Australian Government
Department of Health
Therapeutic Goods Administration

Proposed changes to Required Advisory Statements for Medicine Labels (RASML): Melatonin

Consultation paper

Version 1.0, July 2021

TGA Health Safety Regulation

Confidentiality
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Introduction

Purpose

The Therapeutic Goods Administration (TGA) is seeking comments from interested parties on proposed new advisory statements for labels of over the counter (OTC) medicines containing melatonin, for inclusion in the Required Advisory Statements for Medicine Labels (RASML). The proposal to include advisory statements for melatonin-containing medicines in RASML follows recent down-scheduling of melatonin when supplied under specific conditions, from Schedule 4 to Schedule 3 of the Poisons Standard.

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 RASML statements for melatonin

The following entry in Schedule 3 of the Poisons Standard came into effect for melatonin on 1 June 2021:

> MELATONIN in modified release tablets containing 2 mg or less of melatonin for monotherapy for the short term treatment of primary insomnia characterised by poor quality of sleep for adults aged 55 or over, in packs containing not more than 30 tablets.

Given the anticipated registration of new S3 melatonin medicines as a result of down-scheduling, RASML warnings for S3 melatonin are proposed as shown in the table below. The basis for each warning is included in the table.

Warning statement	Basis for warning
Do not take this medicine if:	
• you are under 55 years of age	In accordance with scheduling restrictions and approved indications
• you are taking any other medicines for sleep	The medicine is specifically indicated, and restricted by the Schedule 3 entry, for use as monotherapy for the short term treatment of primary insomnia.
• you have liver problems	Consistent with approved Product Information (PI), which states that there is no experience of use in patients with liver impairment and therefore it is not recommended in these patients.
• you are pregnant or breastfeeding	Consistent with approved PI, which states it is not recommended in either circumstance. The warning is not relevant to the indicated age group (from 55 years of age), but should be included in case of misuse/off-label use.
Unless a doctor has told you to, do not use:	
• for more than 3 weeks	Consistent with recommendation of the Scheduling Delegate in their reasons for the final decision, that treatment should be limited to a maximum duration of three weeks.
• if you have kidney problems	Consistent with approved PI, which states "Caution should be used when melatonin is administered to such patients"

Warning statement	Basis for warning
• if you have an autoimmune disease	Consistent with approved PI, which states "…not recommended for use in patients with autoimmune diseases".
Consult your pharmacist or doctor before use if you are taking other medicines regularly.	Consistent with approved PI, which specifies several interactions including with fluvoxamine, which substantially increases melatonin plasma levels.
Do not drink alcohol while taking this medicine	Consistent with approved PI, which states that alcohol reduces efficacy and may alter the prolonged-release characteristics of the tablets. Enhanced drowsiness may also occur (British National Formulary).
This medication may cause drowsiness. If affected do not drive or operate machinery.	Consistent with product efficacy and approved PI

In summary, the following RASML entry for melatonin-containing oral medicines is proposed:

Column 1 Substance(s)	Column 2 Conditions	Column 3 Required statement(s)
Melatonin *(Entry 1 of 1)*	In modified-release tablets containing 2 mg or less of melatonin	• Do not use if: - you are under 55 years of age - you are taking any other medicines for sleep - you have liver problems - you are pregnant or breastfeeding • Unless a doctor has told you to, do not use: - for more than 3 weeks - if you have kidney problems - if you have an autoimmune disease • Consult your pharmacist or doctor before use if you are taking other medicines regularly • Do not drink alcohol while taking this medicine • This medication may cause drowsiness. If affected do not drive or operate machinery.

Note: 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.

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 melatonin 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

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Reference/Publication #