South African Health Products
Regulatory Authority
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MAY 2022

SAHPGL-CEM-NS-01: APPLICATION FOR RESCHEDULING OF A SUBSTANCE OR MEDICINE

This document is intended to provide guidance to applicants on the scheduling of substances submitted for registration as medicines. It represents the South African Health Products Regulatory Authority's current thinking on the safety, quality and efficacy of medicines and takes into account the country's obligations in terms of international agreements. It is not intended as an exclusive approach. The Authority reserves the right to request any additional information to establish the scheduling status 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. It is important that applicants adhere to the administrative requirements to avoid delays in the processing and evaluation of applications.

Document History

First document drafted	01 March 2022
Alignment with SAHPRA template and formatted	30 March 2022
Date for implementation	30 May 2022

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CHIEF EXECUTIVE OFFICER

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1. INTRODUCTION

1.2 General information

1.2.1. The application form is to be used for applications regarding rescheduling of a substance or medicine in line with the SAHPGL-CEM-NS-02_v3_Guideline on the Scheduling of Substances and Medicines.

1.2.2. Application can be submitted by applicants who wish to change the schedule status of a registered medicine or applications for rescheduling can be made independent of a registered medicine by any persons or associations.

1.2.3. The same principles as outlined in the SAHPGL-CEM-NS-02_v3_Guideline on the Scheduling of Substances and Medicines would be applied in considering an application for rescheduling. Therefore, to justify a rescheduling from Schedule 3 or 4 to Schedule 2 or 1, evidence would need to be provided to justify use without a prescription. If any of the following criteria were met, prescription status would need to be maintained:

- The substance is likely to present a direct or indirect danger to human health, even when used correctly, if used without supervision by a medical practitioner or dentist;
- The substance is frequently and to a very wide extent used incorrectly or inappropriately, and as a result is likely to present a direct or indirect danger to human health;
- The safety and efficacy of the substance has not yet been adequately described and requires further investigation.

1.2.4. Likewise, in order to justify a Schedule 0 status, evidence would need to be provided that show that the hazard to health, the risk of misuse and the need for special precautions in handling are small, and that wider sale would be a convenience to the consumer.

1.2.5. A product is normally assigned the highest scheduling status appropriate to any one of the registered indications of the product. If application is made to reschedule only selected indications of a specific product to a lower Schedule, a unique name and a separate registration dossier will also be required for such a product. It must be noted that dual scheduling on printed packaging is not permitted. Only products with indications, strengths, routes of administration and/or pack sizes applicable to the lower schedule will qualify for the lower scheduling status.

2. SUBMITTING AN APPLICATION FORM:

2.1 A rescheduling application form (Annexure A) must be submitted to SAHPRA. The completed submission must also include the following documentation and supporting evidence:

a. Copies of referenced material
b. Proof of Payment
c. Professional information/ Patient information leaflets, where relevant

2.2 Applications for the rescheduling of substances or medicines must be submitted via the File Transfer Protocol (FTP).

2.3 Applicants are requested to adhere to the below file naming convention. This will assist SAHPRA to route the application to the relevant technical unit. The applicant is to ensure that the file is correctly named. Incorrectly named files may lead to a delay in the evaluation of the application.

FTP file naming convention	Example
Application number-BAU(V-n&s)-RSCH-Sequence	50000-BAU(V-n&s)-RSCH-Sequence

2.4 The applicant to ensure that all relevant fields are completed and all supporting documentation is attached. Incomplete applications will be identified as deficient and review will not be progressed until deficiencies are addressed.
The prescribed application fee and proof of payment must accompany the application. For the current fee payable, refer to the latest fee schedule as published in the Government Gazette and published on the SAHPRA website.

2.5 Payments should be made as per 17.05 "Guideline on the payment of fees to SAHPRA", accessible here: https://www.sahpra.org.za/wp-content/uploads/2021/01/SAHPRA-Payment-Guideline-Nov-2020.pdf

3. TIMELINES FOR PROCESSING OF RESCHEDULING APPLICATIONS

3.1 Applications will be processed within 120 working days of receipt thereof.

3.2 A query letter will be sent to the applicant in the event that an application does not meet the evaluation criteria. The deficiencies identified within the application will be documented in the query letter.

3.3 The applicant is required to respond to the deficiencies noted in the query letter **within ten working days.**
NOTE: Only two cycles will be permitted, i.e. the applicant will have two opportunities to address deficiencies identified in the application by submitting a response to SAHPRA within the defined timelines.

3.4 If the response/s (limited to a maximum of two cycles) from the applicant does not adequately address the deficiencies identified in the application, the application will not be recommended and the application will be forfeited.

Amendment History

Version	Date	Reason for amendment
V1	May 2022	New draft for application for rescheduling of a substance and medicine.

APPENDIX A:

APPLICATION FORM FOR RESCHEDULING OF A SUBSTANCE OR MEDICINE

This application form includes text in { }. Such text is for guidance only and should be deleted when preparing a submission.

PART 1: COVER PAGE

{The cover / title page should indicate:

i. The subject of the application.
ii. The name and address of the applicant.
iii. The name of a contact person.
iv. The date on which the application was submitted.}

PART 2: TABLE OF CONTENTS

{The table of contents should tabulate and correlate the titles of each section and major subsections of the application with their appropriate page numbers.}

8.4.2 Pharmacology

8.4.3 Clinical Data

8.4.4 Toxicology

8.4.5 Safety Reports

8.4.6 Occupational Health and Safety Information (If applicable)

8.4.7 Pharmaceutical Aspects

8.4.8 Monitoring of the Public Health Impact

8.4.9 Education

8.5 Proposal

8.6 Discussion

8.7 Proposed Indication for Use

8.8 Product Information and Presentation

9 Other Relevant Information

10 Supporting data

11 Bibliography

12 Appendices if required

PART 3: GENERAL INFORMATION	
Applicant	
Name: (Registered Applicant/ Association/ Person)	
Address:	
Contact person/ Responsible Pharmacist (where relevant):	
Telephone no.:	
Cell no.:	
E-mail address:	
Date of application:	

PART 4: *SUBSTANCE/ MEDICINE INFORMATION*	
Registration Number of Medicine (where relevant)	
Proprietary Name of Medicine (where relevant)	
International Non-proprietary name(s) / Active Ingredient(s)	
Pharmaceutical Dosage Form (where relevant)	
Route of Administration	
Therapeutic Indication(s)	
Current Schedule Status	
Proposed Schedule Status	

PART 5: DECLARATION	
Applicants should note that in terms of the provisions of the Medicines and Related Substances Act 101, 1965 (Act 101 of 1965), it is an offence to make false and misleading statements I declare that all information contained in this application form, and in the documents attached, is true and correct at the date of signing.	
Signature of Responsible Person	
Name	
Date	

PART 6: CHECKLIST -*Documents Submitted with Application*		
Application form in the format requested completed	☐Yes	☐No
Professional Information / Patient Information Leaflet, where relevant	☐Yes	☐No
Classification of the product in other jurisdictions recognised by SAHPRA	☐Yes	☐No
Proof of Payment	☐Yes	☐No
Signed declaration	☐Yes	☐No
Checklist completed	☐Yes	☐No

PART 7: SUMMARY OF THE APPLICATION

{The summary should contain a concise, clear statement of -

i. The purpose of the application, including any proposed change involved as well as the reason for the proposed change in scheduling status.
ii. The major points in the argument, including –
    a. The proposals arising from such argument.
    b. An overall summary of the toxicology, clinical data, post-marketing studies and pharmacoepidemiology of the compound.

The arguments must address the criteria listed in the guidelines for the categorisation of medicines or substances in the schedules.

Normally, this summary will not extend beyond a few pages. Tables are favoured as a means of condensing information. Studies reported in the summary should be cross-referenced to the reports in the main submission.}

PART 8: BODY OF THE APPLICATION

{The body of the application should communicate the aims and justification of the proposal in a concise, clear and logical manner. Appropriate data and information must be supplied to demonstrate that the substance or product will be safe for the public when supplied and used in the proposed manner. Whilst the format of each application may vary the Committee recommends the use of a standard framework consisting of the following:}

8.1 Purpose of the Application

8.2 General Background

8.2.1 Current Regulatory Status

{Reference should be made to the current local regulatory status of the product or substance in terms of dosage forms registered, scheduling status and approved indications. If applicable, the registration number must be indicated}.

8.2.2 International Regulatory Status

{Classification / scheduling status in other countries where the product is registered, including information of the approved indications and dosage forms. The availability status should be clearly indicated in terms of e.g. prescription only, pharmacy only, general sales outlets. For regulatory authorities with which the SAHPRA aligns itself, refer to the General Information guideline.}

8.3 Introduction of the data upon which the application is based

8.4 Technical Information

{Additional information on the active pharmaceutical ingredient that was not submitted during the registration of the original product is required. Data that were submitted during the registration process may be summarised.}

8.4.1 Physico-Chemical Properties of the Active Pharmaceutical Ingredient

i. Structural formula or any available information on the structure of the substance.
ii. All relevant chemical and physical properties.

8.4.2 Pharmacology

i. Any known information relating to the structural and pharmacological relationship to other drugs or chemicals
ii. The pharmacodynamic and pharmacokinetic profile
iii. Interactions, incompatibilities, side effects or adverse reactions
iv. Any recognised standard such as a pharmacopoeia monograph.

8.4.3 Clinical Data

i. Post-marketing reports
ii. Additional clinical reports
iii. Adverse drug reaction reports
iv. Epidemiology reports
v. Poisoning reports

8.4.4 Toxicology

i. Summary of the known toxicology of the product.
ii. Summary of the known metabolism of the product.
iii. Relevant details of any published or unpublished toxicological investigations of the product / substance

8.4.5 Safety Reports

i. A summary of animal studies that confirm low general toxicity and no relevant reproductive toxicity, genotoxic, or carcinogenic properties relevant to the experience / exposure of the product.
ii. Information from post-marketing surveillance studies, clinical trials and published literature presenting the issue of drug safety. For OTCs: experience of patient exposure, including data from at least 2 years of use in the relevant or similar population.
iii. Information on adverse drug reactions. In the case of OTC medication, the information should include experience without medical supervision in other countries. Variables such as number of patients treated, demographic details, indications for use and dose should be provided and taken into account in providing and interpreting the data;
iv. Drug interactions with food or commonly prescribed drugs.
v. Consideration of the consequences concerning misuse.

8.4.6 Occupational Health and Safety Information (If applicable)

{A summary of occupational health and safety aspects.}

8.4.7 Pharmaceutical Aspects

{Any intended change in formulation, pack size, packaging, etc should be indicated. However, pharmaceutical data such as stability need not be included. This data must be evaluated as part of a registration application or amendment to the registration application.}

8.4.8 Monitoring of the Public Health Impact

{If evaluation of the public health impact is required, proposals on how this will be managed should be given.}

8.4.9 Education

{If any specific education of professionals, distributors or users are required, details of a process to manage this is required.}

8.5 Proposal

{Indicate proposed schedule}.

8.6 Discussion

{Safety issues must be justified in relation to the schedule for which the application is made. For example: A motivation for rescheduling from Schedule 5 to Schedule 4 will focus on the absence of abuse potential.}

8.7 Proposed Indication for Use

{New indications are evaluated by the Clinical Committee as part of a registration application or an amendment to the registration application after registration. Only thereafter will the possibility of rescheduling be discussed.}

8.8 Product Information and Presentation:

Presentation of the product:

i. Dosage form, strength and pack size
ii. Type of packaging
iii. Label warning or other information that can impact on safety
iv. Proposed professional information
v. Patient information leaflet

PART 9: OTHER RELEVANT INFORMATION

PART 10: SUPPORTING DATA

{An overview summary of the type and details of supporting data included with your application. This is separate from the full bibliography below.
If not contained in the bulk of the documentation, any additional data should be included as addenda to the relevant part, together with additional expert comment that may be provided as a supplement to, or incorporated into, the overall summary.

Where a clinical expert report is submitted, the expert is expected to make an objective and impartial assessment of the application in the light of current scientific knowledge. The expert is required to sign a declaration indicating any competing interests or conflict of interests in providing this report. This declaration is also to include a statement regarding the relationship of the expert to the applicant.}

Where a paper or article is cited in your submission an electronic copy should be included. It is noted that such references are often in PDF format and can comprise a large section of an application.}

PART 11: BIBLIOGRAPHY

PART 12: APPENDICES IF REQUIRED