MEDICINES CONTROL COUNCIL

DEPARTMENT OF HEALTH
Republic of South Africa

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PACKAGE INSERT AMENDMENTS CONCERNING URGENT SAFETY RESTRICTIONS: URGENT SAFETY RESTRICTION NOTICE (USRN)

This guideline is intended to provide recommendations to applicants wishing to submit safety amendments to package inserts. It is not intended as an exclusive approach. Council reserves the right to request any additional information to establish the safety, quality and efficacy of a medicine in keeping with the knowledge current at the time of evaluation. Alternative approaches may be used but these should be scientifically and technically justified. The MCC is committed to ensure that all registered medicines will be of the required quality, safety and efficacy. It is important that applicants adhere to the administrative requirements to avoid delays in the processing and evaluation of applications.

Guidelines and application forms are available from the office of the Registrar of Medicines and the website.

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REGISTRAR OF MEDICINES
MS M HELA

An Urgent Safety Restriction Notice (USRN) is a notice from the applicant to the MCC of an amendment to the content of the package insert for a medicinal product by the applicant or holder of a certificate of registration for a medicine of new information which has a bearing on the safe use of the medicinal product.

1 CHANGES ALLOWED AS AN URGENT SAFETY RESTRICTION NOTICE (USRN)

The following amendments relating to safety without review by MCC will be allowed as an Urgent Safety Restriction Notification USRN:

(i) An USRN may only be used for an amendment which has a more restrictive effect on the use of the medicine than has previously been approved, such as:

- Deletion of an indication.
- Reducing the patient population in which it may be used.
- Adding a contraindication, warning, precaution, interaction or adverse reaction.
- Adding an instruction about dosage and administration that is intended to increase the safe use of the product.

(ii) Changes not allowed include

- additional headings.
- changes which in any way may relax the way in which the medicine is used.
- any wording or information to further qualify ("soften") or elaborate on the new safety-related information, such as "unknown clinical significance", "only occurs at higher dose", "occurs rarely", etc.
- comparative statements.
- class statements, e.g. "as with other beta-blockers."
- additional information on lack of interaction with other substances.
- additional information on treatment of overdose.

(iii) All other safety-related amendments will be subjected to the current process in place, whereby submissions will be reviewed in turn as received.

2 PROCESS FOR AN URGENT SAFETY RESTRICTION NOTICE (USRN)

(i) The applicant submits an Urgent Safety Restriction Notice (USRN), together with the required fee[1].

(ii) Clearly mark an USRN "**URGENT SAFETY RESTRICTION NOTICE**".

(iii) Include hard copies and electronic versions of the following with a submission for a USRN:

- all data in support of the amendment
- justification for being an USRN
- a currently approved package insert
- a package insert with the proposed amendments, as required for any other submission.
- any decision taken or any change made by other regulatory authorities, such as the FDA or EMEA
- a draft Dear Health Care Professional (DHCP)-letter
- a comment on how the amendment will affect the benefit-risk ratio of the use of the medicine.

Such an application for an USRN does not replace any other requirements regarding submissions.

[1] The current fee for a package insert amendment

2 Process for an urgent safety restriction notice (USRN) - continued

(iv) A USRN must address a specific issue and may not include other amendments to the package insert.

(v) After identification of the submission as an USRN, the secretariat shall acknowledge receipt of the USRN. Unless the applicant receives a written objection by fax or e-mail from the secretariat within 30 days of receipt of the submission for an USRN, the applicant shall commence implementation of the urgent safety amendment to the package insert.

(vi) The secretariat shall immediately present the draft DHCP-letter to the DHCP letter review group and the DHCP letter review group shall within a time period of no longer than 30 days (includes interaction with the applicant) of receipt give a response to the secretariat. (See process for Dear Health Care Professional letter)

(vii) The DHCP-letter shall then be distributed by the applicant to the relevant health care professionals within a further 10 - 14 days.

(viii) The printed amended package insert must be made available in the packaging within 90-120 days of commencement of the implementation of the urgent safety amendment.

(ix) The applicant to note that the USRN submission will be processed on the basis of the signed declaration by the authorised person of the applicant that the safety amendment(s) are in line with the requirements of the USRN guideline and that the electronic version is identical to the hard copies submitted.

(x) The MCC may evaluate any information immediately or at a later stage and require further amendments.

(xi) The applicant shall in writing inform MCC whenever an USRN has been implemented and submit a copy of the amended package insert.

(xii) The Clinical Committee will report all USRNs submitted by applicants to Council for noting and comment.

(xiii) If an applicant is found to have implemented an urgent safety amendment to a package insert without complying with the process, the applicant will be required to resubmit full documentation with repayment of the required fee.

3 CHANGES TO PATIENT INFORMATION LEAFLET

The amendment made to the package insert in terms of the USRN shall also apply to the Patient Information Leaflet (PIL) and should be incorporated into the PIL simultaneously.