MEDICINES CONTROL COUNCIL

DEPARTMENT OF HEALTH
Republic of South Africa

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SAFETY-RELATED PACKAGE INSERT NOTIFICATIONS (SR-PINs)

This guideline is intended to provide information to applicants wishing to submit applications regarding safety and safety-related amendments to the package insert of a registered medicine by notification process. It represents the Medicines Control Council's current thinking on the safety, quality and efficacy of medicines. 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. 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.

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Version 2	March 2014
Implementation	With immediate effect
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1 Introduction

The package insert for a medicine is a legal document which must be approved by the Medicines Control Council (MCC). The purpose of this guideline is to provide a process whereby safety and safety-related amendments to package inserts can be implemented by a notification process. This process is referred to as Safety- Related Package Insert Notifications (SR-PINs).

2 SR-PIN Application Requirements

2.1 All proposed SR-PIN applications must be submitted as proposed package insert amendments, and include all source/reference documentation to substantiate/support the proposed safety or safety related amendment(s). Documentation must include an assessment report as to why the proposed safety information amendment(s) to the package insert will not change the already known benefit-risk profile of the medicine. All proposed SR-PINs submitted should contain a cover letter which lists all the proposed safety related amendment(s) to the package insert as well as a declaration, signed by both the Chief Executive Officer (CEO) and the Responsible Pharmacist, or on their behalf by their deputies, that the application/submission is compliant with the requirements of the SR-PIN guideline. The code for a SR-PIN application/submission is "CCC-SRN"

2.3 Any SR-PIN amendment(s) to a package insert must simultaneously be applied to the patient information leaflet of that medicine as well as to the package insert and patient information leaflet for a similar medicine, registered, but currently not marketed by the applicant.

2.3 If the application (submission) does not comply with the requirements of the SR-PIN guideline, it will be rejected as a SR-PIN application by the MCC within 60 working days of receipt at the MCC, which is regarded as the date on the date stamp which serves as proof of delivery of the SR-PIN application, coded as CCC-SRN. If there is no rejection response from MCC after 60 working days of the date, serving as proof of delivery of the SR-PIN application / submission, it can be regarded that the SR-PIN application / submission has been approved / accepted by MCC.

2.4 Safety related package insert amendments approved by the SR-PIN process, must be implemented, and the amended package insert/patient information leaflet included in medicine packages as soon as possible, but not later than 120 working days following the approval/acceptance thereof by MCC. The holder of the certificate of registration (applicant) should inform the MCC of the date of inclusion of the amended package insert/patient information leaflet in medicine packages, and provide the MCC with a copy of the SR-PIN amended package insert and patient information leaflet.

2.5 An applicant must submit an annual report to the MCC by 31 March of each year, listing, in a dated and chronological order, all SR-PIN applications approved or rejected by MCC.

3 Sources/References that can be used to support and/or substantiate a SR-PIN application

3.1 Clinical studies;

3.2 Most recently updated MCC approved innovator package insert, and if medicine is no longer marketed, the most recently updated MCC approved interchangeable multisource medicine package insert;

3.3 Most recently updated package insert(s) of medicine which has been approved by a Regulatory authority with which MCC aligns itself. The data/information which prompted the updating of the relevant section(s) of the package insert should also be submitted;

3.4 Most recently updated Company Core Data Sheet (CCDS). The data/information which prompted the updating of the relevant section(s) in the CCDS should also be submitted;

3.5 Expert reports with data/information relevant to the section(s) to be amended in the package insert;

3.6 Relevant published scientific literature;

3.7 Relevant excerpts from most recent editions of internationally available textbooks e.g. USPDI, Martindale (for safety issues) and Goodman & Gilman (pharmacology); and

3.8 Relevant acts and/or regulations, guidelines/guidance documents published by the MCC or relevant guidelines/standards published by relevant competent bodies.

4 Amendments that do not qualify for the SR-PIN process

4.1 Inclusion of any statement/information other than or in addition to, what is allowed by the SR-PIN guideline.

4.2 Addition of a new indication or a change to an approved indication.

4.3 Changes to the dosage and directions for use.

4.4 Changes to the composition/formulation

4.5 Any safety or safety related amendment to an approved package insert which changes the clinical benefit-risk profile for the use of the medicine, or softens any safety or safety related information already in the package insert or removal of safety or safety related information from the package insert.

4.6 Any safety or safety related issues, that have given rise to significant correspondence/interaction between the applicant and Regulatory Authorities with which the MCC aligns itself, Dear Healthcare Professional (DHCP) letters, public health advisories, press releases or similar safety alerts, or other significant communications to the public or health care professionals in any other countries.

5 Update History

Date	Reason for update	Version & publication
2008	Published for comment	October 2008
July 2012	Released for piloting	v1, November 2012
March 2014	Guideline name changed. Amendment to sections 1, 2.6, 3.2, 3.3 Addition of new 2.10, 4.6	v2
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September 2016	Version 3 published for comment Amendment to sections 1, 2.1, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 4, 4.2, 4.4, 4.5, 4.6, 4.12 Deletion of sections 3.3, 3.4, 3.5, 4.5, 4.6, 4.7, 4.8, 4.9, 4.10, 4.11	v3, November 2016
05 December 2016	Due date for comment	
June 2017	Version 3 finalised Amendment to sections: Purpose of the guideline, 1, 2, 2.1, 2.3, 2.6, 2.8, 4, 4.1, 4.5, 4.6 Deletion of sections: 2.2, 2.4, 2.5, 2.7, 2.9, 2.10, 3, 3.1, 3.2, 3.3, 4.3 Addition of new section 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 4.1	v3, August 2017
August 2017	Implementation	