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GUIDELINE FOR HANDLING DEAR HEALTHCARE PROFESSIONAL LETTERS RELATING TO MEDICINE SAFETY

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This document has been prepared to serve as a guideline to those who prepare and distribute Dear Healthcare Professional letters. It represents South African Health Products Regulatory Authority (SAHPRA) current thinking on the safety, quality and efficacy of medicines. SAHPRA reserves the right to request any additional information to establish the safety, quality and efficacy of a medicine and may make amendments in keeping with the knowledge which is current at the time of consideration of safety data.

Document History

Final Version	Reason for Amendment	Effective Date
1	"Process for handling Dear Dr Letters and Drug Alerts" First version published as Circular	30 July 2003
2	Amended to be in new format of guidelines and communications	May 2006
3	Overall editing int al to address timelines 1.2, new 1.4 2.1, 2.2, 2.3, 2.5, 2.6, 2.7, 2.8, 2.10, 2.13 (now 2.11), 2.14 (now 2.12) and 3 deleted	August 2014 September 2014
4	Change of address for electronic copy of the letter	March 2015
5	Revised to include heading, 1, 2, 3, 4, 5, 6, 7 and addition of a reference	January 2020
6	Changed to SAHPRA revised document template Changed document number from 9.08 to SAHPGL-CEM-PV-05-v6 Corrected email for submissions of dear healthcare professionals letter correspondence pvsubmissions@sahpra.org.za	August 2022

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1 INTRODUCTION

This guideline is intended to assist holders of a certificate of registration(holder)/applicants with the development of the dear healthcare professional (DHCP) letter for safety concerns associated with the use of registered medicines and "Old Medicines" which arise during post-registration and post-marketing. It provides recommendations to holders/applicants and SAHPRA personnel on the expected content and format of a DHCP letter. This includes recommendations on when to distribute a DHCP letter, the principles and process relating to issuing of DHCP letters and how to organise the information so that it is communicated effectively to healthcare practitioners.

Communicating safety information to patients and healthcare professionals is a public health responsibility, and is essential to achieve the objectives of pharmacovigilance in terms of promoting the safe and rational use of medicines and preventing harm from adverse reactions. A DHCP letter may be complemented by other communication tools and channels and the principle of consistent information should apply.

For the purpose of this guideline, "SAHPRA" refers to the South African Health Products Regulatory Authority, hereafter referred to as the Authority, and "NADEMC" refers to the National Adverse Drug Event Monitoring Centre. The terms "holder of certificate of registration" (holder) and "applicant" are used interchangeably. The terms "medicine" and "drug" are also used interchangeably.

2 DEFINITION

A Dear Healthcare Professional (DHCP) letter is a communiqué in a form of a letter intended to convey important medicine safety information, distributed by holders/applicants directly to individual healthcare professionals. The DHCP letter further advises healthcare professionals on the need to take certain action or adapt their practices in relation to the use of the implicated medicine. Such letters can be requested by SAHPRA or initiated by the holder/applicant. Regardless of the initiator of the DHCPL, the letters should always be approved by SAHPRA before distribution to healthcare professionals.

3 LIST OF ABBREVIATIONS

ADRs	Adverse Drug Reactions
DHCP	Dear Health Care Professional
HCP	HealthCare Professional
HCR [HOLDER]	Holder of a Certificate of Registration
PI	Professional Information
PIL	Patient Information Leaflet
USRN	Urgent Safety Restriction Notice
SAHPRA	South African Health Products Regulatory Authority

4 PRINCIPLES

4.1 Communication of safety is considered part of risk assessment and management process throughout the life cycle of a medicine.

4.2 Communicating safety information through DHCP letter should be effectively and adequately coordinated between the holder/applicant and SAHPRA.

4.3 DHCP letters should deliver relevant, clear, concise, accurate and consistent messages and reach the right healthcare professionals at the right time.

4.4 DHCP letter should be tailored to the appropriate healthcare professionals using appropriate terminology and taking into account different levels of knowledge and needs.

4.5 The targeted DHCP letter recipients must be agreed upon by both the holder/applicant and the Authority before an approved DCHP letter can be issued.

4.6 In cases where Allied Health Professionals are to be informed about a safety concern that is related to their profession, SAHPRA should prescribe the Allied Health Professionals to be included in the distribution list.

4.7 The information on risk 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 the adverse reaction.

4.8 New information should be summarised, highlighted and presented using the language used in the proposed updated Professional Information, as appropriate.

4.9 DHCP letters should provide recommendations on how to deal with any safety concerns with regards to a medicine.

4.10 The DHCP letter should include the appropriate contact information (contact details for reporting cases of ADRs) of both the applicant and the Authority and the procedure for reporting suspected ADRs.

4.11 DHCP letter should avoid discussion of noncritical information that could obscure the important information.

4.12 The following information should be avoided as it could obscure or divert attention from the important safety information:

- Marketing information about the medicine including numbers of prescription, patient exposures, approvals and pending approvals,
- Extensive details about the design of a clinical study,
- Information about a safety review panel,
- Plans to further investigate the problem (if not specifically related to the problem) and
- Promotional language/material.

4.13 In a situation where the reason to distribute a DHCP letter is in line with the requirements of an Urgent Safety Restriction Notice (USRN), the USRN procedure as outlined in Guideline 2.08 Variations Addendum for Human and Veterinary Medicines must be followed.

4.14 DHCP letter content should not be longer than five (5) pages.

4.15 DHCP letter should be finalised and approved by SAHPRA within twenty (20) working days of the initial communication from or to the holder/applicant.

4.16 DHCP letter must be distributed to healthcare professionals and published on the applicant's website within five (5) working days subsequent to the Authority communicating the approved letter to the holder/applicant. No safety related DHCP letter should be distributed to HCPs without the Authority's approval.

4.17 The DHCP letter which contains safety information, should be emailed to the relevant HCPs as agreed upon by the Applicant and the Authority.

4.18 In the instance where a PI/PIL updated is necessitated by a DHCP letter, the Authority and the Applicant will agree upon the wording of the label update and this will be indicated in the DHCP letter.

5 PURPOSE

SAHPRA may request the holders/applicants to distribute a DHCP letter in any situation where it is deemed necessary, relevant to the safe and effective use of the medicine. However, holders/applicants may also initiate a DHCP letter. A DHCP letter should be issued in the following situations:

- A change in the risk-benefit balance of a medicine (for example, new data identifying a previously unknown risk or a change in the frequency or severity or a known risk),
- New recommendations for treating or preventing ADRs,
- Important change to the product information, in particular restriction of an indication, new contraindication, change in the recommended dose, major warnings or precautions for use.
- Restriction in availability and accessibility which impact on the medicine's current use by healthcare professionals and patients.
- Suspension, withdrawal or revocation of a marketing authorisation with recall of the medicinal product from the market for safety reasons;
- 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 DHCP letter 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).

6 PROCESS

6.1 The holder/applicant should notify the Authority within five (5) working days of the receipt of the safety concern from other Regulatory Authorities as per. Alternatively, the holder/applicant should respond to the Authority's recommendation to issue a DHCP letter by submitting a draft DHCP letter within five (5) working days of the date of the recommendation letter to the Authority for review.

6.2 The format of the draft DHCP letter should be aligned with the Authority's guideline for handling DHCP letters.

6.3 The holder/applicant should submit to the Authority a draft of the proposed DHCP letter (in a word format), motivation (where relevant), most recently approved Professional Information and the supporting data of the safety information.

6.4 In cases where the process is initiated by the applicant, and the consequence of the new information requires an amendment to the PI/PIL, the applicant must include the proposed PI/PIL in which the proposed changes are indicated at the same time as the proposed DHCP letter. In cases where the process is initiated by the Authority, the amended PI/PIL should only be submitted to the relevant unit once the exact wording for the amendment is provided by the Authority.

6.5 Correspondences between the Authority and the holder/applicant relating to changes in DHCP letter text or corrections should be actioned in a timely manner, within three (3) working days of receipt by the holder/applicant.

6.6 Only three (3) correspondences are permitted between the applicant and the Authority per letter. Should the applicant not be in agreement with the amendments made by the Authority, the matter would be referred to the CEO for decision-making.

6.7 The DHCP letter should only be distributed once the final letter is approved by the Authority.

6.8 The holder/applicant should submit to the Authority a copy of the final DHCP letter signed by the relevant signatory before distribution.

6.9 The Authority should endorse the letter by signing it. Once the letter is signed by the Authority, the applicant can distribute the letter to the target audience with both the Authority and the applicant's signatures.

6.10 An emailed distribution list indicating the number of HCPs who were emailed should be submitted to the Authority within fourteen (14) working days after communication of the approved DHCP letter by the Authority to the applicant.

6.11 NOTE: For safety concerns relating to active substances contained in medicines authorised for more than one (1) holder, (i.e. not necessarily on a specific trade name), a collaborated DHCP letter should be considered.

6.12 A lead holder/applicant should be identified, who will be responsible for coordinating the process of reviewing the collaborated DHCP letter between the Authority and the holders/applicants concerned.

6.13 All communication between the Authority and the holders/applicants relating to the collaborated DHCP letter should be done through the lead holder/applicant, who must then communicate to the other holders/applicants concerned.

6.14 The lead holder/applicant must consolidate all comments from other holders/applicants relating to the DHCP letter and convey them to the Authority.

6.15 A collaborated DHCP letter should follow the same process as an uncollaborated DHCP letter.

7 FORMAT OF DHCP LETTERS

7.1 Contents of a DHCPL

7.1.1 The heading of the letter must read as "Important medicines safety information"

7.1.2 The date of the final approved proposed DHCPL.

7.1.3 Greeting statement (e.g. Dear Healthcare Professional)

7.1.4 The subject line of the letter should be written in bold (underlined or not) or within a border or text box to further draw attention to the information and should include:

a) name of the medicine (international non-proprietary, followed by the trade name), registration number and a concise description of the issue that is addressed in the body of the letter.

b) characterisation of the seriousness of the problem (that is, serious, life-threatening, fatal adverse reactions) and the population at risk. Note: use of vague terms to characterise the incidence of reaction should be avoided, e.g. rare, infrequent.

c) statement regarding a well-defined increase in the magnitude of risk or rate of reaction and rate observed in controlled trials or epidemiological studies can be used, e.g. the rate of reaction X is doubled.

7.1.5 The initial paragraph of the letter should be introductory and may include the following type of information:

a) Purpose of the letter e.g. to inform healthcare professionals about a specific medicine safety issue.
b) A statement on the agreement between the holder/applicant and SAHPRA on the safety information.
c) Description of the safety concern
d) Existing information that has changed, if any e.g. information that is no longer valid in light of the new safety information.

7.1.6 The second paragraph of the letter should briefly summarise the information essential to a healthcare professionals' understanding the nature and management of the problem and actions taken to address the issue. This paragraph may include the following type of information:

a) Description of the safety information,
b) Whether the risk occurred with approved use of the medicine or not,
c) Population at risk,
d) Labelling changes using verbatim language from the prescribing information may be included (summarised) and
e) Rationale for change in indication, usage or dose, if relevant.

7.1.7 The interior paragraphs of the letter should provide background of the medicine(s) and the safety concern and any other additional details that may be helpful in understanding the issue. The information may include the following:

a) Brief description of the indications and usage,
b) Concise description of the issue that gave rise to the new warning or other change in the prescribing information, including the nature and severity of the issue.
c) Degree of risk, if known. Reliable incidence and/or prevalence data from a controlled trial, observational study, or any other reliable source, can be included if available. If the new information is based on spontaneous reports, the number of reports must be included if that number is an important factor in explaining why a regulatory action is taken to revise the prescribing information and alert the healthcare professionals.
d) Attributes of affected patient populations or subsets.
e) Summary of the data or other information that is the basis for a new safety warning (e.g. summary information about a controlled clinical trial, epidemiologic study, or spontaneous adverse event reporting).
f) Limitations of the data and other information (e.g. what is known and what is not known).
g) Mechanism of the adverse reaction if known.
h) Whether the event is common to the medicine class or not.
i) Additional research undertaken to better understand the adverse reaction.

7.1.8 The last paragraphs of the letter should provide advice to healthcare professionals with regards to actions to be taken in response to the new safety issue, if any (management), such as:

a) Recommended action, including but not limited to:
    - Discontinued use,
    - Limitations of use,
    - Dose reduction,

- Patient monitoring for specific clinical findings or laboratory results and
- Additional testing required before prescribing.

b) Patient counselling, including but not limited to:

- Contacting their healthcare professional if they experience a specific clinical sign or symptom,
- Stopping the medicine immediately if they experience a specific clinical sign or symptom or
- Consulting their healthcare professional before discontinuing the medicine.

c) The DHCP letter should include a statement that the Professional Information is in the process of being reviewed to reflect the relevant information, if applicable.

7.1.9 Concluding paragraph should include the following information:

a) Information on how to report new cases of the adverse reaction or other safety issues described in the letter,

b) A list of holder/applicant-specific medicines containing the active ingredient (Trade names) should be provided together with each medicine's registration number and contact information for direct inquiries regarding the safety issue and

c) Contact information of the Authority.

7.2 References where applicable

7.3 Signature(s) of the relevant holder/applicant's personnel

NB: All correspondences between the Authority and the holder/applicant pertaining to DHCP letter must be done through an email (pvsubmissions@sahpra.org.za). The DHCP letter must be distributed to the target groups mainly by email. Post may be used as a supplementary method.

8 REFERENCES

8.1 U.S. Department of Health and Human Services - Food and Drug Administration, 2014. Guidance for Industry and FDA staff: Dear Healthcare Provider Letters: Improving Communication of Important Safety Information. OMB Control No. 0910-075.

8.2 EMA Guideline on Good Pharmacovigilance Practices (GVP) – Module XV – Safety Communication EMA/118465/2012.

9 VALIDITY

This guideline is valid for a period of 5 years from the effective date of revision and replaces. It will be reviewed as and when required.