Australian Government
Department of Health, Disability and Ageing
Therapeutic Goods Administration

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

Consultation paper

Version 1.0, July 2026

Confidentiality

All submissions received will be placed on the TGA's Internet site, unless marked confidential. Any confidential material contained within your submission should be provided under a separate cover and clearly marked "IN CONFIDENCE". Reasons for a claim to confidentiality must be included in the space provided on the TGA submission form. For submission made by individuals, all personal details, other than your name, will be removed from your submission before it is published on the TGA's Internet site. In addition, a list of parties making submissions will be published. If you do not wish to be identified with your submission you must specifically request this in the space provided on the submission form.

Contents

Introduction ____ 4

Purpose ____ 4

Background ____ 4

Advisory statements ---- 4

Required Advisory Statements for Medicine Labels (RASML) ---- 4

Proposed changes to RASML ____ 5

Proposed new entries ____ 5

Celecoxib ---- 5

Melatonin – immediate-release ---- 8

Methenamine ---- 10

Naratriptan ---- 11

Changes to existing entries ____ 12

Antihistamines - first-generation, sedating ---- 12

Cetirizine and Levocetirizine ---- 19

Dextromethorphan ---- 20

Ibuprofen ---- 21

Other minor changes ____ 27

Aspartame ---- 27

Benzoyl peroxide ---- 28

Chelidonium majus ---- 28

Minor editorial changes ---- 28

Consultation questions and responses ____ 30

Introduction

Purpose

The Therapeutic Goods Administration (TGA) is seeking comments from interested parties on proposed changes to the Required Advisory Statements for Medicine Labels (RASML). RASML sets out advisory statements that are required to be included on the labels of specified OTC and registered complementary medicines.

The proposed changes to RASML are:

- addition of entries for three new substances not currently included in RASML - celecoxib, methenamine and naratriptan
- a new entry for immediate-release melatonin preparations for short term treatment of jet lag
- changes to existing entries for sedating antihistamines, cetirizine and levocetirizine, dextromethorphan, and ibuprofen, and
- deletion of the entry for aspartame, minor changes to existing entries for benzoyl peroxide and Chelidonium majus, and other minor editorial changes.

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.

Required Advisory Statements for Medicine Labels (RASML)

RASML sets out advisory statements that are required to be included on the labels of specified OTC and registered complementary medicines. The current version, RASML No. 6, is registered on the Federal Register of Legislation as Schedule 1 to the *Therapeutic Goods (Medicines Advisory Statements) Specification 2021*, a legislative instrument made under subsection 3(5A) of the Act.

Following publication of the outcomes of this consultation, the new and updated entries will be incorporated in the next version of RASML, RASML No. 7. An 18-month transition period from commencement of RASML No. 7 will be provided for the updating of existing medicine labels that do not already comply with the new requirements.

The advisory statements required by 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.

RASML permits the wording of the actual statements that are included on medicine labels to differ from the wording set out in RASML, provided the meaning is the same.

Proposed changes to RASML

Proposed new entries

Celecoxib

The proposal to include advisory statements for celecoxib-containing medicines in RASML follows down-scheduling of celecoxib when supplied under specific conditions, from Schedule 4 to Schedule 3 of the Poisons Standard. The following entry in Schedule 3 came into effect on 1 February 2024:

> CELECOXIB in tablets or capsules each containing 200 mg or less of celecoxib, in a primary pack containing not more than 10 dosage units for the short-term treatment of acute pain due to primary dysmenorrhea or musculoskeletal or soft tissue injuries in adults.

Proposed RASML warnings for S3 celecoxib are specified in the table below, together with the basis for their inclusion.

Warning statement	Basis for warning
Do not use:	
• in children and adolescents aged under 18 years	Consistent with the Product Information (PI) and labelling for the originator product, Celebrex Relief
• if you have a stomach ulcer or intestinal bleeding	Consistent with the Celebrex Relief PI and labelling.
• if you are allergic to celecoxib, other anti-inflammatory medicines or sulfonamides	Consistent with the Celebrex Relief PI and labelling.
• if you have liver or kidney problems	Consistent with Celebrex Relief labelling. The Celebrex Relief PI specifies contraindication in severe renal impairment (estimated creatinine clearance <30 mL/min) and moderate to severe hepatic impairment (Child-Pugh# score ≥7; with a note that this is more restrictive than for prescription celecoxib). In the context of OTC use and label warnings, it is appropriate to simplify the contraindication to “liver or kidney problems” as included for Celebrex Relief labelling.
• if you have heart failure or have had a heart attack or stroke in the last 3 months	Based on the Celebrex Relief PI and similar to Celebrex Relief label warnings. The Celebrex Relief PI includes the following relevant contraindications: • *Unstable ischaemic heart disease of thrombus aetiology or documented myocardial infarction or stroke within 3 months.* • *Congestive heart failure (NYHA II-IV).* While heart failure is qualified in the PI as “congestive heart failure *(NYHA II-IV)”,* in the context of OTC use it is appropriate to simplify this to “heart failure” (as specified on the Celebrex Relief label). Given the range of different heart conditions and symptoms and their varying risks in relation to use of celecoxib, it is appropriate to also include a warning to “*Consult your doctor or pharmacist before use if*

Warning statement	Basis for warning
	you have heart problems", in addition to the proposed contraindication warning (see further cardiovascular warnings below). Related Celebrex Relief label warnings are: "*Do not take… if you have heart problems causing chest pain, had a heart attack or stroke in the last 3 months or have heart failure*."
• if you have asthma, unless advised by a doctor	Consistent with the Celebrex Relief PI and labelling and with existing RASML entries for other NSAIDS.
• if trying to become pregnant, or during the first 6 months of pregnancy, unless a doctor has told you to. Do not use at all during the last 3 months of pregnancy	Consistent with the Celebrex Relief PI and labelling and with existing RASML entries for other NSAIDS.
• with products containing aspirin or other anti-inflammatory medicines, or with other medicines that you are taking regularly, unless advised by your doctor or pharmacist	Consistent with the Celebrex Relief PI and labelling and existing RASML entries for other NSAIDS.
• if you are aged 65 years or over, unless advised by a doctor	Consistent with the Celebrex Relief PI and labelling. Several of celecoxib's contraindications and precautions involve conditions particularly applicable to the elderly, there is increased risk of elderly patients taking the medicine with other interacting medicines, elderly patients are more likely to be at risk of adverse events, and the medicine is only recently available over the counter (in Australia and worldwide). The warning is already required for unscheduled ibuprofen products and is proposed in this consultation to apply to all OTC ibuprofen-containing medicines, regardless of schedule (see proposed changes to ibuprofen entries below).
Consult your doctor or pharmacist before use:	
• if you have heart problems or risk factors for heart disease, including diabetes, high blood pressure or high cholesterol.	Based on the Celebrex Relief PI, which includes the following warnings/precautions regarding cardiovascular risks: *CELEBREX RELIEF should be used with caution in patients with significant established ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease as well as patients at high risk of cardiovascular disease including those with significant and multiple risk factors (e.g. diabetes, hypertension, hypercholesterolaemia, cardiac failure and smokers).*
• if you have a blood vessel disorder.	Based on the Celebrex Relief PI, which states to use "*with caution in patients with….peripheral arterial disease and/or cerebrovascular disease".*
• if you have fluid retention causing swelling in your feet or legs.	Consistent with Celebrex Relief labelling and based on the PI, which states: *Fluid retention and oedema have been observed in some patients taking celecoxib…Therefore, CELEBREX RELIEF should be used with caution in patients with fluid retention, hypertension, heart*

Warning statement	Basis for warning
	failure, compromised cardiac function, pre-existing oedema or other conditions predisposing to, or worsened by, fluid retention including those taking diuretic treatment or otherwise at risk of hypovolaemia. Patients with pre-existing congestive heart failure or hypertension should be closely monitored.
Do not use for more than 5 days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage.	Consistent with the Celebrex Relief PI and labelling. RASML entries for other NSAIDs specify similar: *"Do not use for more than a few days at a time unless…"*
If you get an allergic reaction, stop taking and see your doctor immediately	Consistent with Celebrex Relief labelling and RASML entries for other NSAIDs.

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

Substances	Circumstances	Required statements
Celecoxib	In medicines for oral use	• Do not use: – in children and adolescents aged under 18 years – If you have a stomach ulcer or intestinal bleeding – if you are allergic to celecoxib, other anti-inflammatory medicines or sulfonamides – if you have liver or kidney problems – if you have heart failure or have had a heart attack or stroke in the last 3 months – if you have asthma, unless advised by a doctor – if trying to become pregnant, or during the first 6 months of pregnancy, unless a doctor has told you to. Do not use at all during the last 3 months of pregnancy – with products containing aspirin or other anti-inflammatory medicines, or with other medicines that you are taking regularly, unless advised by your doctor or pharmacist – if you are aged 65 years or over, unless advised by a doctor • Consult your doctor or pharmacist before use: – if you have heart problems or risk factors for heart disease, including diabetes, high blood pressure or high cholesterol – if you have a blood vessel disorder – if you have fluid retention, causing swelling in your feet or legs • Do not use for more than 5 days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage. • If you get an allergic reaction, stop taking and see your doctor immediately.

Note: RASML permits the wording of the actual statements that are included on medicine labels to differ from the wording set out in RASML, provided the meaning is the same.

Melatonin – immediate-release

RASML currently contains a single entry for melatonin, which applies to modified-release tablets containing 2 mg or less of melatonin. It is proposed to include a new RASML entry for immediate-release preparations for short term treatment of jet lag. This follows down-scheduling of these medicines from prescription-only to OTC availability and the recent registration of the first such product. Additional registration applications are anticipated.

Proposed RASML warning statements and their basis for inclusion are detailed in the table below.

Warning statement	Basis for warning
Do not use:	
• in children and adolescents under 18 years of age	Consistent with approved indications and scheduling.
• if you are taking medicines for sleep	PIs for melatonin-containing medicines state that melatonin may enhance the sedative effects of hypnotics.
• if you have liver problems	PIs for melatonin-containing medicines state: "*Limited data indicates that daytime endogenous blood melatonin concentration is markedly elevated in patients with hepatic impairment due to reduced clearance. Therefore, [melatonin] is not recommended for patients with hepatic impairment.*" Contraindication is consistent with the current RASML entry for melatonin in modified-release preparations.
• if you are pregnant or breastfeeding	PIs for melatonin-containing medicines state that they are not recommended in pregnancy or breastfeeding. The proposed warning is consistent with the current RASML entry for melatonin in modified-release preparations.
Talk to your doctor before use if:	
• you have an autoimmune disease or kidney problems	<u>Autoimmune disease</u> PIs for melatonin-containing medicines state "*There is no data concerning the use of melatonin in patients with autoimmune diseases. Therefore* [melatonin] *is not recommended in patients with autoimmune diseases.*" <u>Kidney problems</u> PIs for immediate-release melatonin medicines state "*Limited data is available for the use of melatonin in patients with renal impairment. Therefore,* [melatonin] *is not recommended for patients with renal impairment.*" PIs for modified-release melatonin medicines state "*The effect of any stage of renal insufficiency on melatonin pharmacokinetics has not been studied. Caution should be used when melatonin is administered to such patients.*" The proposed warnings are consistent with those required by RASML for melatonin in modified-release preparations.
Talk to your doctor or pharmacist before use if:	
• you are at risk of seizures	Consistent with PIs for immediate-release melatonin medicines, which state "*Melatonin may increase seizure frequency in patients experiencing seizures (e.g. epileptic patients). Patients suffering from seizures must be informed about this possibility before using melatonin. Melatonin may promote or increase the incidence of*

Warning statement	Basis for warning
	seizures in children and adolescents with multiple neurological defects." PIs for modified-release melatonin medicines do not refer to increased risk of seizures, hence the absence of such a warning in the current RASML entry for these medicines.
• you are taking any other medicines regularly	Consistent with approved PIs for melatonin-containing medicines, which specify several interactions including with fluvoxamine, which substantially increases melatonin plasma levels. Also consistent with the current RASML entry for melatonin in modified-release preparations.
This medication may cause drowsiness. If affected do not drive or operate machinery. Avoid alcohol	Consistent with approved PIs for immediate-release melatonin medicines.

In summary, the following additional RASML entry (*Entry 2 of 2*, shown in red) for melatonin in immediate-release preparations for short-term treatment of jet lag is proposed (existing entry shown in black):

Substances	Circumstances	Required statements
Melatonin *(Entry 1 of 2)*	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 a 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.
Melatonin *(Entry 2 of 2)*	In immediate-release preparations for short-term treatment of jet lag	• Do not use: – in children and adolescents under 18 years of age – if you are taking medicines for sleep – if you have liver problems – if you are pregnant or breastfeeding • Talk to your doctor before use if: – you have an autoimmune disease or kidney problems • Talk to your doctor or pharmacist before use if: – you are at risk of seizures – you are taking any other medicines regularly • This medication may cause drowsiness. If affected do not drive or operate machinery. Avoid alcohol

Note: RASML permits the wording of the actual statements that are included on medicine labels to differ from the wording set out in RASML, provided the meaning is the same.

Methenamine

The proposal to include advisory statements for methenamine-containing oral medicines in RASML follows a recent increase in applications for registration of these medicines.

Methenamine was unscheduled for many years but was included in Schedule 3 of the Poisons Standard in October 2025. The S3 entry is "*METHENAMINE in preparations for therapeutic use.*"

Proposed RASML warning statements and their basis for inclusion are detailed in the table below.

Warning statement	Basis for warning
Do not use:	
• in children under 12 years of age	Consistent with approved product information (PIs) for existing products, which do not include dosing in children under 12 years of age and state that use in this age group is not recommended.
• if you are taking sulfonamides, acetazolamide or a urinary alkaliniser	Consistent with current product information and labelling for most existing products. Methenamine should not be used with urinary alkalinisers as efficacy requires acidic urine. Approved PIs also state not to administer concurrently with sulfonamides because of the possibility of crystalluria and that "concurrent use with acetazolamide should be avoided as the desired effect [of methenamine] will be lost".
• if you have gout, or impaired kidney or liver function or are severely dehydrated	Consistent with current product information and labelling for most existing products.
Talk to your doctor or pharmacist before use if:	
• you are taking any other medicines	While a specific warning regarding concurrent use with sulfonamides, acetazolamide or urinary alkalinisers is considered appropriate, additional inclusion of a more general warning is also considered appropriate. Most consumers would not know if they were taking a sulfonamide and some consumers may not be familiar with 'urinary alkalinisers'. The PI for Hiprex also refers to antacids potentially decreasing the effect of methenamine hippurate due to increased urinary pH. The proposed warning is consistent with current labelling for most existing products.
• you have any medical conditions or use a catheter	While reference to "any medical condition" is general, it covers patients who might have metabolic acidosis for reasons other than kidney or liver problems (metabolic acidosis is a contraindication) and further safeguards against potential use with sulfonamides. It also covers those for whom methenamine hippurate may be ineffective, such as those with neuropathic bladder or renal tract abnormalities (as per PI). The PIs for most existing products advise against use in those using long-term catheters. The proposed warning is consistent with current labelling for most existing products.

Warning statement	Basis for warning
See your doctor as soon as signs of a urinary tract infection (UTI) appear.	Consistent with current product information and labelling for most existing products. Patients may delay or forgo seeking medical attention in the expectation that methenamine hippurate treatment will resolve the UTI, whereas prompt clinical assessment and appropriate treatment of the UTI is essential.

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

Substances	Circumstances	Required statements
Methenamine	In medicines for oral use	• Do not use: – in children under 12 years of age – if you are taking sulfonamides, acetazolamide or a urinary alkaliniser – if you have gout, or impaired kidney or liver function or are severely dehydrated • Talk to your doctor or pharmacist before use if: – you are taking any other medicines – you have any medical conditions or use a catheter • See your doctor as soon as signs of a urinary tract infection (UTI) appear

Note: RASML permits the wording of the actual statements that are included on medicine labels to differ from the wording set out in RASML, provided the meaning is the same.

Naratriptan

A RASML entry for naratriptan is proposed. Naratriptan is one of several triptans available as a Schedule 3 Pharmacist Only medicine for treatment of migraine. It is the latest triptan to become available as an OTC medicine (see Scheduling Delegate's final decision notice) and is currently the only OTC triptan without a RASML entry.

Naratriptan has risks similar to those of existing triptans, except in relation to medicine interactions. Unlike several triptans, naratriptan does not interact with monoamine oxidase inhibitors (MOAIs), but can interact with selective serotonin reuptake inhibitors (SSRIs) and serotonin-noradrenaline reuptake inhibitors (SNRIs), ergotamine and derivatives, other triptans and other 5-HT1 agonists, and possibly with St John's Wort. These medicines are approved for use in migraine, depression and anxiety. The current PI (for Naramig) does not specify any other medicine interactions for naratriptan.

Accordingly, the proposed new RASML entry for naratriptan specifies the same label warnings as for other triptans, except that the proposed warning for medicine interactions is as follows:

> *Consult your doctor or pharmacist before use if you are taking other medicines for migraine, depression or anxiety.*

The proposed full RASML entry for naratriptan is as follows:

Substances	Circumstances	Required statements
Naratriptan	In divided oral preparations for relief of migraine	• Do not use: – without a previous diagnosis of migraine by a doctor – if you have heart disease, peripheral vascular disease (a blood vessel disorder) or high blood pressure or have previously had a heart attack or stroke. • Consult your doctor or pharmacist before use:

Substances	Circumstances	Required statements
		– if you think you may be at risk of heart disease (including if you are post-menopausal or a male over the age of 40) – if you have liver or kidney problems or any other medical conditions – if you are taking other medicines for migraine, depression or anxiety – if you are pregnant or breastfeeding. • Speak to a doctor or pharmacist if your migraine attacks become more frequent. Overuse of this medicine may worsen your condition. • This medicine may cause drowsiness. If affected, do not drive a vehicle or operate machinery.

Note: RASML permits the wording of the actual statements that are included on medicine labels to differ from the wording set out in RASML, provided the meaning is the same.

Changes to existing entries

Antihistamines - first-generation, sedating

Changes are proposed to the RASML entries for the first-generation sedating antihistamines alimemazine (trimeprazine), brompheniramine, chlorphenamine, dexchlorpheniramine, diphenhydramine, doxylamine, pheniramine, promethazine, and triprolidine. Following a post-market safety review, it is proposed that these entries be revised to contraindicate use in children under 6 years of age for all indications. It is also proposed to delete the class entry “Antihistamines” and to add reference to dimenhydrinate in the entries for diphenhydramine.

Background

First-generation sedating antihistamines are variously approved for use in children for a range of indications, including cough, cold and flu, allergy, sedation, nausea and vomiting, and travel sickness. Current RASML entries for first-generation sedating antihistamines include warning statements contraindicating use in children under 6 years of age when used for cough, cold and flu, and under 2 years of age for other indications.

In January 2022, the Advisory Committee for Medicines (ACM) provided advice on the use of first-generation sedating antihistamines and use in children 2 to 5 years of age. The ACM meeting statement noted the following (ACM meeting statement, Meeting 31, 3-4 February 2022 | Therapeutic Goods Administration (TGA)):

- A lack of efficacy data to support the use of first-generation sedating antihistamine-containing products in children aged 2 to 5 years for the treatment of coughs and colds and allergic indications.
- Current clinical guidelines for allergy treatment in children recommend use of non-sedating antihistamines.
- First-generation sedating antihistamines should be at least Schedule 3.
- Any first-generation sedating antihistamine products for use in children aged 2 to 5 years be discontinued and removed from the Australian Register of Therapeutic Goods (ARTG).

In 2024 the sponsor of Phenergan (containing promethazine hydrochloride and indicated for allergy, nausea and vomiting, travel sickness and sedation) advised the TGA that cumulative safety data in children between 2 to 5 years of age (inclusive) supported a causal association between

promethazine (and combinations) and safety concerns relating to psychiatric and central nervous system (CNS) adverse events. Consequently, the Product Information and labelling for Phenergan were revised to include relevant warnings and to contraindicate use in children under 6 years of age (see Safety Update).

It is biologically plausible for similar risks to be present for other first-generation sedating antihistamines. Clinical guidelines (such as the Australian Therapeutic Guidelines and UpToDate) and evidence-based resources (such as Australian Family Physician, the National Prescribing Service (NPS) MedicineWise and resources provided by the Royal Children's Hospital Melbourne) advise against the use of first-generation sedating antihistamines in children and adolescents.

Reports of CNS or psychiatric adverse events involving first-generation sedating antihistamines in children have been reported to the TGA adverse event database.

A literature review retrieved multiple articles relevant to this issue. CNS impairments highlighted in these articles include impaired learning and cognitive function, manifesting as attention and memory problems[1,2], slowed processing and reaction times, diminished motor responses, and reduced examination performance[3,4]. Memory problems, confusion, inattention, slowed processing speed and motor responses, and difficulties with language and communication have been documented[2]. The scientific literature noted the known adverse effects in children to include CNS effects of sedation, impaired learning ability, attention, and academic performance, and memory problems with first-generation sedating antihistamines. There is a recognised paradoxical CNS stimulatory effect of first-generation sedating antihistamines with increased aggression and psychomotor activity in young children.

A study by Kim et al. (2024)[5] also revealed a 22% increased risk of seizure events in children prescribed first-generation sedating antihistamines. This risk was significantly higher in younger children (6-24 months) with a 49% increased risk, compared to a 24% increase in risk in those aged 25 months to 6 years.

Given the above evidence, the TGA considers there are sufficient safety grounds to support the extension of contraindication to children less than 6 years of age for all indications. The TGA has subsequently contacted sponsors of relevant OTC products requesting corresponding changes to product information (PI) and labelling, including the addition of further warnings to the PI. Sponsors have agreed to make these changes and almost all affected products have now been updated accordingly.

To ensure that future products are labelled appropriately, amendments are proposed to the currently required advisory statements in RASML for first-generation sedating antihistamines.

In addition to contraindicating use of first-generation sedating antihistamines in children below 6 years of age, the TGA has proposed to reschedule these medicines when labelled for use in children under 12 years of age, to Schedule 3 of the Poisons Standard where they are not already included in Schedule 3. This proposal was considered by the ACMS in March 2026 and the delegate is still to make an interim decision. The outcome is unlikely to impact on changes to the RASML entries as proposed below, but will be considered as part of any final proposed changes if necessary.

Proposed changes

RASML currently contains a consolidated 'Antihistamines' entry covering first-generation sedating antihistamines, while also including separate entries for each individual antihistamine, namely: alimemazine (trimeprazine), brompheniramine, chlorphenamine, dexchlorpheniramine, diphenhydramine, doxylamine, pheniramine, promethazine, and triprolidine.

[1] Simons FE, Simons KJ. H1 antihistamines: current status and future directions. World Allergy Organ J. 2008;1(9):145-55.

[2] Reimers A, Odin P, Ljung H. Drug-Induced Cognitive Impairment. Drug Saf. 2024.

[3] Church MK, Maurer M, Simons FE, Bindslev-Jensen C, van Cauwenberge P, Bousquet J, et al. Risk of first-generation H(1)-antihistamines: a GA(2)LEN position paper. Allergy. 2010;65(4):459-66.

[4] Gober HJ, Li KH, Yan K, Bailey AJ, Carleton BC. Hydroxyzine Use in Preschool Children and Its Effect on Neurodevelopment: A Population-Based Longitudinal Study. Front Psychiatry. 2021;12:721875.

[5] Kim JH, Ha EK, Han B, Han T, Shin J, Chae KY, et al. First-Generation Antihistamines and Seizures in Young Children. JAMA Netw Open. 2024;7(8):e2429654.

The following changes to the entries are proposed:

1. Amend the entries so that all medicines containing first-generation sedating antihistamines require the warning "*Do not give to children under 'x' years of age*", where x must not be less than **6**. Currently, only the entries for medicines indicated for cough, cold or flu specify a minimum age of 6 years (entries 3 and 4), while other entries specify a minimum age of 2 years. Applying the 6-year minimum age across all of the medicines renders entries 3 and 4 redundant and they can be removed.

   Note: There are no entries 3 & 4 for alimemazine (trimeprazine)

2. Delete the class entry of "Antihistamines", for the following reasons:

   - Pregnancy warnings are only required for alimemazine and promethazine, which then requires separate statements for these substances within the 'Antihistamines' entries.
   - Reference to "Antihistamines" can be readily misinterpreted to refer to *all* antihistamines, despite the entries stating "when NOT separately specified in this table". The entries are only intended to apply to first-generation sedating antihistamines.
   - If a new antihistamine becomes available, it is automatically captured by the 'Antihistamines' entries even if the warnings are not appropriate, unless an update to RASML is made.

3. Amend the "Diphenhydramine" entry to "Diphenhydramine (including as dimenhydrinate)". Dimenhydrinate (Australian Approved Name) is the 8-chlorotheophylline salt of diphenhydramine, so the entry is applicable to dimenhydrinate, but some readers may not be aware that dimenhydrinate contains diphenhydramine.

The current individual entries are presented below, with the proposed changes indicated in red, strikethrough and underlined text. Several entries are identical, so only representative examples are shown (i.e. entries are the same for brompheniramine, chlorphenamine, dexchlorpheniramine, pheniramine and triprolidine and entries for doxylamine and diphenhydramine are also the same).

Alimemazine (trimeprazine):

Substances	Circumstances	Required statements
Alimemazine (trimeprazine) *Entry 1 of 2*	In oral medicines that ~~are NOT 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 ~~2~~6) ~~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. • If pregnant or likely to become pregnant, consult a doctor or pharmacist before use.
Alimemazine (trimeprazine) *Entry 2 of 2*	In oral medicines ~~that are NOT indicated for cough cold or flu,~~ that ONLY include dosage instructions for CHILDREN aged between 'x' and 'y' years (where	• This medication may cause drowsiness. • Do not give to children under 'x' years of age.

Substances	Circumstances	Required statements
	'x' must not be less than ~~2~~6, and 'y' must not be more than 11)	• Do not give to children between 'x' and 'y' years of age, except on the advice of a doctor, pharmacist or nurse practitioner. • If pregnant or likely to become pregnant, consult a doctor or pharmacist before use.

Brompheniramine (and same for chlorphenamine, dexchlorpheniramine, pheniramine and triprolidine):

Substances	Circumstances	Required statements
Brompheniramine *(Entry 1 of ~~4~~2)*	In oral medicines that include dosage instructions for adults and children aged from 'x' years (**where 'x' must not be less than ~~2~~6**) ~~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.
Brompheniramine *(Entry 2 of ~~4~~2)*	In oral medicines that ONLY include dosage instructions for CHILDREN aged between 'x' and 'y' years (**where 'x' must not be less than ~~2~~6, 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.
~~Brompheniramine~~ ~~*(Entry 3 of 4)*~~	~~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.~~
~~Brompheniramine~~ ~~*(Entry 4 of 4)*~~	~~In oral preparations indicated for COUGH, COLD OR FLU:~~	~~• This medication may cause drowsiness.~~ ~~• Do not give to children under 'x' years of age.~~

Substances	Circumstances	Required statements
	~~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)~~	• ~~*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.~~

Diphenhydramine (and same for doxylamine):

Substances	Circumstances	Required statements
Diphenhydramine *(includes dimenhydrinate)* *(Entry 1 of ~~53~~)*	In oral medicines that include dosage instructions for adults and children aged from 'x' years (where 'x' must not be less than ~~2~~6) ~~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.
Diphenhydramine *(includes dimenhydrinate)* *(Entry 2 of ~~53~~)*	In oral medicines that ONLY include dosage instructions for CHILDREN aged between 'x' and 'y' years (where 'x' must not be less than ~~2~~6, 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.
~~Diphenhydramine~~ ~~*(Entry 3 of 5)*~~	~~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.~~

Substances	Circumstances	Required statements
~~Diphenhydramine~~ ~~*(Entry 4 of 5)*~~	~~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 nurse practitioner.~~
Diphenhydramine *(includes dimenhydrinate)* *(Entry ~~5 of 5~~3 of 3)*	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~~6) *(Note: Diphenhydramine medicines indicated for sedation that only include dosage instructions for children aged < 12 years are subject to 'Diphenhydramine (Entry 2 of ~~5~~3))*	• This product should be taken on medical or pharmacist advice. • Do not give to children under 'x' years of age. • If breastfeeding, 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.

Promethazine (same as doxylamine and diphenhydramine except that promethazine includes a pregnancy warning):

Substances	Circumstances	Required statements
Promethazine *(Entry 1 of ~~5~~3)*	In oral medicines that include dosage instructions for adults and children aged from 'x' years (where 'x' must not be less than ~~2~~6) ~~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. • If pregnant or likely to become pregnant, consult a doctor or pharmacist before use.
Promethazine *(Entry 2 of ~~5~~3)*	In oral medicines that ONLY include dosage instructions for CHILDREN aged between 'x' and 'y' years (where 'x' must	• This medication may cause drowsiness. • Do not give to children under 'x' years of age.

Substances	Circumstances	Required statements
	not be less than ~~2~~6, and 'y' must not be more than 11) ~~when NOT separately specified in this table~~	• Do not give to children between 'x' and 'y' years of age, except on the advice of a doctor, pharmacist or nurse practitioner. • If pregnant or likely to become pregnant, consult a doctor or pharmacist before use.
~~Promethazine~~ ~~*(Entry 3 of 5)*~~	~~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.~~ ~~• If pregnant or likely to become pregnant, consult a doctor or pharmacist before use.~~
~~Promethazine~~ ~~*(Entry 4 of 5)*~~	~~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 nurse practitioner.~~ ~~• If pregnant or likely to become pregnant, consult a doctor or pharmacist before use.~~
Promethazine *(Entry ~~5 of 5~~3 of 3)*	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~~6) *(Note: Promethazine medicines indicated for sedation that only include dosage instructions for children aged < 12 years are subject to 'Promethazine (Entry 2 of ~~5~~3))*	• This product should be taken on medical or pharmacist advice. • Do not give to children under 'x' years of age. • If pregnant or likely to become pregnant, or if breastfeeding, 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.

Note: RASML permits the wording of the actual statements that are included on medicine labels to differ from the wording set out in RASML, provided the meaning is the same.

Cetirizine and Levocetirizine

It is proposed to add warning statements regarding use when pregnant or breastfeeding (extend requirement to children's-only products) and use in renal impairment.

Use in pregnancy & breastfeeding

It is proposed to amend the RASML entry for cetirizine (and levocetirizine; 'Entry 2 of 2' for both) to include the warning "*If you are pregnant or breastfeeding, check with your doctor or pharmacist before using this medicine.*"

Entry 2 applies to preparations labelled exclusively for use in children aged 1 to 12 years and does not require a pregnancy warning or drowsiness warnings that refer to driving, operating machinery or drinking alcohol - the only required warning is "*This medication may cause drowsiness*".

Whilst there is a rationale for these reduced warning requirements for products labelled exclusively for use in children, the omission of a pregnancy warning statement is inconsistent with the following TGO 92 label requirement (s.8(1)(k)(ii)):

where:

(A) the medicine is for oral use; and

(B) the medicine contains active ingredient(s) included in category 'B' (including 'B1', 'B2, 'B3') or category 'C' in the document titled 'Prescribing medicines in pregnancy database' published on the TGA website as on the date of commencement of this Order; and

(C) the medicine is not subject to other specific warning statement(s) relating to use during pregnancy,

the required statement is: 'If pregnant or likely to become pregnant, consult a pharmacist or a doctor before use' or words to this effect

The above TGO 92-required pregnancy warning is required even when the medicine is labelled exclusively for use in children. Therefore, the current RASML cetirizine/levocetirizine "Entry 2" is inconsistent with TGO 92 and creates confusion as to the legally required warning. The following points are further noted:

- There is a risk that pregnant women might still use the children's-only product or at least infer from the lack of warning that use of cetirizine/levocetirizine in pregnancy does not require caution.
- There are no other examples in RASML where a pregnancy warning is excluded from an entry on the basis that the medicine is intended solely for use in children. For example, pregnancy warnings are included in the RASML entries for ibuprofen medicines intended specifically for children (current entries 3 and 4).
- Other second-generation antihistamines (fexofenadine, loratadine, desloratadine) do not have RASML entries for children's-only medicines and the pregnancy and breastfeeding warnings apply in all cases.

Given the above points, it is proposed to apply the pregnancy and breastfeeding warning statement currently specified in "Entry 1 of 2" for cetirizine/levocetirizine to "Entry 2 of 2" also, as shown below.

It is noted that a similar argument could be made to require the full drowsiness warning (i.e.. with reference to driving, operating machinery and drinking alcohol) for children's-only products. However, this has not been required for other sedating antihistamines and should similarly not be required for cetirizine and levocetirizine, which have substantially lower sedation risk than first-generation sedating antihistamines.

Use in renal impairment

The approved PI for Zyrtec states:

> *Cetirizine clearance is reduced in patients with renal impairment. In patients with renal insufficiency, dosage should be reduced to half the usual recommended dose. Zyrtec is contraindicated in patients with severe renal impairment (less than 10 mL/min creatinine clearance).*

Consistent with this, the originator Zyrtec products include a label warning to "*Ask your doctor before use if you have … kidney disease*". Most, but not all generic cetirizine-containing products also include a label warning to this effect. It is therefore proposed to include the warning "*Ask your doctor before use if you have kidney problems*" in Entry 1 and 2 for cetirizine and levocetirizine.

Proposed entry changes

The proposed changes are shown in red below.

Substances	Circumstances	Required statements
Cetirizine *(Entry 1 of 2)* *and* Levocetirizine (Entry 1 of 2)	In preparations for oral use that are NOT specifically labelled for use only in children (between 1 year and 12 years of age)	• *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. • If you are pregnant or breastfeeding, check with your doctor or pharmacist before using this medicine. • Ask your doctor before use if you have kidney problems.
Cetirizine *(Entry 2 of 2)* *and* Levocetirizine (Entry 2 of 2)	In preparations for oral use specifically labelled for use only in children (between 1 year and 12 years of age)	• This medication may cause drowsiness. • If you are pregnant or breastfeeding, check with your doctor or pharmacist before using this medicine. • Ask your doctor before use if you have kidney problems.

Dextromethorphan

The addition of warning statements regarding medicine interactions is proposed.

The current RASML entry for dextromethorphan does not include a warning regarding medicine interactions. Dextromethorphan is contraindicated in those taking monoamine oxidase inhibitors (MAOIs), or who have taken MAOIs within 14 days, due to risk of serotonin toxicity.

The following points are noted:

- MAOIs are used in depression (phenelzine, moclobemide), Parkinson's disease (selegiline/rasagiline/safinamide) and serious infection (linezolid).

- Some non-MAOI antidepressants can also potentially interact with dextromethorphan to cause serotonin toxicity, but the risk is lower than for MAOIs. The Product Information for Bisolvon Dry states that "*dextromethorphan should not be used with MAOIs and be used with caution in patients receiving other serotonergic drugs.*"
- The recently deleted OTC Medicine Monograph (for N2 application pathway) required the following warning: "*Do not take this medicine if you are taking a monoamine oxidase inhibitor (MAOI) or an antidepressant, or have taken the MAOI or antidepressant medicine within the past two weeks."*

Based on the above, the following warnings are proposed:

- Do not take this medicine if you are taking, or have taken in the past 14 days, a monoamine oxidase inhibitor (MAOI).
- Talk to a doctor or pharmacist before use if you are taking medicine for depression or anxiety.

The current RASML entries are presented below with the proposed additional warnings in red:

Substances	Circumstances	Required statements
Dextromethorphan *(Entry 1 of 2)*	In oral preparations indicated for cough, cold or flu which DO NOT include dosage instructions for children aged under 12 years	• Do not give to children under 12 years of age. • If [coughing/symptoms] persist(s), consult your doctor or pharmacist. • Do not take this medicine if you are taking, or have taken in the past 14 days, a monoamine oxidase inhibitor (MAOI). • Talk to a doctor or pharmacist before use if you are taking medicine for depression or anxiety.
Dextromethorphan *(Entry 2 of 2)*	In oral preparations indicated for cough, cold or flu which include dosage instructions for children aged from 'x' to 11 years (where 'x' is 6, 7, 8, 9, 10 or 11)	• Do not give to children under 'x' years of age. • *either (if 'x' is 11)* – Do not give to children aged 11 years, except on the advice of a doctor, pharmacist or nurse practitioner. *or (if 'x' is 6, 7, 8, 9 or 10)* – Do not give to children aged between 'x' and 11 years of age, except on the advice of a doctor, pharmacist or nurse practitioner. • If [coughing/symptoms] persist(s), consult your doctor or pharmacist. • Do not take this medicine if you are taking, or have taken in the past 14 days, a monoamine oxidase inhibitor (MAOI). • Talk to a doctor or pharmacist before use if you are taking medicine for depression or anxiety.

Ibuprofen

Addition of a warning regarding use in those aged 65 years and over

Currently RASML only requires the warning statement "*Unless a doctor has told you to, do not use if you are aged 65 years or over*" for unscheduled ibuprofen-containing medicines (Entries 1 and 3; Item nos. 128 and 130) and not for S2 or S3 medicines (Entries 2 and 4). It is proposed to address this

inconsistency by amending the entries to similarly require scheduled (S2 and S3) ibuprofen-containing medicines to require the same warning.

Background

A sponsor-initiated request to remove the RASML-required warning statement regarding use in those aged 65 years and over from unscheduled ibuprofen-containing medicines was considered in 2024. Consideration included review of relevant up-to-date published literature regarding safety of ibuprofen use in older populations.

Consideration of the request found that the available evidence did not support removal of the warning. While serious adverse events associated with short-term, over-the-counter use of ibuprofen are relatively rare, the evidence suggests that older adults are at higher risk of adverse effects, particularly gastrointestinal events. The available data are limited by confounding factors (including higher doses, longer durations of use, and comorbidities) but nevertheless support the need for caution in this population.

Older patients are more likely to have underlying risk factors or concomitant medication use that may increase the likelihood or severity of adverse effects associated with non-steroidal anti-inflammatory drugs (NSAIDs). These include increased risk of gastrointestinal bleeding and ulceration, renal impairment (including in the context of concomitant ACE inhibitor or diuretic use), cardiovascular effects, and drug interactions (e.g. with anticoagulants or antiplatelet agents).

The warning statement is intended to mitigate these risks by prompting consumers aged 65 years and over to seek medical advice prior to use, particularly where individual risk factors may not be readily identifiable. This is considered especially important given the potential for repeated short-term use in the management of chronic or recurrent pain in older populations.

The United States Food and Drug Administration (FDA) requires labelling of NSAIDs to include warnings highlighting an increased risk of stomach bleeding in individuals aged 60 years and over and directs such patients to seek medical advice prior to use.

Extending the existing warning requirement to scheduled ibuprofen products addresses the current inconsistency in RASML.

While the current ‘Entry 4’ applies to medicines for use in children under 12 years of age, such medicines may also be used by older consumers. The inclusion of the warning is consistent with the current ‘Entry 3’, which likewise applies to children under 12 years of age but still includes the warning statement regarding use in those aged 65 years and over. A similar approach is taken with pregnancy warnings for products intended for paediatric use.

Proposed change

Current Entries 1 and 2 include the same warnings except that Entry 2 does not include the warning regarding use in those aged 65 years and over. In requiring this warning in Entry 2, Entries 1 and 2 can be merged, to cover “*preparations for oral use in adults and children aged 12 years and over*”.

Entries 3 and 4 apply to children under 12 years of age and include the children-specific warning “*Ask your doctor or pharmacist before use of the medicine in children suffering from dehydration through diarrhoea and/or vomiting.*” Entry 3, which applies only to unscheduled products, also includes the warning “*Do not use in children under 6 years of age*”. Because of this difference, it is intended to retain Entries 3 and 4 (to become Entries 2 & 3) and add the warning regarding use in those aged 65 years and over to the current Entry 3 (to be Entry 2).

Changes to format and wording without changes in meaning

The following changes are proposed:

- It is proposed to revise the presentation of the warnings to improve readability and efficient use of label space, by grouping some of the warnings in a single dot point (warnings for stomach ulcer, impaired kidney function and heart failure), grouping some warnings under the lead-in “*Do not use if you*” and adjusting the order of information.

It should be noted that the wording and format set out in RASML are not mandatory. Alternative wording may be used, provided the meaning is unchanged, and sponsors may adopt more restrictive statements where appropriate. These proposed changes to format and wording of the RASML entries do not necessitate changes to existing compliant labelling.

It is acknowledged that there are multiple different ways this information could be presented in RASML (e.g. through different lead-ins or subheadings); however, the proposed format is considered to provide an appropriate balance of clarity, conciseness and prioritisation of key risks. Currently, sponsors often replicate the wording and order in RASML verbatim, which may not result in the most effective presentation, or alternatively attempt to group warnings in a suboptimal or incorrect manner.

- It is proposed to change the current warning statement in Entry 3 from "*Do not use in children 6 years of age or less*" to "*Do not use in children under 7 years of age*". There is no change to the meaning, and either wording would comply with the required meaning. However, the current wording can be misinterpreted and has caused confusion in the past, while the proposed wording is consistent with other similar age restriction warnings in RASML. Therefore, the proposed wording is preferred.

Proposed changes (overall)

Proposed changes are indicated below in red text, or green for relocated text. A clean version of the proposed entries is included further below.

Substances	Circumstances	Required statements
Ibuprofen *(Entry 1 of ~~65~~)*	~~For the purpose of exclusion from the schedules to the current Poisons Standard, when the~~ In preparations ~~is~~ for oral use in adults and children aged 12 years and over.	• Do not use if you: – have a stomach ulcer, impaired kidney function or heart failure – have asthma, unless advised by a doctor ~~• Do not use if you have impaired kidney function.~~ ~~• Do not use if you have heart failure.~~ – are trying to become pregnant, or during the first 6 months of pregnancy, except on the advice of a doctor. Do not use at all during the last 3 months of pregnancy – are aged 65 years or over, except on the advice of a doctor – ~~Do not use if you~~ are allergic to ibuprofen or other anti-inflammatory medicines. ~~• If you get an allergic reaction, stop taking and see your doctor immediately.~~ ~~• Unless a doctor has told you to, do not use if you have asthma.~~ • Unless advised by ~~your~~ a doctor or pharmacist, do not use with products containing ibuprofen, aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly. • Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage. ~~• Do not use if trying to become pregnant, or during the first 6 months of pregnancy, except on doctor's advice. Do not use at all during the last 3 months of pregnancy.~~ ~~• Unless a doctor has told you to, do not use if you are aged 65 years or over.~~

Substances	Circumstances	Required statements
		• If you get an allergic reaction, stop taking and see ~~your~~ a doctor immediately.
~~Ibuprofen *(Entry 2 of 6)*~~	~~When included in a schedule to the current Poisons Standard for oral use in adults and children aged 12 years and over~~	~~• Do not use if you have a stomach ulcer.~~ ~~• Do not use if you have impaired kidney function.~~ ~~• Do not use if you have heart failure.~~ ~~• Do not use if you are allergic to ibuprofen or other anti-inflammatory medicines.~~ ~~• If you get an allergic reaction, stop taking and see your doctor immediately.~~ ~~• Unless a doctor has told you to, do not use if you have asthma.~~ ~~• Unless advised by your doctor or pharmacist, do not use with products containing ibuprofen, aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly.~~ ~~• Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage.~~ ~~• Do not use if trying to become pregnant, or during the first 6 months of pregnancy, except on doctor's advice. Do not use at all during the last 3 months of pregnancy.~~
Ibuprofen *(Entry ~~32~~ 32 of ~~65~~ 65)*	For the purpose of exclusion from the schedules to the current Poisons Standard, for oral use in children under 12 years of age	• Do not use if you: – have a stomach ulcer, impaired kidney function or heart failure – have asthma, unless advised by a doctor ~~• Do not use if you have impaired kidney function.~~ ~~• Do not use if you have heart failure.~~ – are trying to become pregnant, or during the first 6 months of pregnancy, except on the advice of a doctor. Do not use at all during the last 3 months of pregnancy – are aged 65 years or over, except on the advice of a doctor – ~~Do not use if you~~ are allergic to ibuprofen or other anti-inflammatory medicines. • Do not use in children ~~6~~ under 7 years of age ~~or less~~ ~~• If you get an allergic reaction, stop taking and see your doctor immediately.~~ ~~• Unless a doctor has told you to, do not use if you have asthma.~~ • Unless advised by ~~your~~ a doctor or pharmacist, do not use: – with products containing ibuprofen, aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly. – in children suffering from dehydration through diarrhoea and/or vomiting • Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage.

Substances	Circumstances	Required statements
		• ~~Do not use if trying to become pregnant, or during the first 6 months of pregnancy, except on doctor's advice. Do not use at all during the last 3 months of pregnancy.~~ • ~~Ask your doctor or pharmacist before use of the medicine in children suffering from dehydration through diarrhoea and/or vomiting.~~ • ~~Unless a doctor has told you to, do not use if you are aged 65 years or over.~~ • If you get an allergic reaction, stop taking and see ~~your~~ a doctor immediately. • ~~Do not use in children 6 years of age or less~~
Ibuprofen *(Entry ~~43~~ of ~~65~~)*	When included in a schedule to the current Poisons Standard for oral use in children under 12 years of age	• Do not use if you: – have a stomach ulcer, impaired kidney function or heart failure – have asthma, unless advised by a doctor • ~~Do not use if you have impaired kidney function.~~ • ~~Do not use if you have heart failure.~~ – are trying to become pregnant, or during the first 6 months of pregnancy, except on the advice of a doctor. Do not use at all during the last 3 months of pregnancy – are aged 65 years or over, except on the advice of a doctor – ~~Do not use if you~~ are allergic to ibuprofen or other anti-inflammatory medicines. • ~~If you get an allergic reaction, stop taking and see your doctor immediately.~~ • ~~Unless a doctor has told you to, do not use if you have asthma.~~ • Unless advised by ~~your~~ a doctor or pharmacist, do not use: – with products containing ibuprofen, aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly. – in children suffering from dehydration through diarrhoea and/or vomiting • Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage. • ~~Do not use if trying to become pregnant, or during the first 6 months of pregnancy, except on doctor's advice. Do not use at all during the last 3 months of pregnancy.~~ • ~~Ask your doctor or pharmacist before use of the medicine in children suffering from dehydration through diarrhoea and/or vomiting.~~ • If you get an allergic reaction, stop taking and see ~~your~~ a doctor immediately.
Ibuprofen *(Entry ~~54~~ of ~~65~~)*	In combination with paracetamol, in medicines for oral use	< Warnings unchanged >

Substances	Circumstances	Required statements
Ibuprofen *(Entry ~~65~~ of ~~65~~)*	In preparations for external use	< Warnings unchanged >

Proposed entries (without mark-up):

Substances	Circumstances	Required Statements
Ibuprofen *(Entry 1 of 5)*	In preparations for oral use in adults and children aged 12 years and over.	• Do not use if you: – have a stomach ulcer, impaired kidney function or heart failure – have asthma, unless advised by a doctor – are trying to become pregnant, or during the first 6 months of pregnancy, except on the advice of a doctor. Do not use at all during the last 3 months of pregnancy – are aged 65 years or over, except on the advice of a doctor – are allergic to ibuprofen or other anti-inflammatory medicines. • Unless advised by a doctor or pharmacist, do not use with products containing ibuprofen, aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly. • Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage. • If you get an allergic reaction, stop taking and see a doctor immediately.
Ibuprofen *(Entry 2 of 5)*	For the purpose of exclusion from the schedules to the current Poisons Standard, for oral use in children under 12 years of age	• Do not use if you: – have a stomach ulcer, impaired kidney function or heart failure – have asthma, unless advised by a doctor – are trying to become pregnant, or during the first 6 months of pregnancy, except on the advice of a doctor. Do not use at all during the last 3 months of pregnancy – are aged 65 years or over, except on the advice of a doctor – are allergic to ibuprofen or other anti-inflammatory medicines. • Do not use in children under 7 years of age • Unless advised by a doctor or pharmacist, do not use: – with products containing ibuprofen, aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly. – in children suffering from dehydration through diarrhoea and/or vomiting • Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage.

Substances	Circumstances	Required Statements
		• If you get an allergic reaction, stop taking and see a doctor immediately.
Ibuprofen *(Entry 3 of 5)*	When included in a schedule to the current Poisons Standard for oral use in children under 12 years of age	• Do not use if you: – have a stomach ulcer, impaired kidney function or heart failure – have asthma, unless advised by a doctor – are trying to become pregnant, or during the first 6 months of pregnancy, except on the advice of a doctor. Do not use at all during the last 3 months of pregnancy – are aged 65 years or over, except on the advice of a doctor – are allergic to ibuprofen or other anti-inflammatory medicines. • Unless advised by a doctor or pharmacist, do not use: – with products containing ibuprofen, aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly. – in children suffering from dehydration through diarrhoea and/or vomiting • Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage. • If you get an allergic reaction, stop taking and see a doctor immediately.
Ibuprofen *(Entry 4 of 5)*	In combination with paracetamol, in medicines for oral use	< Warnings unchanged >
Ibuprofen *(Entry 5 of 5)*	In preparations for external use	< Warnings unchanged >

Other minor changes

Aspartame

It is proposed that this entry, shown below, be deleted. The declaration of aspartame on product labelling under the heading 'Warnings' is already required by Therapeutic Goods Order No. 92 (TGO 92). Retention of the entry in RASML is unnecessary duplication and is inconsistent with the regulatory approach under which warnings for numerous other excipients (e.g. gluten, sugars, sugar alcohols) are captured exclusively under TGO 92. While TGO 92 currently only requires reference to "Contains aspartame", it is intended to revise the Order to require reference to "Contains aspartame (phenylalanine)", which is considered appropriate and sufficient to alert consumers, including those with phenylketonuria.

Substances	Circumstances	Required statements
~~Aspartame~~	~~When for oral ingestion and included in medicines as an active or excipient ingredient~~	~~• Phenylketonurics are warned that this product contains aspartame (phenylalanine).~~

Benzoyl peroxide

It is proposed to revise the wording for the circumstance in which the specified warnings apply from "*In Schedule 2 to the current Poisons Standard*" to "*In dermal preparations*", so that warning requirements also apply to unscheduled products (which contain 5% or less of benzoyl peroxide). This is consistent with the current Australian Regulatory Guidance for OTC Medicines (ARGOM) and with previously approved and currently registered medicines. Other minor editorial changes to the warning statements are also proposed, as below:

Proposed amendments:

Substances	Circumstances	Required statements
Benzoyl peroxide	In ~~Schedule 2 to the current Poisons Standard~~ dermal preparations	• Keep from eyes, lips, mouth and sensitive areas of the neck. • If excessive swelling, irritation, redness or peeling occurs, discontinue use. See a doctor if these persist. • ~~If these persist, consult a physician.~~ • Avoid excessive exposure to sunlight and other sources of ~~ultra violet~~ ultraviolet light.

Chelidonium majus

It is proposed to revise the current RASML entry to be consistent with the entry in the Permitted Ingredients Determination, which was updated in 2024 after public consultation to the following:

Item	Ingredient Name	Purpose	Specific requirements
1332	CHELIDONIUM MAJUS	A, E, H	• When the medicine is for oral or sublingual use, the following warning statement is required on the medicine label: • (CELAND1) 'In rare cases, Chelidonium majus may harm the liver. Stop use and see a doctor if you have yellowing skin/eyes or unusual: fatigue, nausea, appetite loss, abdominal pain or dark urine.'

Accordingly, the following changes are proposed to the RASML entry:

Substances	Circumstances	Required statements
Chelidonium majus	When the preparation is for oral use	• ~~Warning: Greater Celandine may harm the liver in some people.~~ In rare cases, Chelidonium majus may harm the liver. Stop use and see a doctor if you have yellowing skin/eyes or unusual: fatigue, nausea, appetite loss, abdominal pain or dark urine. • Use only under the supervision of a healthcare professional.

Note: There is currently only one registered product containing this ingredient.

Minor editorial changes

- Removal of the signal words 'CAUTION' and 'WARNING' from several RASML advisory statements. TGO 92 requires advisory statements to be presented under the heading 'Warnings' in the consumer health information (CHI) panel. The inclusion of 'CAUTION' or 'WARNING' within

individual statements is unnecessary, may reduce readability and is inconsistent with statements for other entries. Affected entries are as follows:

Substance	Required statements
H2 antagonists: cimetidine, famotidine, nizatidine, ranitidine Proton pump inhibitors: esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole	• ~~CAUTION:~~ This preparation is for the relief of minor and temporary ailments and should be used strictly as directed.
Alclometasone	• ~~CAUTION –~~ Do not use for children under 2 years old unless a doctor has told you to.
Clobetasone	• ~~CAUTION –~~ Do not use for children under 12 years old unless a doctor has told you to.
Diethyltoluamide (DEET)	• ~~WARNING –~~ May be dangerous, particularly to children, if you use large amounts on the skin, clothes or bedding or on large areas of the body, especially if you keep using it for a long time.
Hydroquinone	• ~~WARNING –~~ If a pigmented spot or mole has recently become darker, changed colour, become enlarged or itchy, or bleeds, do not use this product, see your doctor immediately.
Iodine	• ~~CAUTION –~~ Total iodine intake may exceed recommended level when taking this preparation. • ~~WARNING –~~ Contains iodine - do not take when pregnant except on physician's advice.
Piper methysticum	• ~~WARNING:~~ Not for prolonged use
Podophyllin (Entry 1 of 2) and Podophyllotoxin (Entry 1 of 2)	• ~~WARNING –~~ Do not use on face or on anal or genital areas except on doctor's advice.
Podophyllin (Entry 1 of 2) and Podophyllotoxin (Entry 2 of 2)	• ~~WARNING –~~ Do not use on face or on anal or genital areas.
Silver salts	• ~~WARNING –~~ Overuse may stain the skin or mouth.
Zinc compounds	• *either* – ~~WARNING –~~ This medication may be dangerous when used in large amounts or for a long period. *or* – ~~WARNING –~~ Contains zinc, which may be dangerous when used in large amounts or for a long period.

Warning statements for pyridoxal and pyridoxine entries (4) also include "WARNING". However, these specific entries are to be considered separately at a later date in relation to further required changes.

- **Amethocaine (tetracaine)** – delete these entries (item nos. 5 and 6) and amend item nos. 252 and 253 from “Tetracaine (amethocaine)” to “Tetracaine”, as mandatory dual naming of tetracaine-containing medicines expired in April 2025.
- **Lidocaine (Lignocaine)** – amend item nos. 151 to 154 from “Lidocaine (Lignocaine)” to “Lidocaine”. The transition period for moving to the single name expired in April 2026.
- **Iodine** (Entry 2 of 2; Item no 136) – replace ‘physician’ with ‘doctor’

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 should be relevant to matters specifically raised in this consultation and must be received by the closing date.

Question (for each substance entry and for ‘other minor changes’)

Do you support the proposed wording of the advisory statements and proposed changes to existing entries?

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 ‘Online Survey’ on the consultation page and include your response using the free text fields 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 / Complementary and OTC Medicines Branch	July 2026

Therapeutic Goods Administration

PO Box 100 Woden ACT 2606 Australia
Email: info@tga.gov.au Phone: 1800 020 653 Fax: 02 6203 1605
https://www.tga.gov.au

Reference D26-3272343