Australian Government
Department of Health
Therapeutic Goods Administration

Proposed minor changes to Required Advisory Statements for Medicine Labels (RASML): Chlorhexidine, hydrocortisone, ibuprofen

Consultation paper

Version 1.0, July 2021

TGA Health Safety Regulation

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Introduction

Purpose

The Therapeutic Goods Administration (TGA) is seeking comments from interested parties on proposed minor changes to advisory statement requirements for labels of over the counter (OTC) medicines containing chlorhexidine, hydrocortisone or ibuprofen, for inclusion in the Required Advisory Statements for Medicine Labels (RASML). The proposed changes involve minor changes to existing RASML entries to correct or clarify intended requirements and in most cases should not require changes to existing product labels.

Background

Advisory statements

Consumers rely on information from their health practitioner, pharmacist and medicine label in order to use medicines safely and effectively. However, the enhanced access and availability of OTC medicines means that consumers may not always receive comprehensive advice from a practitioner or pharmacist.

In the context of self-medication, the medicine label is the primary source of information for the consumer; so the label must contain the directions and advisory statements that are needed for safe and effective use of these medicines.

The TGA Labelling Orders require medicine labels to include 'warning statements' where these apply to the medicines, including any advisory statements specified in the instrument made under subsection 3(5A) of the *Therapeutic Goods Act 1989* ('the Act'), as in force from time to time.

The Required Advisory Statements for Medicine Labels (RASML)

The RASML is registered on the Federal Register of Legislative Instruments under subsection 3(5A) of the Act, as the Therapeutic Goods (Medicines Advisory Statements) Specification 2019 ('the Specification'). The RASML sets out advisory statements that are required to be included on the labels of specified OTC and registered complementary medicines.

The most recent version of the Specification is the Therapeutic Goods (Medicines Advisory Statements) Specification 2019, which comprises RASML No. 5. The transition period for compliance with RASML No. 5 ended on 31 August 2020 and labels must now comply with the advisory statements specified in RASML No. 5.

Finalised advisory statements for melatonin would be included in the next version, RASML No. 6. A transition period of 18 months from commencement of the new RASML is provided to allow for existing medicines that do not already comply with new requirements to have their labelling updated.

The advisory statements required by the RASML are designed to inform consumers about specific risks related to the use of medicines that have been identified during development and evaluation of new medicines, or subsequent pharmacovigilance activities, testing, adverse event reports or from other scientific or clinical information.

The RASML permits the wording of the actual statements that are included on medicine labels to differ from the wording set out in the RASML, as long as the intent is the same.

Proposed changes to RASML entries for chlorhexidine

The current RASML entries for chlorhexidine are as follows:

Column 1 Substance(s)	Column 2 Conditions	Column 3 Required statement(s)
Chlorhexidine *(Entry 1 of 2)*	In topical products, including preparations for topical use on mucosal surfaces.	• Avoid contact with eyes. • If in eyes, rinse well with water. • WARNING – This product contains chlorhexidine. Severe allergic reactions can occur. Stop use if this occurs.
Chlorhexidine *(Entry 2 of 2)*	In topical products OTHER THAN preparations for topical use on mucosal surfaces.	• Avoid contact with eyes. • If in eyes, rinse well with water. • Mild irritation may occur; stop use if it becomes severe.

The above entries are confusing and ambiguous as to whether a warning regarding "severe allergic reactions" is required for dermal-only products and whether a mild irritation warning is required for products used both mucosally and dermally. Dermally-applied chlorhexidine may cause skin irritation, an issue not appropriately covered by the current "severe allergic reactions" warning. However, the allergic reaction and mild irritation warnings are somewhat conflicting and confusing if both are included on labelling as currently worded. Improvements are proposed to clarify requirements and improve wording.

To more clearly specify warning requirements, it is proposed to include separate entries for mucosal and dermal preparations and to include a note that if both mucosal and dermal uses apply, then all warnings (ie. as specified for dermal preparations; Entry 2) are required. It is also proposed to:

- amend the severe allergic reaction warning to direct those suffering a severe allergic reaction to "seek immediate medical assistance" rather than merely to "stop use", and
- amend the mild irritation warning to state "Mild <u>skin</u> irritation may occur; stop use if it becomes <u>more</u> severe", to more clearly indicate this is only relevant to dermal-application and because use should stop before irritation becomes "severe".

In summary, the proposed changes are as follows (additions/deletions in bold red/strikethrough text):

Column 1 Substance(s)	Column 2 Conditions	Column 3 Required statement(s)
Chlorhexidine *(Entry 1 of 2)*	In ~~topical products,~~ ~~including~~ preparations for topical use on mucosal surfaces. **Note: If also for dermal use, Entry 2 below applies.**	• Avoid contact with eyes. • If in eyes, rinse well with water. • ~~WARNING – This product contains chlorhexidine.~~ **Chlorhexidine can cause** ~~S~~**s**evere allergic reactions ~~can occur. Stop use if this occurs~~. **Seek immediate medical assistance if this occurs.**
Chlorhexidine *(Entry 2 of 2)*	In ~~topical products OTHER THAN~~ preparations for ~~topical~~ **dermal** use ~~on mucosal surfaces~~.	• Avoid contact with eyes. • If in eyes, rinse well with water. • Mild **skin** irritation may occur; stop use if it becomes **more** severe. • **Chlorhexidine can cause severe allergic reactions. Seek immediate medical assistance if this occurs.**

The final proposed entries are therefore as follows:

Column 1 Substance(s)	Column 2 Conditions	Column 3 Required statement(s)
Chlorhexidine *(Entry 1 of 2)*	In preparations for topical use on mucosal surfaces. Note: If also for dermal use, Entry 2 below applies.	• Avoid contact with eyes. • If in eyes, rinse well with water. • Chlorhexidine can cause severe allergic reactions. Seek immediate medical assistance if this occurs.
Chlorhexidine *(Entry 2 of 2)*	In preparations for dermal use.	• Avoid contact with eyes. • If in eyes, rinse well with water. • Mild skin irritation may occur; stop use if it becomes more severe. • Chlorhexidine can cause severe allergic reactions. Seek immediate medical assistance if this occurs.

Proposed changes to RASML entries for hydrocortisone

The current RASML entry for hydrocortisone specifies "do not use for children under 2 years of age unless a doctor has told you to". However, the Schedule 2 and 3 entries for hydrocortisone in the Poisons Standard exclude use in children under 12 years of age in some circumstances when hydrocortisone is combined with antifungals or aciclovir. While the RASML warning is less restrictive and does not preclude a more restrictive warning, it is misleading and can potentially lead to incorrect labelling.

It is therefore proposed to amend the current RASML entry for hydrocortisone to indicate that in some circumstances the more restrictive warning, "Do not use for children under 12 years old", is required.

Given the details involved in describing the circumstances when the more restrictive statement is required by the Poisons Standard (in Schedules 2 and 3 of the Standard for Uniform Scheduling of Medicines and Poisons; SUSMP), it is considered sufficient and clearer to amend the RASML entry to simply specify the statement as required "if Schedule 2 or 3 to the SUSMP excludes use in children under 12 years of age", as shown below. Reference to "CAUTION" in the current Entry 2 is considered redundant, given that TGO 92 requires warnings to be included under the heading "Warnings", so "CAUTION" will be deleted from the warning.

In summary, the following changes are proposed (additions/deletions in bold red/strikethrough text):

Column 1 Substance(s)	Column 2 Conditions	Column 3 Required statement(s)
Hydrocortisone *(Entry 1 of 2)*	In preparations for dermal use	• ***either*** - ~~CAUTION -~~ Do not use for children under 2 years of age unless a doctor has told you to. ***or (if Schedule 2 or 3 to the SUSMP excludes use in children under 12 years of age)*** - **Do not use for children under 12 years of age** • Do not use in the eyes. • Do not use for acne. • Do not use under waterproof bandages unless a doctor has told you to. • Do not use for more than 7 days unless a doctor has told you to.
Hydrocortisone *(Entry 2 of 2)*	In preparations for topical rectal use	• ~~CAUTION -~~ Do not use for children under 2 years of age unless a doctor has told you to. • Do not use for more than 7 days unless a doctor has told you to.

Proposed correction to RASML entry for ibuprofen

Amendment of one warning statement in RASML Entry 3 of 6 for ibuprofen is proposed in order to correct a discrepancy between the Poisons Standard and RASML requirements for unscheduled ibuprofen for use in children under 12 years of age.

The current RASML Entry 3 of 6 specifies warnings for unscheduled ibuprofen-containing medicines for oral use in children under 12 years of age. One of the included warnings in the entry is "Unless a doctor has told you to, do not use in children 6 years of age or less". However, the Poisons Standard specifies that exemption from schedule 2 requires the medicine to be "not labelled for the treatment of children 6 years of age or less."

In order for the RASML to be consistent with the requirements of the Poisons Standard for exclusion from scheduling, it is proposed to amend the current ibuprofen Entry 3 of 6 warning to

remove the qualification of “Unless a doctor has told you to” from the warning statement. The revised wording proposed is “Do not use in children under 7 years of age.”

Consultation questions and responses

The TGA is requesting comments that will help ensure that the proposed advisory statements are appropriate and support the quality use of the medicines. Submissions must be relevant to warning statements for OTC medicines containing either chlorhexidine, hydrocortisone or ibuprofen and must be received by the closing date.

Question

Do you support the proposed conditions and wording of the advisory statements?

If there are aspects you do not support, please explain why you do not support them. You may make suggestions for alternative wording or additional statements that you think are suitable.

You may wish to include an assessment of how the proposed changes will impact on you; that is, what do you see as the likely benefits or costs to you (these may be financial or non-financial).

To provide your feedback click ‘Make a submission’ on the consultation page and include your response using the free text field and/or file upload function.

All feedback will be considered after the consultation period ends and will be published on the TGA website with your consent.

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	OTC Medicines Evaluation Section	July 2021

Therapeutic Goods Administration

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Reference/Publication #