the final agreed version of the DHPC must be submitted to the HPRA on approval.

~~4~~5 COMMUNICATION PLANNING FOR A DHPC

~~The MAH should submit a draft distribution plan to the HPRA that includes: objective, timetable, an up-to-date list of recipients, dissemination method, communication plan, related communications and post-communication strategy.~~
The MAH must also submit the HPRA 'National Submission Form for Direct Health Care Professional Communications and Communication Plans for Marketing Authorisation Holders' form (available on the HPRA website) to the HPRA. Where appropriate, the DHPC recipient groups proposed by the European Medicines Agency (EMA) or Reference Member State (RMS) may be adapted or supplemented to reflect the Irish healthcare system. The MAH should also consider including professional societies and patient organisations in the list of recipient groups, where relevant. The Vigilance Assessment section of the Human Products Monitoring department of the HPRA should also be included on the distribution list (see National Submission Form for contact details).

DHPCs should be disseminated in hard copy; however, additional modalities for dissemination in parallel may also be proposed. As the national communication plan may require amendment following assessment, the national submission form may be updated and the final agreed version of the national communication plan must be submitted to the HPRA on approval.

~~5~~6 JOINT DHPCS

In the event that a DHPC is required for an active substance or for products of the same therapeutic class and two or more MAHs are obliged to distribute the same DHPC, the HPRA

recommends that MAHs collaborate to distribute a single joint DHPC, where appropriate[1]. ~~The HPRA will facilitate the joint submission of DHPCs, where appropriate.~~ In these circumstances, MAHs are encouraged to appoint one MAH to represent all concerned MAHs as the contact point for the HPRA during the assessment process. Such coordination will ensure that healthcare professionals receive one approved DHPC encompassing all of the medicinal products affected by the particular safety concern. The HPRA will facilitate the joint submission of DHPCs, where appropriate. The MAH acting as contact point for the HPRA and on behalf of all other MAHs should be specified in the national submission form and communication plan to facilitate coordination.

~~6~~7 TEMPLATE FOR PREPARING A DHPC AND NATIONAL COMMUNICATION PLAN

~~The DHPC template should be followed and is provided as Annex II to GVP Module XV. In summary, the template shows that the letter should be arranged with the following sections:~~

~~6.0 Heading~~

~~The heading should specify the main message of the DHPC.~~

~~6.0 Summary~~

~~Provide a brief description of safety concern and recommendations for risk minimisation (this section should be in a larger font size compared to the rest of the text and preferably be in bullet points).~~
~~Include a statement indicating that the information is being sent in agreement with the national competent authority or EMA, if applicable.~~

~~6.0 Further information on the safety concern and recommendations~~

~~Include the following details:~~
- ~~Important details about the safety concern (adverse reaction, seriousness, statement on the suspected causal relationship);~~
- ~~Reason for disseminating the DHPC at this point in time;~~
- ~~If needed, details on the recommendations for risk minimisation;~~

~~Placing of the risk in the context of the benefit;~~ For DHPCs, GVP Annex II – Templates: DHPC (Rev 1) (also included in GVP Module XV – Safety Communications (Rev 1)) should be followed. For national communication plans, the HPRA 'National Submission Form for Direct Health Care Professional Communications and Communication Plans for Marketing Authorisation Holders' should be used.

- ~~An~~ ~~estimation of the frequency of the adverse reaction or reporting rates with estimated patient exposure;~~

[1] It is acknowledged that it may not always be possible to collaborate due to differences in formulations or routes of administration, etc., that could impact on the information being provided.

- Statement indicating any association between the adverse reaction and off-label use, if applicable.

11.0 Follow-up actions

A schedule for follow-up action(s) by the MAH or national competent authority should be included, if applicable.

7.5 Further information

Include a link or reference to other available relevant information, such as information on the website of a competent authority.

198 7.6 CALL FOR REPORTING OF SUSPECTED ADVERSE REACTIONS

Include a reminderThe following wording reminding healthcare professionals of the need and mechanism for reporting adverse reactions in accordance with the HPRA national spontaneous reporting system as per the QRD template, Appendix V, Adverse Drug Reaction Reporting Details. Requested wording is as follows:, must be included:

Call for reporting:
Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, website: www.hpra.ie.

7.7 Company contact point

Provide contact point details for access to further information, including relevant website address(es), telephone numbers

9 NATIONAL DHPC IDENTIFIER – 'IMPORTANT MEDICINE SAFETY INFORMATION APPROVED BY THE HPRA'

To facilitate the identification and a postal address.

7.8 Annexes

Include revised product information, detailed scientific information, reference list including literature references, and distinction of DHPCs from other information.

Note that safety communications should deliver relevant, clear, accurate and consistent messages.

Other editorial suggestions include:
- It may be useful to refer at least once to the recommended International Nonproprietary Name (rINN) as well as the medicine's brand name;
- Avoid abbreviations that may be unfamiliar toreceived by healthcare professionals; if they are necessary, spell them out first time and include the abbreviation in brackets after;
- Avoid over-use of bold and italics for emphasis; block italics can be difficult to read;
- , a specific HPRA identifier should be included on all DHPCs submitted for approval to the HPRA. The use of S.I. units;

~~Consider that the audience may be a wide range of healthcare professionals (e.g. range of disciplines and level of specialist knowledge relating to the safety information). The language~~identifier should ~~reflect a potentially diverse audience:~~be included at the top of the first page of the DHPC and should not be modified. The identifier is available to download from the HPRA website in JPG, EPS and PDF formats. ~~at the information may be relevant to professionals wider than those who prescribe or administer a medicine (e.g. consider dispenser/community-facing roles and those who may identify an adverse reaction). link below:~~

~~HPRA.XXXX.jpeg~~

10 PUBLICATION OF APPROVED DHPCs

The HPRA will publish the final approved DHPC on the HPRA website. The timing of publication will be aligned to that of the dissemination of the DHPC nationally.

11 SUBMISSION OF DHPC COMMUNICATIONS AND COMMUNICATION PLANS TO THE HPRA

The following must be submitted as part of a DHPC submission to the Vigilance Assessment section via medvigilance@hpra.ie:

- ~~Core version of~~ DHPC ~~submission form for MAHs, please see the 'Publications~~ and ~~Forms' section of www.hpra.ie~~
- ~~Draft DHPC letter~~
- communication plan as agreed by PRAC/CHMP/CMD(h)/RMS (as applicable)
- ~~List of recipients~~

- Draft DHPC letter for national approval
- Draft communication plan for national approval (HPRA 'National Submission Form for Direct Health Care Professional Communications and Communication Plans for Marketing Authorisation Holders')
- Final DHPC and Final national communication plan on approval

HPRA
~~05 May 2020~~24 January 2022~~<Date>~~