Australian Government
Department of Health
Therapeutic Goods Administration

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

Consultation paper

Version 1.0, March 2021

TGA Health Safety Regulation

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Introduction

Purpose

The Therapeutic Goods Administration (TGA) is seeking comments from interested parties on changes to current requirements for advisory statements for labels of non-prescription medicines containing antihistamines indicated for short term use in insomnia (diphenhydramine, doxylamine and promethazine), as included in the Required Advisory Statements for Medicine Labels (RASML) document.

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.

Any changes required to RASML No. 5 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 antihistamine entries

Proposed deletion of pregnancy warnings for sedating antihistamines

The TGA considers that the current RASML pregnancy warnings for doxylamine and diphenhydramine when used for insomnia are not required due to the absence of safety concerns. The warnings are inconsistent with the TGA's pregnancy categorisation of these substances (Category A in the TGA's 'Prescribing medicines in pregnancy database') and with available safety evidence. Doxylamine is frequently recommended by doctors for treatment of nausea and vomiting in pregnancy, consistent with the Therapeutic Guidelines[1] and Australian Medicines Handbook[2]. The current warnings create confusion and concern for pregnant women advised by healthcare professionals to take doxylamine and can potentially lead to the use of less safe alternatives.

Promethazine is category C in the TGA's 'Prescribing medicines in pregnancy database' and a pregnancy warning on labelling is therefore required by TGO 92 for promethazine regardless of the RASML entry. While already specified in TGO 92, it is proposed nevertheless, to retain the pregnancy warning for promethazine in RASML for completeness. For consistency, the pregnancy warning will also be added to other RASML entries for promethazine (and for alimemazine, which is also pregnancy Category C).

Proposed minor changes to the breastfeeding warning for sedating antihistamines

It is proposed to simplify the current breastfeeding warnings by deleting the option to use the words "Not recommended for use by breastfeeding women" and to maintain the existing warning of "If breastfeeding, consult a doctor or pharmacist before use".

[1] *eTG complete* [digital]. Melbourne: Therapeutic Guidelines Limited; 2020 Aug. <https://www.tg.org.au>
[2] Australian Medicines Handbook [digital]. Adelaide: Australian Medicines Handbook Pty Ltd; 2020 Jul. <https://amhonline.amh.net.au>

Proposed changes to RASML antihistamine entries (deletions in strikethrough, additions in red)

Column 1 Substance(s)	Column 2 Conditions	Column 3 Required statement(s)
Antihistamines *(Entry 1 of 5)* including: • Alimemazine (trimeprazine) • Brompheniramine • Chlorphenamine • Dexchlorpheniramine • Diphenhydramine • Doxylamine • Pheniramine • Promethazine • Triprolidine when NOT separately specified in this table	In oral medicines that include dosage instructions for adults and children aged from 'x' years (**where 'x' must not be less than 2**) when NOT separately specified in this table	• *either* - This medication may cause drowsiness. If affected do not drive a vehicle or operate machinery. Avoid alcohol. *or* - This medication may cause drowsiness and may increase the effects of alcohol. If affected do not drive a motor vehicle or operate machinery. • Do not give to children under 'x' years of age. • *and (if 'x' < 12)* - Do not give to children between 'x' and 11 years of age, except on the advice of a doctor, pharmacist or nurse practitioner. • *(for alimemazine and promethazine only)* If pregnant or likely to become pregnant, consult a doctor or pharmacist before use.
Antihistamines *(Entry 2 of 5)* including: • Alimemazine (trimeprazine) • Brompheniramine • Chlorphenamine • Dexchlorpheniramine • Diphenhydramine • Doxylamine • Pheniramine • Promethazine • Triprolidine when NOT separately specified in this table	In oral medicines that ONLY include dosage instructions for CHILDREN aged between 'x' and 'y' years (**where 'x' must not be less than 2, and 'y' must not be more than 11**) when NOT separately specified in this table	• This medication may cause drowsiness. • Do not give to children under 'x' years of age. • Do not give to children between 'x' and 'y' years of age, except on the advice of a doctor, pharmacist or nurse practitioner. • *(for alimemazine and promethazine only)* If pregnant or likely to become pregnant, consult a doctor or pharmacist before use.

Column 1 Substance(s)	Column 2 Conditions	Column 3 Required statement(s)
Antihistamines *(Entry 3 of 5)* including: • Brompheniramine • Chlorphenamine • Dexchlorpheniramine • Diphenhydramine • Doxylamine • Pheniramine • Promethazine • Triprolidine when NOT separately specified in this table	In oral preparations indicated for COUGH, COLD OR FLU: • which include dosage instructions for adults and children aged from 'x' years (where 'x' must not be less than 6)	• *either* – This medication may cause drowsiness. If affected do not drive a vehicle or operate machinery. Avoid alcohol. *or* – This medication may cause drowsiness and may increase the effects of alcohol. If affected do not drive a motor vehicle or operate machinery. • Do not give to children under 'x' years of age. • *and (if 'x' < 12)* – Do not give to children between 'x' and 11 years of age, except on the advice of a doctor, pharmacist or nurse practitioner. • *(for promethazine only)* If pregnant or likely to become pregnant, consult a doctor or pharmacist before use.
Antihistamines *(Entry 4 of 5)* including: • Brompheniramine • Chlorphenamine • Dexchlorpheniramine • Diphenhydramine • Doxylamine • Pheniramine • Promethazine • Triprolidine when NOT separately specified in this table	In oral preparations indicated for COUGH, COLD OR FLU: • which ONLY include dosage instructions for CHILDREN aged between 'x' and 'y' years (where 'x' must not be less than 6 and 'y' must not be more than 11)	• This medication may cause drowsiness. • Do not give to children under 'x' years of age. • *and (if 'x' < 12)* – Do not give to children between 'x' and 11 years of age, except on the advice of a doctor, pharmacist or • *(for promethazine only)* If pregnant or likely to become pregnant, consult a doctor or pharmacist before use.

Column 1 Substance(s)	Column 2 Conditions	Column 3 Required statement(s)
Antihistamines *(Entry 5 of 5)* including: • Diphenhydramine • Doxylamine • Promethazine	In oral medicines indicated for SHORT TERM USE IN INSOMNIA: • which include dosage instructions for adults and children aged from 'x' years (where 'x' must not be less than 2) *(Note: Antihistamine medicines indicated for sedation that only include dosage instructions for children aged < 12 years are subject to 'Antihistamines (Entry 2 of 5))*	• This product should be taken on medical or pharmacist advice. • Do not give to children under 'x' years of age. ~~• *either (if the substance is in pregnancy category B or C):*~~ ~~- If pregnant or [likely/trying] to become pregnant, or if breastfeeding, consult a doctor or pharmacist before use.~~ ~~*or (if the substance is in pregnancy category A):*~~ ~~*either*~~ ~~- Not recommended for use by pregnant or breastfeeding women.~~ ~~*or*~~ ~~- If pregnant or breastfeeding, consult a doctor or pharmacist before use.~~ • If breastfeeding, consult a doctor or pharmacist before use. • *(for promethazine only)* If pregnant or likely to become pregnant, consult a doctor or pharmacist before use. • Do not take this medicine for more than a few days. • This preparation is to aid sleep. Drowsiness may continue the following day. If affected do not drive or operate machinery. Avoid alcohol.

Individual RASML entries for alimemazine, diphenhydramine, doxylamine and promethazine would be similarly amended.

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 and that any label changes that would be required for these medicines are made in the most convenient, efficient and cost-effective way.

Submissions must be relevant to warning statements for OTC medicines containing antihistamines 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	March 2021

Therapeutic Goods Administration

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Reference/Publication #