Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

Consultation: Proposed amendments to the Poisons Standard – ACMS, ACCS and Joint ACMS-ACCS meetings, November 2023

1 September 2023

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About this consultation

Subdivision 3D.2 of the *Therapeutic Goods Regulations 1990* (the **Regulations**) sets out the procedure to be followed where the Secretary receives an application under section 52EAA of the *Therapeutic Goods Act 1989* (the **Act**) to amend the current Poisons Standard or decides to amend the Poisons Standard on his or her own initiative and decides to refer the proposed amendment to an expert advisory committee. These include, under regulation 42ZCZK, that the Secretary publish (in a manner the Secretary considers appropriate) the proposed amendment to be referred to an expert advisory committee, the committee to which the proposed amendment will be referred, and the date of the committee meeting. The Secretary must also invite public submissions to be made to the expert advisory committee by a date mentioned in the notice as the closing date, allowing at least 20 business days after publication of the notice.

In accordance with regulation 42ZCZK of the Regulations, the Secretary invites public submissions on scheduling proposals referred to the November 2023 meetings of the Advisory Committee on Medicines and Chemicals Scheduling. Submissions must be received by close of business **29 September 2023.**

Submissions should be provided through our consultation hub. Any submission about any of the proposals to amend the Poisons Standard will be considered at the next meeting of the Advisory Committee on Medicines Scheduling (ACMS), meeting of the Advisory Committee on Chemicals Scheduling (ACCS), or a joint meeting of these two committees.

This consultation closes on 29 September 2023.

We aim to provide documents in an accessible format. If you're having problems using this document, please contact medicines.scheduling@health.gov.au.

1 Proposed amendments referred for scheduling advice to ACMS meeting #43, November 2023

1.1 Astodrimer sodium

Proposal

The applicant has proposed an amendment of the Schedule 3 entry relating to astodrimer sodium. The proposed amendment would exempt astodrimer sodium from scheduling when in a barrier nasal spray preparation. Astodrimer sodium is currently approved for use as an active ingredient in medical devices only.

CAS number

676271-69-5

Alternative names

2, 6-Bis-{(1-napthalenyl-3,6-disulfonic acid)-oxyacetamido}-2,6-bis-2,6-bis-2,6-bis-(2,6-diamino-hexanoylamino)-2,6-diamino-hexanoic acid (diphenylmethyl)-amide, polysodium salt; SPL7013

Applicant

Private applicant

Proposed Scheduling

Astodrimer sodium is currently listed in Schedule 3, Appendix F and Appendix H of the Poisons Standard.

The applicant's proposed amendments to the Poisons Standard are:[1]

Schedule 3 – Amend Entry

ASTODRIMER SODIUM except when used in:

(a) a condom lubricant; or
(b) a barrier nasal spray.

Index

ASTODRIMER SODIUM

Schedule 3
Appendix F, clause 4
Appendix H, clause 1

[1] Proposed additions are shown in green underlined font, proposed deletions are shown in red strikethrough font, and text without this formatting represents the current text in the Poisons Standard.

Appendix F, clause 4 – Poisons that must be labelled with warning statements and safety directions.

Item	Poison	Warning statement
30	ASTODRIMER SODIUM – for the treatment and relief of bacterial vaginosis	**63** – See a doctor (or) (dentist) if no better after (Insert number of days as approved Product Information) days.
		64 – If getting better, keep using for (Insert number of days as per approved Product Information) days.
		69 – If symptoms recur within two weeks of completing the course, consult a doctor.
		75 – Do not use under waterproof bandages unless a doctor has told you to.
		109 – See your healthcare provider is you consider that you may be at risk of a Sexually Transmitted Infection (STI).
		110 – See a doctor if you plan to become pregnant or are breastfeeding or plan to breastfeed.
31	ASTODRIMER SODIUM – for the prevention of recurrent bacterial vaginosis	**63** – See a doctor (or) (dentist) if no better after (Insert number of days as approved Product Information) days.
		75 – Do not sue under waterproof bandages unless a doctor has told you to.
		109 – See your healthcare provider is you consider that you may be at risk of a Sexually Transmitted Infection (STI).
		110 – See a doctor if you plan to become pregnant or are breastfeeding or plan to breastfeed.

Appendix H, clause 1 – Schedule 3 medicines permitted to be advertised.

Item	Poison
3	ASTODRIMER SODIUM – for the treatment and relief of bacterial vaginosis and for the prevention of recurrent bacterial vaginosis

Background

Astodrimer sodium is a low toxicity, non-antibiotic, microbicidal that is used in the treatment of bacterial vaginosis as a topical gel and the prevention of sexually transmitted diseases (STD) as a condom lubricant.

Astodrimer sodium is currently a Schedule 3 medication (except when used in condom lubricants) with labelled warning statements of ‘for the treatment and relief of bacterial vaginosis’ and ‘for the prevention of recurrent bacterial vaginosis.’ The Appendix H entry permits advertising of Schedule 3 preparations containing astodrimer for these indications.

Summary of applicant's reasons for the proposal

- The non-serious and self-limiting nature of the condition (the common cold) is consistent with the risk profile of over-the-counter (OTC) medicines. Similar products used in the treatment of the condition are OTC medicines and readily available in Australia.
- The purpose of astodrimer sodium inclusion in a nasal spray product is to act as a physical barrier to trap and block cold viruses such as the common cold, allowing the body's natural defences to remove them with the nasal mucus.
- Astodrimer sodium poses low risk of harm, as noted in the delegate's previous decision in November 2021. The risks associated with misuse, abuse and overuse are very low. Astodrimer sodium is not systemically absorbed when used as a barrier nasal spray.
- Adverse effects are rare and well-characterised; with no known interactions with commonly used food and consumables, or contra-indications. The risk profile of the substance is well defined, and risks can be appropriately managed through labelling and packaging.
- The use of astodrimer sodium in a nasal spray is not likely to mask the symptoms or delay diagnosis of a serious condition. Appropriate labelling and packaging can manage any perceived risk.

Key uses / expected use

Used in medical devices.

Australian regulations

- According to the TGA Ingredient Database, astodrimer sodium is:
  - Available for use as an Active ingredient in Devices
  - Available for use as an Excipient in Devices
  - Not available as an Equivalent Ingredient in any application
- As of July 2023, there were no medicines containing astodrimer sodium on the Australian Register of Therapeutic Goods (ARTG).
- Astodrimer sodium is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination No.3 of 2023.
- Astodrimer sodium is not listed in the TGA prescribing medicines in pregnancy database.
- There are no warning statements pertaining to astodrimer sodium in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.
- As of July 2023, there were no reports of adverse events for products containing astodrimer sodium as an active ingredient on the Database of Adverse Event Notifications (DAEN).
- As of July 2023, there were no products containing astodrimer sodium as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS).

International regulations

- Astodrimer sodium is not included in the Health Canada drug product database, the United States Food and Drug Administration's approved drug products database, the New Zealand Inventory of Chemicals, the New Zealand Medicines and Medical Devices Safety Authority (MedSafe), the European Commission database for information on cosmetic substances and ingredients, or Ireland's Health Products Regulatory Authority medicines database.

1.2 Bilastine

Proposal

The applicant proposed to extend the availability of bilastine through a pharmacist without requiring a prescription by removing the current phrasing which limits the Schedule 3 entry to divided preparations and reducing the age restriction from 12 to 6 years of age. The applicant has not proposed any changes to the Appendix H entry.

CAS number

202189-78-4

Alternative names

4-[2-[4-[1-(2-Ethoxyethyl)-1*H*-benzimidazol-2-yl]-1-piperidinyl]ethyl]-α,α-dimethylbenzeneacetic acid

Applicant

Private applicant

Proposed Scheduling

The applicant's proposed amendments to the Poisons Standard are:[2]

Schedule 3 – Amend entry

BILASTINE in ~~divided~~ oral preparations when labelled with a recommended daily dose not exceeding ~~containing~~ 20 mg ~~or less~~ of bilastine for the treatment of adults and children ~~adolescents~~ 6~~12~~ years of age and older.

Index

BILASTINE
Schedule 4
Schedule 3
Appendix H, clause 1

Appendix H, clause 1 – Schedule 3 medicines permitted to be advertised.

Item	Poison
4	BILASTINE

2 Proposed additions are shown in green underlined font, proposed deletions are shown in red strikethrough font, and text without this formatting represents the current text in the Poisons Standard.

Background

Bilastine is an antihistamine that is used for the symptomatic treatment of seasonal and perennial allergic rhino-conjunctivitis and urticaria. Bilastine is currently available as 20 mg tablets in pack sizes of 10 and 30. Over the counter preparations of bilastine were permitted in 2021 in divided oral preparations containing 20 mg or less for adults and adolescents 12 years of age and older.

Summary of applicant's reasons for the proposal

- Allergic rhinitis (commonly known as hay fever), both seasonal and perennial, is the most common allergic condition in Australia with an estimated 10% of the total population self-reporting the condition in 2017-2018. Allergic rhinitis is a risk factor for developing asthma and Australia has amongst the highest incidence of developed countries.
- Allergic rhino-conjunctivitis is known to be most prevalent during the school age years but is rare in children below 5 years of age. Sleep disruption often results in daytime fatigue, increased class distraction or absenteeism, reduced focus on schoolwork and other curricular activities. Therefore, symptomatic treatment is as important in school age children as in adults.
- Bilastine is a non-sedating antihistamine which provides an effective once a day relief for common symptoms such as itchy, red or watery eyes, sneezing, runny or blocked nose, itchy throat, coughing and skin rashes/hives (urticaria) caused by allergies to certain plant and animal material.
- The extension of treatment to the younger population necessitates the development of more palatable formulations such as an oral liquid or orally disintegrating tablets. An oral liquid formulation under the current scheduling would be classified as a prescription only medicine (current Schedule 3 entry limits preparations to 'divided' medicines only).
- Other paediatric formulations of non-sedating antihistamines have been available in Australia without a physician's prescription for more than 25 years. Although bilastine is relatively new in Australia, the substance is indicated for the treatment of similar conditions and has a comparable safety profile to other non-sedating antihistamines.

Key uses / expected use

Medicines

Australian regulations

- According to the TGA Ingredient Database, bilastine is:
  - Available for use as an Active Ingredient in Export Only, Over the Counter and Prescription Medicines
  - Not available as an Excipient Ingredient in any application
  - Not available as an Equivalent Ingredient in any application.
- As of July 2023, there was one medicine currently active on the Australian Register of Therapeutic Goods (ARTG) that contain bilastine as an active ingredient. It is a non-prescription medicine.
- Bilastine is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination No.3 of 2023.

- The TGA prescribing medicines in pregnancy database classifies bilastine as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Bilastine	B3	Allergy and Immune System	Antihistamines	
Category B3 – Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed. Studies in animals have shown evidence of an increased occurrence of foetal damage, the significance of which is considered uncertain in humans.				

- There are no warning statements pertaining to bilastine in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.
- As of July 2023, there were 6 reports of adverse events for products containing bilastine as an active ingredient on the Database of Adverse Event Notifications (DAEN), with 6 reports where bilastine was the single suspected medicine. The reported events were diverse in nature.
- As of July 2023, there were no products containing bilastine as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS).

International regulations

- Bilastine is not found in the US FDA database. However, it is listed in the US Global Substance Registration System.
- In the EU according to the European Medicines Agency, bilastine is available in 20 mg preparations.
- The Ireland Health Products Regulation Authority has approved 6 products containing bilastine as an active ingredient. These products consist of 2.5 mg/mL oral solution, 6 mg/mL eye drop solution and 20 mg tablet preparations.
- New Zealand Medicines and Medical Devices Safety Authority (MedSafe) list bilastine as a Prescription Only medicine, except when in divided solid dosage forms for oral use containing 20 mg or less for the treatment of allergic rhino-conjunctivitis (seasonal and perennial) and urticaria.
- The UK Electronic Medicines Compendium (emc) has approved bilastine in 10 and 20 mg tablets for oral use to treat allergic rhino-conjunctivitis (seasonal and perennial) and urticaria, for adults and adolescents aged 12 years and over. The emc also lists a 2.5 mg/mL oral solution for the same indication for children aged 6-11 years of age, with a body weight of at least 20 kg.
- Health Canada has bilastine approved as a prescription only medicine and has a 10 mg and 20 mg oral tablet preparation, and a 2.5 mg/mL oral solution.

1.3 BPC-157

Proposal

The TGA is seeking public comment regarding the creation of a Schedule 4 entry for BPC-157, with an additional entry Appendix D, clause 5 entry. The new entries would restrict access to BPC-157 to be a prescription-only medicine with possession of the substance without authority being illegal.

CAS number

137525-51-0

Alternative names

Bepecin, Body protection compound 157, PL-10, PL-14736, PLD-116

Applicant

Delegate of the Secretary of the Department of Health and Aged Care (Delegate-initiated proposal).

Proposed Scheduling

BPC-157 is not currently listed on the Poisons Standard, nor is it regarded as a derivative of any listed substance on the Standard.

The Delegate's proposed amendments to the Poisons Standard are:[3]

Schedule 4 – New Entry

BPC-157

Appendix D, clause 5 – New Entry

Item	Poison
4a	BPC-157

Index – New Entry

BPC-157

Schedule 4
Appendix D, clause 5

Background

BPC-157 is a synthetic pentadecapeptide with unsubstantiated claims for enhancement of human healing from injuries and organ damage (including bone or joint healing, stomach ulcers, and organ damage) and enhanced athletic performance. In January 2022, BPC-157 was listed under the S0 Non-Approved Substances category of the World Anti-Doping Agency (WADA) list[4] and is prohibited for use in sports at all times (in and out of competition).

[3] Proposed additions are shown in green underlined font, proposed deletions are shown in red strikethrough font, and text without this formatting represents the current text in the Poisons Standard.

Summary of the reasons for the proposal

- BPC-157 is acknowledged in open sources as an experimental therapy with no related clinical data in humans. The experimental nature of BPC-157 justifies medical professional oversight to monitor for potential side effects, especially for continued or repeated use.
- Group entries for growth hormone releasing hormones, peptides and secretagogues are included under Schedule 4 and Appendix D of the Act. Similar substances, such as THYMOSIN BETA-4, AOD-9604, CJC-1295, PRALMORELIN, GROWTH HORMONE RELEASING PEPTIDE 6, HEXARELIN, and IPAMORELIN have been included in Schedule 4 with additional Appendix D conditions.
- The limited available research on the risks and benefits of use and associated toxicity, the experimental nature of the substances, and the potential for abuse given that the substances are used as performance enhancing drugs satisfy criteria for inclusion in Schedule 4 and Appendix D (Item 5) of the Act.
- BPC-157 aligns with several Schedule 4 factors in the SPF, particularly:
    1. The ailments or symptoms that the substance is used for require medical, veterinary or dental intervention,
    2. The use of the substance requires adjunctive therapy or evaluation or specialised handling for administration, and
    8. The experience of the use of the substance under normal clinical conditions is limited.

Key uses / expected use

Medicines

Australian regulations

- BPC-157 is not a listed ingredient on the TGA Ingredient Database.
- As of August 2023, there were no medicines currently active on the Australian Register of Therapeutic Goods (ARTG) that contain BPC-157 as an active ingredient.
- BPC-157 is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination No.3 of 2023.
- The TGA prescribing medicines in pregnancy database does not include a classification for BPC-157.
- There are no warning statements pertaining to BPC-157 in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.
- As of August 2023, there was one report of an adverse event for products containing BPC-157 as an active ingredient on the Database of Adverse Event Notifications (DAEN), with no reports where BPC-157 was the single suspected medicine. The report related to a hypersensitive reaction.
- As of August 2023, there were no products containing BPC-157 as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS).

International regulations

- BPC-157 is not registered with the United States Food and Drug Administration, the European Commission database for information on cosmetic substances and ingredients or the European Commission Union Register of medicinal products. Similarly, BPC-157 is not listed in the New Zealand MedSafe database, the Canadian Drug Product Database, the United Kingdom MHRA database or the HPRA of Ireland database.

1.4 Glycopyrronium

Proposal

The applicant has proposed an Appendix H listing for glycopyrronium to allow the advertisement of Schedule 3 preparations containing this substance.

CAS number

596-51-0

Alternative names

Glycopyrrolate; 3-[2-Cyclopentyl(hydroxy)phenylacetoxy]-1,1-dimethylpyrrolidinium bromide

Applicant

Private applicant

Proposed Scheduling

Glycopyrronium is currently listed in Schedules 3 and 4 of the Poisons Standard.

The applicant's proposed amendments to the Poisons Standard are:[5]

Schedule 4

GLYCOPYRRONIUM in preparations for injection.

Schedule 3

GLYCOPYRRONIUM except when included in Schedule 4.

Index – Amend entry

GLYCOPYRRONIUM

Schedule 4
Schedule 3
Appendix H, clause 1

[5] Proposed additions are shown in green underlined font, proposed deletions are shown in red strikethrough font, and text without this formatting represents the current text in the Poisons Standard.

Appendix H – New Entry

Item	Poison
19a	GLYCOPYRRONIUM

Background

Glycopyrronium is an anticholinergic medicine that is available for inhalation for the symptomatic relief in patients with chronic obstructive pulmonary disease (COPD). It is also available in preparations for injection for the reduction of salivary and tracheobronchial secretions and the reversal of residual non-depolarising neuromuscular block. Glycopyrronium for topical use, in the treatment of excessive underarm sweating (primary axillary hyperhidrosis) in adults and adolescents 9 years and older was first approved by the FDA in 2018 as a prescription medication.

Summary of applicant's reasons for the proposal

- The applicant is proposing to include glycopyrronium in Appendix H of the Poisons Standard to permit advertising of a proposed Schedule 3 (Pharmacist Only) product, a topical cream that contains glycopyrronium as an active ingredient, for the treatment of primary axillary hyperhidrosis in adults.
- Primary hyperhidrosis is a stigmatising disease characterised by excessive perspiration. The physical and psychological symptoms affect a patients' quality of life, including limitations to daily activities, social relationships, study and work life and emotional wellbeing.
- A medical diagnosis is required to confirm primary hyperhidrosis and to rule out secondary hyperhidrosis (i.e., resulting from an underlying medical condition). However, following initial medical diagnosis, primary hyperhidrosis is suitable for self-treatment and management by the patient and does not require close medical management by a doctor. Being a Schedule 3 medicine, the availability of a pharmacist may also assist in the monitoring of safe ongoing use of the medicine following the initial diagnosis by a doctor.
- Advertising of Schedule 3 glycopyrronium medicines will not exacerbate any potential issues that cannot be mitigated by pharmacist supervision and none that are of concern to public health. It will only serve to inform sufferers of primary axillary hyperhidrosis of the availability of a non-invasive, efficacious and generally well tolerated medicine for the treatment of their condition.

Key uses / expected use

Medicines

Australian regulations

- According to the TGA Ingredient Database, glycopyrronium is:
  - Available for use as an Active Ingredient in Export Only, Prescription Medicines
  - Not available as an Excipient Ingredient in any application
  - Not available as an Equivalent Ingredient in any application.

- As of July 2023, there were 20 medicines currently active on the Australian Register of Therapeutic Goods (ARTG) that contain glycopyrronium as an active ingredient. All were prescription medicines.
- Glycopyrronium is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination No.3 of 2023.
- The TGA prescribing medicines in pregnancy database classifies glycopyrronium as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Glycopyrronium bromide	B2	Alimentary System	Antispasmodics	
Glycopyrronium bromide	B2	Cholinergic and Anticholinergic Agents		
Glycopyrronium bromide	B3	Respiratory System	Inhalation agents	Bronchospasm relaxants
Glycopyrronium bromide / formoterol fumarate	B3	Respiratory System	Inhalation agents	
indacaterol maleate / Glycopyrronium bromide	B3	Respiratory System	Inhalation agents	
Indacaterol/Glycopyrronium	B3	Respiratory System	Inhalation agents	Bronchospasm relaxants

Category B2 – Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed.

Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of foetal damage.

Category B3 – Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed.

Studies in animals have shown evidence of an increased occurrence of foetal damage, the significance of which is considered uncertain in humans.

- There are no warning statements pertaining to glycopyrronium in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.
- From July 2013 to July 2023, there were 130 reports of adverse events for products containing glycopyrronium as an active ingredient on the Database of Adverse Event Notifications (DAEN), with 88 reports where glycopyrronium was the single suspected medicine. The major of reports appear to be related to preparations for inhalation and involved pulmonary and cardiac disorders, including dyspnoea, COPD and bradycardia.
- As of July 2023, there were no products containing glycopyrronium as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS).

International regulations

- The United States Food and Drug Administration Approved Drug Products Database lists 45 active approved products containing glycopyrronium. Of these 44 of these products are in the form of oral tablets, injections and inhalers that contain glycopyrrolate as an active ingredient, and 1 product contains glycopyrronium tosylate for topical use. All of these are available by prescription only.
- The European Commission Union Register of medical products lists 15 approved products containing glycopyrronium. These products are available as inhalers and oral solution. Glycopyrronium cream is approved as a prescription only medicine in Austria, Sweden, Finland and the Netherlands.
- New Zealand Medicines and Medical Devices Safety Authority (Medsafe) lists glycopyrronium as prescription only.
- Canada's Drug Product Database lists 15 approved products containing glycopyrronium in the form of inhalers, oral solution and injectables. All of these products are listed as prescription only products except for injectables which are classified as ethical products.
- The UK Electronic Medicines Compendium (emc) lists 22 approved products containing glycopyrronium. These products are present in the form of inhalers, oral tablets, oral solution and injections. All of these are available by prescription only.
- The Ireland Health Products Regulation Authority has 25 approved products containing glycopyrronium. These products are in the form of topical cream, inhaler, injection and oral solution. All are listed as prescription-only medicines.

1.5 Methenamine

Proposal

The applicant has proposed to create a Schedule 2 entry for methenamine and its derivatives, in preparations for oral therapeutic use. Methenamine is approved for the suppression or elimination of bacteriuria associated with chronic or recurrent urinary tract infections (UTIs) and is currently available for general sale.

CAS number

5714-73-8

Alternative names

Methenamine hippurate; Hexamine hippurate

Applicant

Private applicant

Proposed Scheduling

Methenamine is currently listed in Schedule 5 of the Poisons Standard.

The applicant's proposed amendments to the Poisons Standard are:[6]

Schedule 5

METHENAMINE in cosmetic preparations, **except** in preparations containing 0.15% or less of methenamine

Schedule 2 – New entry

METHENAMINE and its derivatives in preparations for oral therapeutic use

Index – Amend Entry

METHENAMINE
cross reference: 1,3,5,7-TETRAAZATRICYLO[3.3.1.1^{3,7}] DECANE, HEXAMINE, HEXAMETHYLENETETRAMINE

Schedule 5
Schedule 2

Background

Methenamine has several uses across the cosmetic, therapeutic, domestic, and industrial environments. Methenamine has not previously been considered for scheduling for therapeutic purposes but was placed in Schedule 5 for cosmetic uses in March 2014. Methenamine hippurate has been supplied and sold in therapeutic products in Australia since 1991.

Summary of applicant's reasons for the proposal

- The applicant has proposed to create a Schedule 2 entry for therapeutic use of methenamine. This amendment would require all products currently available at the general sales level, to be sold in pharmacies only.
- The availability of methenamine to suppress or eliminate bacteriuria associated with chronic or recurrent urinary tract infection (UTI) poses a risk to public health as the indications could mask a more serious disease, ailment, or injury. Access to discussion with a pharmacist to ensure proper use of the substance is required.
- The move to pharmacy only medicine (Schedule 2), would ensure that a pharmacist is available to assist patients who are new to the product that it is the correct treatment option for their condition and patients who are familiar with using the product will continue to be able to access it as needed over the counter in a pharmacy.
- Moving therapeutic use of methenamine to Schedule 2 will align with the controls of other international regulatory bodies and the scheduling factors for pharmacy only medicines in Australia.

[6] Proposed additions are shown in green underlined font, proposed deletions are shown in red strikethrough font, and text without this formatting represents the current text in the Poisons Standard.

Key uses / expected use

Medicines, cosmetics, domestic use, industrial use, food (preservative)

Australian regulations

- According to the TGA Ingredient Database, methenamine (hippurate) is:
  - Available for use as an Active Ingredient in Biologicals, Export Only, Over the Counter and Prescription Medicines.
  - Available for use as an Excipient ingredient in Biologicals, Devices and Prescription Medicines.
  - Not available as an Equivalent Ingredient in any application.
- As of July 2023, there were 10 medicines currently active on the Australian Register of Therapeutic Goods (ARTG) that contain methenamine (hippurate) as an active ingredient, all of which are non-prescription products.
- Methenamine is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination No.3 of 2023.
- The TGA prescribing medicines in pregnancy database classifies methenamine as:

Drug name	Category	Classification Level 1	Classification Level 2
Methenamine	A	Genitourinary system	Urinary antiseptics
Category A – Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed			

- There are no warning statements pertaining to methenamine in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.
- Between July 2013 and July 2023, there were 21 reports of adverse events for products containing methenamine as an active ingredient on the Database of Adverse Event Notifications (DAEN), with 17 reports where methenamine was the single suspected medicine. The reported events were diverse in nature.
- As of July 2023, there were no products containing methenamine as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS).

International regulations

- The US Food and Drug Administration database lists 4 products which contain methenamine. All products are prescription only medicines.
- In 2022, the New Zealand Medicines and Medical Devices Safety Authority (Medsafe) announced that products containing methenamine will be reclassified from general sale to pharmacy only medicines. The decision is due to be implemented in December 2023.
- The UK's Electronic Medicines Compendium (emc) lists 3 products containing methenamine, 2 prescription only medicines and one pharmacy only medicine.
- No products containing methenamine are listed in the Ireland Health Product Regulation Authority database.

- Health Products Canada lists methenamine products as ethical and OTC products. Ethical products do not require a prescription but are generally prescribed by a medical practitioner.

1.6 Naratriptan

Proposal

The applicant has proposed to create a new Schedule 3 entry for certain preparations of naratriptan for the acute relief of migraine in patients who have a stable, well-established pattern of symptoms. The proposal includes listing naratriptan in Appendix H to permit advertising for Schedule 3 preparations. The proposal would align the scheduling of naratriptan with other substances in the triptan class, including sumatriptan, zolmitriptan, eletriptan and rizatriptan.

CAS number

121679-13-8

143388-64-1 (as hydrochloride)

Alternative names

Naratriptan hydrochloride; *N*-Methyl-3-(1-methyl-4-piperidinyl)-1*H*-indole-5-ethanesulfonamide

Applicant

Private applicant

Proposed Scheduling

Naratriptan is currently listed in Schedule 4 of the Poisons Standard.

The applicant's proposed amendments to the Poisons Standard are:[7]

Schedule 4 – Amend Entry

NARATRIPTAN **except** when included in Schedule 3.

Schedule 3 – New Entry

NARATRIPTAN when in divided oral preparations containing 2.5 mg or less per dosage unit and when sold in a pack containing not more than 2 dosage units for the acute relief of migraine in patients who have a stable, well-established pattern of symptoms.

Index – Amend Entry

NARATRIPTAN

Schedule 4
Schedule 3
Appendix H, clause 1

[7] Proposed additions are shown in green underlined font, proposed deletions are shown in red strikethrough font, and text without this formatting represents the current text in the Poisons Standard.

Appendix H – New Entry - Schedule 3 medicines permitted to be advertised.

Item	Poison
30a	NARATRIPTAN

Background

Naratriptan belongs to a class of medicines known as 5HT1-receptor agonists (selective serotonin agonists) or are known more commonly as triptans. They are used for the treatment of acute migraine attacks with or without aura. Triptans work by stimulating the serotonin receptors in the brain and this eases the symptoms of migraine. They are designed to stop a migraine attack as the attack begins. Naratriptan is currently available as 2.5 mg oral tablets by prescription only. Naratriptan was listed in the Poisons Standard in 1998 as a Schedule 4 substance and has not been considered since.

Summary of applicant's reasons for the proposal

- Migraine is a common and debilitating recurrent condition that affects 12-20% of women and 6% of men. In Australia, approximately 2.3 million people could potentially require triptan medication for the treatment of migraine.
- Naratriptan is currently available by prescription only and this restriction may delay patients from receiving acute migraine relief. A fundamental requirement for the efficacy of triptans (5HT-1 agonists) in the acute treatment of migraine is to administer within one hour of the onset of migraine headache.
- Delay in treatment increases the risk of more severe and prolonged headache pain, inappropriate simple analgesic use, medication overuse headache, chronic migraine, and increases the economic and productivity costs to Australia.
- The proposal aims to facilitate timely access to naratriptan through community pharmacy for patients diagnosed with migraine headaches, so that treatment may be initiated at the early stages of an attack. Pharmacists have appropriate skills and knowledge to appropriately assess migraine symptoms and the medical history of consumers.
- Other triptan medicines such as sumatriptan, zolmitriptan, eletriptan and rizatriptan were re-scheduled and made available for Pharmacist Only sale in 2021.
- Triptans are considered to have low abuse potential. Medication overuse headache (MOH) is considered the most likely unintended outcome associated with misuse or abuse of naratriptan. The prevalence of MOH is approximately 0.5–2.0% of the population.

Key uses / expected use

Medicines

Australian regulations

- According to the TGA Ingredient Database, naratriptan is:
  - Available for use as an Active Ingredient in Biologicals and Prescription Medicines;
  - Available for use as an Excipient Ingredient in Biologicals, Devices and Prescription Medicines;

  - Available for use as an equivalent Ingredient in Prescription Medicines.

- As of August 2023, there was one medicine currently active on the Australian Register of Therapeutic Goods (ARTG) that contains naratriptan (as hydrochloride) as an active ingredient. The product is a prescription only medicine.
- Naratriptan is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination No.3 of 2023.
- The TGA prescribing medicines in pregnancy database classifies naratriptan as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Naratriptan	B3	Cardiovascular system	Antimigraine preparations	
Category B3 – Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed. Studies in animals have shown evidence of an increased occurrence of foetal damage, the significance of which is considered uncertain in humans.				

- There are no warning statements pertaining specifically to naratriptan in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021. However, there are specific warning statements required for eletriptan, rizatriptan, sumatriptan and zolmitriptan.
- Between July 2013 and July 2023, there were 4 reports of adverse events for products containing naratriptan as an active ingredient on the Database of Adverse Event Notifications (DAEN), with no reports where naratriptan was the single suspected medicine.
- As of August 2023, there were no products containing naratriptan as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS).

International regulations

- The US FDA database of approved drugs contains 6 products with naratriptan as an active ingredient, all of which are prescription only medicines.
- MedSafe New Zealand lists one product containing naratriptan which was previously marketed as a prescription only medicine. The approval status now denotes “Approval lapsed” indicating that the product may no longer be marketed in New Zealand.
- The Health Products Regulatory Authority of Ireland database contains one product containing naratriptan as an active ingredient. The product is a prescription only medicine and is authorised to be advertised to health professionals only.
- The Electronic Medicines Compendium (UK) includes one product with naratriptan as an active ingredient. The product is a prescription only medicine.
- The European Medicines Agency lists naratriptan as being available in several European countries at a dose of 2.5 mg.
- The Drug and Health Product Database of Canada lists 5 products containing naratriptan as an active ingredient, all of which are prescription only medicines.

1.7 Paracetamol

Proposal

The applicant has proposed to amend the entry under Schedule 2 to create an exception for effervescent paracetamol preparations of 16 tablets or less packed in a container with a child-resistant closure (instead of blister or strip packaging) and made available for general sale.

CAS number

103-90-2

Alternative names

Acetaminophen, 4-Acetamidophenol and *N*-(4-Hydroxyphenyl) acetamide

Applicant

Private applicant

Proposed scheduling

Paracetamol is currently listed in Schedules 2, 3 and 4, and Appendix F, Part 3 and H, of the Poisons Standard.

The applicant has proposed amendments to the paracetamol entry under Schedule 2:[8]

Schedule 4

PARACETAMOL:

a) when combined with aspirin or salicylamide or any derivative of these substances **except** when separately specified in these Schedules; or

b) when combined with ibuprofen in a primary pack containing more than 30 dosage units; or

c) in modified release tablets or capsules containing more than 665 mg paracetamol; or

d) in non-modified release tablets or capsules containing more than 500 mg paracetamol; or

e) in individually wrapped powders or sachets of granules each containing more than 1000 mg paracetamol; or

f) in tablets or capsules enclosed in a primary pack containing more than 100 tablets or capsules **except** in Schedule 2 or Schedule 3; or

g) in individually wrapped powders or sachets of granules enclosed in a primary pack containing more than 50 wrapped powders or sachets of granules **except** when included in Schedule 2; or

[8] Proposed additions are shown in green underlined font, proposed deletions are shown in red strikethrough font, and text without this formatting represents the current text in the Poisons Standard.

h) for injection; or

i) for the treatment of animals.

Schedule 3

PARACETAMOL:

a) when combined with ibuprofen in a primary pack containing 30 dosage units or less **except** when included in Schedule 2; or

b) in modified release tablets or capsules containing 665 mg or less paracetamol enclosed in a primary pack containing not more than 100 tablets or capsules; or

c) in modified release tablets or capsules containing 665 mg or less paracetamol enclosed in a primary pack containing more than 100 tablets or capsules intended only as a bulk medicine and labelled 'For dispensing only' and 'This pack is not to be supplied to a patient'; or

d) in liquid preparations for oral use **except** when in Schedule 2.

Schedule 2

PARACETAMOL for therapeutic use:

a) in liquid preparations for oral use containing a maximum of 10 g of paracetamol per container; or

b) when combined with ibuprofen in preparations for oral use when labelled with a recommended daily dose of 1200 mg or less of ibuprofen in divided doses in a primary pack containing no more than 12 dosage units per pack; or

c) in tablets or capsules enclosed in a primary pack containing not more than 100 tablets or capsules; or

d) in tablets or capsules enclosed in a primary pack containing more than 100 tablets or capsules intended only as a bulk medicine pack and labelled 'For dispensing only' and 'This pack is not to be supplied to a patient'; or

e) in individually wrapped powders or sachets of granules enclosed in a primary pack containing not more than 50 wrapped powders or sachets of granules; or

f) in individually wrapped powders or sachets of granules enclosed in a primary pack containing more than 50 wrapped powders or sachets of granules intended only as a bulk medicine pack and labelled 'For dispensing only' and 'This pack is not to be supplied to a patient'; or

g) in other preparations **except**:

i) when included in Schedule 3 or 4; or

ii) in individually wrapped powders or sachets of granules each containing 1000 mg or less of paracetamol as the only therapeutically active constituent (other than caffeine, phenylephrine and/or guaifenesin or when combined with effervescent agents) when:

(A) enclosed in a primary pack that contains not more than 10 such powders or sachets of granules,

(B) compliant with the requirements of the Required Advisory Statements for Medicine Labels,

(C) not labelled for the treatment of children 6 years or age or less, and

(D) not labelled for the treatment of children under 12 years of age when combined with caffeine, phenylephrine and/or guaifenesin; or

iii) in effervescent tablets containing 500mg or less of paracetamol as the only therapeutically active constituent (other than caffeine, phenylephrine and/or guaifenesin) when:

(A) packed in a container with a child-resistant closure that contains not more than 16 tablets,

(B) compliant with the requirements of the Required Advisory Statements for Medicine Labels,

(C) not labelled for the treatment of children 6 years of age or less, and

(D) not labelled for the treatment of children under 12 years of age when combined with caffeine, phenylephrine and/or guaifenesin; or

iv) in tablets or capsules each containing 500 mg or less of paracetamol as the only therapeutically active constituent (other than caffeine, phenylephrine and/or guaifenesin or ~~when combined with effervescent agents)~~ when:

(A) packed in blister or strip packaging ~~or in a container with a child-resistant closure~~,

(B) in a primary pack containing not more than 20 tablets or capsules,

(C) compliant with the requirements of the Required Advisory Statements for Medicine Labels,

(D) not labelled for the treatment of children 6 years of age or less,

(E) and not labelled for the treatment of children under 12 years of age when combined with caffeine, phenylephrine and/or guaifenesin.

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PARACETAMOL
cross reference: ASPIRIN, IBUPROFEN, METOCLOPRAMIDE, SALICYLAMIDE, CAFFEINE

Schedule 4
Schedule 3
Schedule 2
Appendix F, clause 4
Appendix H, clause 1

Background

Paracetamol is the most widely used over the counter (OTC) analgesic agent in the world. While paracetamol has well-established favourable safety and toxicity profiles, the wide use is paralleled by a high prevalence of accidental paracetamol poisoning in the community in both adults and children.

The TGA has been aware of concerns, particularly of families of affected consumers of paracetamol, regarding the number of poisonings and deliberate overdoses from paracetamol obtained from general retail outlets without restrictions to children and adolescents.

The TGA published a final decision on 3 May 2023 (with an implementation date of 1 February 2025) to increase regulatory controls on paracetamol, which included requirements for blister strip packaging and smaller pack sizes for general sale.

Summary of applicant's reasons for the proposal

- Effervescent tablets are more difficult to dry swallow compared to conventional tablets due to the difference in size, and the preparation required for consuming multiple tablets at once is arduous and time consuming.
- The time taken to dissolve tablets (up to 5 minutes) presents an interruption to the consumer that would impede or discourage intentional paracetamol overdose using these preparations, similar to that intended to be presented by the packaging changes in the recent scheduling on paracetamol.
- One primary pack of 16 effervescent tablets contains the same total amount of paracetamol contained in one primary pack of 'Lemsip Hot Drink Oral Powder Sachet' sold in grocery stores.
- Taking account of the above factors, the applicant has requested that the Delegate consider amending the Schedule 2 entry to exempt from scheduling, packs of 16 or less effervescent tablets containing 500 mg or less of paracetamol when packed in a container with a child-resistant closure.

Key uses / expected use

Medicines

Australian regulations

- According to the TGA Ingredient Database, paracetamol is:
  - Available for use as an Active Ingredient in Biologicals, Export Only, Over the Counter and Prescription Medicines
  - Available for use as an Excipient Ingredient in Biologicals, Devices and Prescription Medicines
  - Available as an equivalent ingredient in Export Only, Over the Counter and Prescription Medicines.
- As of July 2023, there were 634 medicines currently active on the Australian Register of Therapeutic Goods (ARTG) that contain paracetamol as an active ingredient. These include:
  - 78 prescription only medicines
  - 544 over the counter medicines
  - 12 export only medicines.
- Paracetamol is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination No. 3 of 2023.
- The TGA prescribing medicines in pregnancy database classifies paracetamol as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Paracetamol	A	Central Nervous System	Analgesics and Antipyretics (see also non-steroidal anti-inflammatory agents)	
Category A – Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed.				

- There are three warning statements pertaining to paracetamol in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.

Item	Substance	Circumstances	Required Statements
191	Paracetamol (Entry 1 of 3)	For the purpose of exclusion from the schedules to the current Poisons Standard	• Adults: Keep to the recommended dose. Do not take this medicine for longer than a few days at a time unless advised to by a doctor. • Children and adolescents: Keep to the recommended dose. Do not give this medicine for longer than 48 hours at a time unless advised to by a doctor. • If an overdose is taken or suspected, ring the Poisons Information Centre (Australia 13 11 26, New Zealand 0800 764 766) or go to hospital straight away even if you feel well because of the risk of delayed, serious liver damage. • Do not take with other products containing paracetamol, unless advised to do so by a doctor or pharmacist.

192	Paracetamol (Entry 2 of 3)	In Schedule 2 or 3 to the current Poisons Standard	• either or both - Adults: Keep to the recommended dose. Do not take this medicine for longer than a few days at a time unless advised to by a doctor. - Children and adolescents: Keep to the recommended dose. Do not give this medicine for longer than 48 hours at a time unless advised to by a doctor. • If an overdose is taken or suspected, ring the Poisons Information Centre (Australia 13 11 26, New Zealand 0800 764 766) or go to hospital straight away even if you feel well because of the risk of delayed, serious liver damage. • Do not take with other products containing paracetamol, unless advised to do so by a doctor or pharmacist.

193	Paracetamol (Entry 3 of 3)	In combination with ibuprofen, in medicines for oral use	• Do not give to children under 12 years of age. • Adults: Keep to the recommended dose. Do not take this medicine for longer than a few days at a time unless advised to by a doctor. • Children and adolescents: Keep to the recommended dose. Do not give this medicine for longer than 48 hours at a time unless advised to by a doctor. • Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage. • Do not use if pregnant or trying to become pregnant. • 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 a doctor has told you to, do not use if you are aged 65 years or over. • Do not take with other products containing paracetamol, ibuprofen, aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly, unless advised to do so by a doctor or pharmacist. If an overdose is taken or suspected, ring the Poisons Information Centre (Australia 13 11 26, New Zealand 0800 764 766) or go to hospital straight away even if you feel well because of the risk of delayed, serious liver damage.

- As of July 2023, there were 5,204 reports of adverse events for products containing paracetamol as an active ingredient on the Database of Adverse Event Notifications (DAEN), with 2,348 reports where paracetamol was the single suspected medicine. There were 333 reports of deaths associated with paracetamol use. The recorded adverse events were widely varied in nature.

International regulations

- The scheduling of paracetamol varies considerably within the Organisation for Economic Co-operation and Development (OECD) countries, with respect to immediate release and modified release formulations (MR), sales outside of pharmacies and maximum pack sizes available.
- Many European countries do not allow any sales outside of pharmacies and have lower limits on pharmacy pack sizes. In addition, MR paracetamol is not available in most European countries. Some countries have implemented restrictions while others have no limits on the quantities per pack or number of packs that can be purchased (predominantly in Eastern Europe and Russia). Fourteen countries have implemented pack size restrictions within pharmacies in the last two decades ranging from 8-30 g (which are lower than in Australia).
- Furthermore, in twelve countries paracetamol-containing analgesics are not available outside of pharmacies, with larger quantities only available with a valid prescription from a doctor. Only seven countries allow the sale of paracetamol from outside of pharmacies, with six countries limiting the range between 5-8 g of paracetamol per pack and Russia allowing unlimited quantities for sale. Sweden now only markets effervescent tablet formulations for general sale. This indicates that apart from Russia all remaining European countries have tighter restrictions on access outside of pharmacies compared to Australia (either through smaller quantities or no access at all without a prescription).
- The UK has tighter scheduling of paracetamol compared to Australia, which it enacted in 1998 as a response to self-poisoning. They now have low pack limits (16 tablets), purchase limits (2 packs) for general sale and a 32-tablet pack size limit from pharmacies. In 2017 Modified-release (MR) paracetamol was removed from the UK market since overdoses with MR paracetamol products can be unpredictable and complex to manage.
- The US, Canada and Singapore do not have significant limits placed on the pack sizes of standard paracetamol products.
- Refer to *Chapter 3: International comparisons of scheduling and paracetamol poisoning* in the independent expert report on the risks of intentional self-poisoning with paracetamol for a comprehensive overview.

2 Proposed amendments referred for scheduling advice to the Joint ACMS-ACCS meeting #35

2.1 Adrenaline

Proposal

The applicant has proposed the inclusion of topical preparations containing 0.1% or more of adrenaline in the existing Schedule 4 entry for adrenaline. Adrenaline is typically included in gels and lotions with local anaesthetic substances for the treatment of wounds. An independent evaluation of the risks associated with the use of adrenaline on wounds has recommended that relevant products should be available by prescription-only (Schedule 4). The proposal also seeks to clarify the existing entries for adrenaline with regards to injectable preparations.

CAS Number

329-63-5 (racemic hydrochloride)

Alternative names

Epinephrine, adrenalin

Applicant

Department of Health and Aged Care

Proposed Scheduling

Adrenaline is currently listed in Schedules 3 and 4 of the Poisons Standard.

The applicant's proposed amendments to the Poisons Standard are the following:[9]

Schedule 4 – Amend Entry

ADRENALINE ~~**except**~~in:

(a) ~~when included in Schedule 3~~topical preparations for wound management in humans; or

(b) other preparations containing more than 1% of adrenaline.~~in preparations containing 0.02% or less of adrenaline unless packed and labelled for injection.~~

Schedule 3 – Amend Entry

ADRENALINE in

a) preparations for injection containing 1% or less of adrenaline; or ~~**except** in preparations containing 0.02% or less of adrenaline unless packed and labelled for injection.~~

[9] Proposed additions are shown in green underlined font, proposed deletions are shown in red strikethrough font, and text without this formatting represents the current text in the Poisons Standard.

b) other preparations containing 1% or less of adrenaline **except**

i) when included in Schedule 4, or

ii) those containing 0.02% or less of adrenaline.

Index

ADRENALINE

Schedule 4
Schedule 3
Appendix H, clause 1

Appendix H, clause 1 – Schedule 3 medicines permitted to be advertised.

Item	Poison
2	ADRENALINE

Background

Adrenaline is a hormone that may be used medicinally (under the synonym epinephrine), in combination with local anaesthetics, for topical application to superficial wounds and lacerations to provide localised surface anaesthesia for wound closure. It may be used to provide topical anaesthetic relief for cleaning, irrigation and debridement of painful minor wounds.

Summary of the reasons for the proposal

- A TGA evaluation of a gel containing adrenaline includes a recommendation for consideration of such products to be sold as prescription only medicines. Currently products containing less than 1% of adrenaline, are classified as Schedule 3 (pharmacist only medicines) medicines.
- The recommendation is based on concerns regarding the potential for inappropriate use, such as in the treatment of burns, abrasions and ulcers, where the vasoconstrictive properties of adrenaline may result in ischemia and, skin necrosis and in rare cases death. There is also the potential for inappropriate use in cosmetic procedures.
- The risks of adverse reactions and inappropriate use suggest a requirement for medical oversight consistent with a Schedule 4 medicine.

Key uses / expected use

Medicines, cosmetic, veterinary

Australian regulations

- According to the TGA Ingredient Database, adrenaline (as anhydrous)[10] is:
  - Available for use as an Active Ingredient in Biologicals, Export Only, Listed Medicines, Over the Counter and Prescription Medicines
  - Available for use in Listed Medicines as a Homeopathic Ingredient only

[10] Adrenaline is also included in the Ingredient Database as the acid tartrate and hydrochloride salts

  - Available for use as an Excipient Ingredient in Biologicals, Devices and Prescription Medicines
  - Available for use as an Equivalent Ingredient in Prescription Medicines.

- As of August 2023, there were 56 medicines currently active on the Australian Register of Therapeutic Goods (ARTG) that contain adrenaline as an active ingredient. These include 53 prescription and 3 medicines for export only.
- According to the Therapeutic Goods (Permissible Ingredients) Determination No.3 of 2023, adrenaline is permitted to be included in listed medicines as follows:

Item	Ingredient Name	Purpose	Specific requirements
414	ADRENALINE (EPINEPHRINE)	H	Only for use as an active homeopathic ingredient.
H = homoeopathic preparation ingredient meaning an ingredient that is a constituent of a homoeopathic preparation			

- The TGA prescribing medicines in pregnancy database classifies adrenaline as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Adrenaline (epinephrine)	A	Cardiovascular system	Adrenergic stimulants	
Category A – Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.				

- There are no warning statements pertaining to adrenaline in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.
- Between January 2013 and July 2023, there were 313 reports of adverse events for products containing adrenaline as an active ingredient on the Database of Adverse Event Notifications (DAEN), with 201 reports where adrenaline was the single suspected medicine. The most common adverse events were associated with ineffectiveness of the drug and product quality/failure, and anaphylactic reactions.
- As of August 2023, there were 2 products containing adrenaline (as tartrate) as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS). These are an injection (co-formulated with lignocaine) and a wound anaesthetic and antiseptic solution (containing 0.0025% adrenaline tartrate co-formulated with local anaesthetics and cetrimide).
- In 2009-2019 the following adverse experiences were recorded for adrenaline in the APVMA Adverse Experience Reporting Program (AERP) database:
  - Three reports of probable incidents classified as related to human health (2013, 2017-18 and 2018-19).

International regulations

- New Zealand Medsafe's Medicines Classification Database lists adrenaline as follows:

Ingredient	Conditions (if any)	Classification
Adrenaline	in medicines containing more than 1%	Prescription

Adrenaline	in medicines containing 1% or less except in medicines for injection containing 0.02% or less; except in medicines for injection containing 0.1% or less for use in practice in an emergency by a dental therapist, an oral health therapist, an oral health therapist or a dental hygienist registered with the Dental Council.	Restricted
Adrenaline	in medicines for injection containing 0.02% or less	General sale

- Ireland's Health Products Regulatory Authority regulates 27 products containing adrenaline in solutions for infusion, injection, and pre-filled pens in various strengths. All are listed as prescription-only medicines.
- Health Canada's Drug Product Database includes 57 marketed products containing adrenaline (as epinephrine), including injections, sprays and topical solutions. Most registered products are classified as 'ethical' medicines (available without a prescription from a medical practitioner).
- The US Food and Drug Administration's Drugs@FDA database lists 59 active products containing adrenaline, most of which are injectable preparations that are listed as prescription medicines. One product, a metered dose aerosol, is listed as an over-the-counter medicine.

2.2 Benzoic acid

Proposal

The applicant has proposed new entries in Schedules 5, 6 and 7 for benzoic acid, which is presently unscheduled. The new entries in Schedules 5 and 6 would place labelling requirements on the use of benzoic acid in agricultural and veterinary products, while the Schedule 7 entry would impose controls on preparations containing more than 10% benzoic acid.

CAS Number

65-85-0

Alternative names

Benzenecarboxylic acid, dracylic acid

Applicant

Australian Pesticides and Veterinary Medicines Authority (APVMA)

Proposed Scheduling

Benzoic acid is not specifically scheduled in the current Poisons Standard.

The applicant has proposed the following new entries:[11]

Schedule 7 – New Entry

BENZOIC ACID in preparations containing greater than 10% of benzoic acid.

[11] Proposed additions are shown in green underlined font, proposed deletions are shown in red strikethrough font, and text without this formatting represents the current text in the Poisons Standard.

Schedule 6 – New Entry

BENZOIC ACID in preparations containing less than 10% of benzoic acid in agricultural and veterinary chemical products **except** when included in Schedule 5.

Schedule 5 – New Entry

BENZOIC ACID in preparations containing less than 1% of benzoic acid in agricultural and veterinary products.

Index – New Entry

BENZOIC ACID
Schedule 7
Schedule 6
Schedule 5

Background

Benzoic acid is a naturally occurring anti-bacterial and anti-fungal substance that has widespread use as a food preservative and in cosmetics, pharmaceutical and personal hygiene products. Benzoic acid is also currently present in numerous agricultural and veterinary (agvet) products, as an excipient or active constituent.

Summary of applicant's reasons for the proposal

- Toxicity data on benzoic acid has been collected over decades, relating to the long history of use in food, cosmetics, pharmaceuticals and as a disinfectant, and giving a robust database for the hazard assessment and risk assessment of benzoic acid.
- Benzoic acid has low acute toxicity by the oral, dermal and inhalation routes. The substance is a slight skin irritant, not a skin sensitiser, but is corrosive to the eye and potential respiratory irritant. The toxicology profile of benzoic acid is consistent with the Scheduling Policy Framework for inclusion in Schedule 7 of the Poisons Standard, based on its corrosive eye irritation.
- The substance may be suitable for a Schedule 6 entry based on appropriate risk mitigation measures. Additionally, the GHS cut-offs for Category 1 eye irritants may be suitable for inclusion of low concentration products in Schedule 5.
- Benzoic acid is present in products as diverse as mouth washes, topical ointments, veterinary medicines, and agricultural products. Benzoic acid (and sodium, potassium and calcium benzoates) is permitted as a food additive at levels up to 0.1%.

Key uses / expected use

Medicines, cosmetics, domestic products, veterinary medicines, agricultural products, industrial use.

Australian regulations

- According to the TGA Ingredient Database, benzoic acid is:
  - Available for use as an Active Ingredient in Biologicals, Export Only, Listed Medicines, Over the Counter and Prescription Medicines
  - Available for use in Listed Medicines as a Homeopathic Ingredient only

  - Available for use as an Excipient Ingredient in Biologicals, Devices, Export Only, Listed Medicines, Over the Counter and Prescription Medicines
  - Not available as an Equivalent Ingredient in any application.

- As of August 2023, there were 10 medicines currently active on the Australian Register of Therapeutic Goods (ARTG) that contain benzoic acid as an active ingredient. These include 10 non-prescription medicines.
- According to the Therapeutic Goods (Permissible Ingredients) Determination No.3 of 2023, benzoic acid is permitted to be included in listed medicines as follows:

Item	Ingredient name	Purpose	Specific requirements
801	BENZOIC ACID	E, H	
E = excipient for a medicine meaning an ingredient that is not an active ingredient or a homoeopathic preparation ingredient H = homoeopathic preparation ingredient meaning an ingredient that is a constituent of a homoeopathic preparation			

- The TGA prescribing medicines in pregnancy database does not include benzoic acid.
- There are no warning statements pertaining to benzoic acid in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.
- Between January 1971 and July 2023, there were 23 reports of adverse events for products containing benzoic acid as an active ingredient on the Database of Adverse Event Notifications (DAEN), with 22 reports where benzoic acid was the single suspected medicine. The reported events were diverse in nature and affected various organ classes.
- As of August 2023, there were 6 products containing benzoic acid as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS).
- In 2010-2020 there were no adverse experiences were recorded for benzoic acid in the APVMA Adverse Experience Reporting Program (AERP) database.
- Benzoic acid is listed on the Australian Inventory of Industrial Chemicals, without any specific information requirements or conditions of introduction or use.

International regulations

- The United States Food and Drug Administration's Drugs@FDA database includes 6 products containing sodium benzoate as an active ingredient. All are prescription-only intravenous solutions.
- The European Union's CosIng database lists benzoic acid as a fragrance, preservative and pH adjuster.
- New Zealand Medsafe's Medicines Classification Database lists benzoic acid as approved for general sale.
- New Zealand's Inventory of Chemicals lists benzoic acid as 'may be used under an appropriate group standard'.

- Health Canada's Drug Product Database includes one marketed product that contains benzoic acid as an active ingredient, an ear cleaning solution for veterinary use that is regulated as an over-the-counter medicine.
- The European Chemicals Agency lists benzoic acid as causing damage to organs through prolonged or repeated exposure, serious eye damage and skin irritation.
- Ireland's Health Products Regulation Agency regulates one product containing benzoic acid as an active ingredient, an antifungal ointment that is available as a non-prescription medicine.

2.3 Meloxicam

Proposal

The applicant has proposed an amendment to the Schedule 6 entry for meloxicam to include certain injectable veterinary vaccines containing less than 1% of meloxicam for single use in lambs undergoing routine animal husbandry procedures. Meloxicam is an anti-inflammatory medicine that can be used for pain relief; the amendment would enable farmers to access the medicine in a co-formulation with certain vaccines, without the requirement for a prescription.

CAS Number

71125-38-7

Applicant

Australian Pesticides and Veterinary Medicines Authority (APVMA)

Proposed Scheduling

Meloxicam is currently listed in Schedules 4 and 6 of the Poisons Standard.

The applicant's proposed amendments to the Poisons Standard are:[12]

Schedule 6 – Amend Entry

MELOXICAM in:

(a) oral transmucosal preparations containing 1% or less meloxicam for pre-surgical treatment and pain management in livestock during routine husbandry procedures; or

(b) injectable vaccines containing bacterial antigens and 1% or less of meloxicam for single use in lambs undergoing husbandry procedures at marking.

Schedule 4

MELOXICAM **except** when included in Schedule 6.

Index

[12] Proposed additions are shown in green underlined font, proposed deletions are shown in red strikethrough font, and text without this formatting represents the current text in the Poisons Standard.

MELOXICAM
Schedule 6
Schedule 4

Background

Meloxicam is a non-steroidal anti-inflammatory drug (NSAID) and is a cyclooxygenase-2-(COX-2) inhibitor, with a well-established safety profile available in a number of human and veterinary therapeutic products. Meloxicam is available in several different dosage forms for the relief of muscular pain, fever and inflammation. Meloxicam was available by prescription-only until 2022, when a new Schedule 6 entry was created for transmucosal preparations containing 1% or less of meloxicam for use in certain animal husbandry procedures.

Summary of applicant's reasons for the proposal

- Meloxicam is available in a number of registered products for various animals including cattle, sheep, pigs, and horses. All injectable forms of meloxicam are presently Schedule 4 prescription-only medicines.
- There are currently a number of registered bacterial antigen (killed cultures) vaccines for sheep which contain toxoid and cell concentrates prepared from formalin killed cultures and are not currently subject to controls under the Poisons Standard.
- A novel combination vaccine for lambs, incorporating existing registered bacterial antigens (killed cultures or inactivated vaccine) with meloxicam, is presently in development. Subsequently, an application has been made to amend the Schedule 6 entry for meloxicam to include injectable vaccines containing bacterial antigens and 1% or less meloxicam for single use in lambs undergoing husbandry procedures at marking.

Key uses / expected use

Medicines, veterinary

Australian regulations

- According to the TGA Ingredient Database, meloxicam is:
  - Available for use as an Active Ingredient in Biologicals, Export Only and Prescription Medicines.
  - Available for use as an Excipient Ingredient in Biologicals, Devices and Prescription Medicines.
  - Not available as an Equivalent Ingredient in any application.
- As of August 2023, there were 61 medicines currently active on the Australian Register of Therapeutic Goods (ARTG) that contain meloxicam as an active ingredient. These include 60 prescription medicines and one for export only.
- Meloxicam is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination No.3 of 2023.
- The TGA prescribing medicines in pregnancy database classifies meloxicam as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Meloxicam	C	Musculoskeletal System	Non-steroidal anti-inflammatory drugs (NSAIDS)	
Category C – Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human foetus or neonate without causing malformations. These effects may be reversible. Accompanying texts should be consulted for further details.				

- There are no warning statements pertaining to meloxicam in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021
- Between July 2013 and July 2023, there were 213 reports of adverse events for products containing meloxicam as an active ingredient on the Database of Adverse Event Notifications (DAEN), with 121 reports where meloxicam was the single suspected medicine. The majority of reports related to gastrointestinal disorders such as nausea and haemorrhages, or skin tissue disorders such as rash or pruritus.
- As of August 2023, there were 72 products containing meloxicam as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS). These were in a variety of dosage forms including oral suspensions, injections, tablets and transmucosal gels.
- In 2015-2020 the following adverse experiences were recorded for meloxicam in the APVMA Adverse Experience Reporting Program (AERP) database:
  - 74 reports of incidents classified as related to animal health
  - One report of an incident related to lack of efficacy.

International regulations

- Ireland's Health Products Regulatory Authority regulates 4 products containing meloxicam. All are prescription-only tablets.
- Health Canada's Drug Product Database includes 32 marketed products containing meloxicam. These include 22 products for veterinary use. All marketed products containing meloxicam are only available by prescription.
- New Zealand's Medicines Classification Database lists meloxicam as a prescription medicine for all preparations and applications.
- The United States Food and Drug Administration's Drugs@FDA database includes 18 current products containing meloxicam, in tablets, capsules and oral suspensions. All are regulated as prescription medicines.

2.4 Palmitoylethanolamide (PEA)

Proposal

The applicant has proposed a new Schedule 6 entry for palmitoylethanolamide (PEA) with an exemption for use in listed human medicines. The proposal would require products containing PEA that are not listed as human medicines, such as veterinary products, to have distinctive packaging with strong warnings and safety directions on the label.

CAS Number

544-31-0

Alternative names

Palmidrol, PEA, palmitic acid monoethanolamide

Applicant

Australian Pesticides and Veterinary Medicines Authority (APVMA)

Proposed Scheduling

Palmitoylethanolamide is not specifically scheduled in the current Poisons Standard.

The applicant's proposed amendments to the Poisons Standard are:[13]

Schedule 6 – New Entry

PALMITOYLETHANOLAMIDE **except** in listed human medicines

Index – New Entry

PALMITOYLETHANOLAMIDE
cross reference: PALMIDROL

Schedule 6

Background

Palmitoylethanolamide (PEA) is a new veterinary active constituent in Australia and is not listed in the Poisons Standard. Palmitoylethanolamide is typically used as a dietary supplement or food additive internationally and in listed human medicines in Australia. It is purported to have a role as an anti-inflammatory, antihypertensive, neuroprotective and anticonvulsant agent.

Summary of applicant's reasons for the proposal

- The findings from the applicant indicate that PEA has low acute toxicity by the oral, dermal and inhalation routes, but is a severe eye and skin irritant and a potential respiratory irritant.

Key uses / expected use

Medicines, veterinary

Australian regulations

- According to the TGA Ingredient Database, palmitoylethanolamide is:
  - Available for use as an Active Ingredient in Export only and Listed Medicines
  - Not available as a Homeopathic Ingredient in Listed Medicines

[13] Proposed additions are shown in green underlined font, proposed deletions are shown in red strikethrough font, and text without this formatting represents the current text in the Poisons Standard.

  - Available for use as an Excipient Ingredient in Devices and for Export Only
  - Not available as an Equivalent Ingredient in any application

- As of August 2023, there were 23 medicines currently active on the Australian Register of Therapeutic Goods (ARTG) that contain palmitoylethanolamide (PEA) (under palmidrol) as an active ingredient, all of which are listed medicines.
- According to the Therapeutic Goods (Permissible Ingredients) Determination No.3 of 2023, palmitoylethanolamide is permitted to be included in listed medicines as follows:

Item	Ingredient Name	Purpose	Specific requirements
3651	PALMIDROL	A	Only permitted for use in medicines limited to oral routes of administration. The maximum recommended daily dose of the medicine must not provide more than 600 mg of palmidrol. The following warning statements (or words to the same effect) are required on the medicine label: - (ANALG) 'The medicine may interact with other prescription analgesic medicines, please consult your healthcare practitioner before use.' - (ADULT) 'Adults only.' - (21DAYS) 'Not to be used for more than 21 consecutive days.'
H = active ingredient meaning an ingredient has the same meaning as in the Regulations.			

- According to the TGA prescribing medicines in pregnancy database, palmitoylethanolamide is not categorised.
- There are no warning statements pertaining to palmitoylethanolamide in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021
- Between January 2013 and July 2023, there were 4 reports of adverse events for products containing palmitoylethanolamide (palmidrol) as an active ingredient on the Database of Adverse Event Notifications (DAEN), with 4 reports where palmitoylethanolamide was the single suspected medicine.
- As of August 2023, there were no products containing palmitoylethanolamide as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS).

International regulations

- New Zealand Medsafe's Medicines Classification Database does not include palmitoylethanolamide.
- Ireland's Health Products Regulatory Authority do not list any products containing palmitoylethanolamide.
- Health Canada's Drug Product Database does not list any products containing palmitoylethanolamide.

- The US Food and Drug Administration's Drugs@FDA database does not list any products containing palmitoylethanolamide.

3 Proposed amendments referred for scheduling advice to ACCS meeting #37

3.1 Animal Blood Products

Proposal

An applicant has proposed to create a new Schedule 4 entry for animal blood products for veterinary use. Animal blood products are currently unscheduled and have not previously been considered for scheduling. Human blood products are currently captured in Appendix A which provides a general exemption from the controls set out in the Poisons Standard.

Applicant

Australian Pesticides and Veterinary Medicines Authority

Proposed Scheduling

Animal blood products are not specifically scheduled in the current Poisons Standard.

The applicant's proposed amendments to the Poisons Standard are:[14]

Schedule 4 – New entry

ANIMAL BLOOD PRODUCTS for veterinary use including:

(a) whole blood;

(b) blood components including red cells, white cells, platelets, and plasma (including cryoprecipitate); and

(c) the following plasma-derived therapeutic proteins; and their equivalent recombinant alternatives:

(i) albumin;

(ii) anticoagulation complex;

(iii) C1 esterase inhibitors;

(iv) clotting factors;

(v) fibrinogen;

(vi) protein C;

(vii) prothrombin complex concentrate (PCC);

(viii) thrombin

INDEX – New entry

ANIMAL BLOOD PRODUCTS
Schedule 4

[14] Proposed additions are shown in green underlined font, proposed deletions are shown in red strikethrough font, and text without this formatting represents the current text in the Poisons Standard.

Background

Animal blood products are used in transfusions in other animals to support the treatment of surgical procedures following various ailments and injuries such as snake bites, anaemia, cancers, bleeding disorders, after a traumatic accident, and other medical conditions or diseases.

Animal blood products are currently extracted in private veterinary practices and used in-house for other animals. Additionally, there are some commercial suppliers who supply through wholesalers direct to veterinary practices.

Summary of applicant's reasons for the proposal

- There are currently several registered animal blood products with the APVMA for various animals including companion animals and production animals. While human blood products are regulated by the Therapeutic Goods Administration (TGA) and the National Blood Authority (NBA), there is no equivalent authority for the regulation of animal blood products.
- Schedule 4 would be the most appropriate schedule to regulate access and supply as animal blood products must be administered by a veterinarian.
- The human health risks associated with collection, handling and administration are low due to the products being handled only by appropriately trained staff.

Key uses / expected use

Veterinary use only.

Australian regulations

- Animal blood products are not present in the TGA Ingredient Database.
- As of July 2023, there were no medicines currently active on the Australian Register of Therapeutic Goods (ARTG) that contain animal blood products as an active ingredient.
- Animal blood products are not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination No. 3 of 2023.
- Animal blood products are not listed in the TGA prescribing medicines in pregnancy database.
- There are no warning statements pertaining to animal blood products in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.
- As of August 2023, there were no reports of adverse events for products containing animal blood products as an active ingredient on the Database of Adverse Event Notifications (DAEN).
- As of August 2023, there were 3 products containing animal blood products listed on the Public Chemical Registration Information System Search (PubCRIS).

International regulations

- Animal blood products in the United Kingdom are regulated by the Veterinary Medicines Directorate, an executive agency who are sponsored by The Department for Environment, Food and Rural Affairs. A permit granted by the Non-Food Animal Blood Bank Authorisation is required in order to collect, store and supply animal blood to a veterinary surgeon for treatment of non-food producing animals. These products can only be supplied to a vet and only a veterinarian

surgeon, or someone acting under a veterinary surgeon's direction may administer the animal blood products.

3.2 Bile acids

Proposal

The applicant proposed to amend the Schedule 4 entry for three bile acids (chenodeoxycholic acid, cholic acid, and deoxycholic acid). The proposed amendment would exempt these substances from scheduling when used as an animal feed additive or in feed pre-mixes.

CAS Number

Chenodeoxycholic acid: 474-25-9

Cholic acid: 81-25-4

Deoxycholic acid: 83-44-3

Alternative names

Chenodeoxycholic acid: 3α,7α-Dihydroxy-5β-cholanic acid, 5β-Cholanic acid-3α,7α-diol, Chenodiol

Cholic acid: 3α,7α,12α-Trihydroxy-5β-cholanic acid, Cholanic acid

Deoxycholic acid: Deoxycholate, Desoxycholic acid, 3α, 12α-Dihydroxy-5β-cholanic acid

Applicant

Private applicant

Proposed Scheduling

Chenodeoxycholic acid, Cholic acid, and Deoxycholic acid are currently listed in Schedule 4 of the Poisons Standard.

The applicant's proposed amendments to the Poisons Standard are:[15]

Schedule 4 – Amend Entry

CHENODEOXYCHOLIC ACID **except** when used as an animal feed additive or in animal feed pre-mixes.

Schedule 4 – Amend Entry

CHOLIC ACID **except** when used as an animal feed additive or in animal feed pre-mixes.

Schedule 4 – Amend Entry

DEOXYCHOLIC ACID **except** when used as an animal feed additive or in animal feed pre-mixes.

Index – Amend Entries

[15] Proposed additions are shown in green underlined font, proposed deletions are shown in red strikethrough font, and text without this formatting represents the current text in the Poisons Standard.

CHENODEOXYCHOLIC ACID

Schedule 4

CHOLIC ACID

Schedule 4

DEOXYCHOLIC ACID

Schedule 4

Background

Chenodeoxycholic acid, cholic acid and deoxycholic acid are bile acids naturally found in mammals. These substances have therapeutic applications in the treatment of primary biliary cirrhosis and gallstones, bile acid synthesis disorders due to single enzyme defects, and for peroxisomal disorder such as Zellweger syndrome. There are also cosmetic applications as they can be used to destroy submental fat cells and reduce facial fullness or convexity in adults.

Chenodeoxycholic acid was first listed in Schedule 4 in March 1980, whilst cholic acid and deoxycholic acid were listed under Schedule 4 in March 2015 and March 2016 respectively.

Summary of applicant's reasons for the proposal

- Chenodeoxycholic acid, cholic acid and deoxycholic acid are naturally occurring steroid acids found in the bile of mammals and other vertebrates.
- The addition of exogenous bile acid to animal feed in conventional or reduced protein diets is intended to enhance animal health and performance. It is not intended to alleviate any animal illness or disease.
- The proposed animal feed formulation comprises 30% bile acids, made up of a minimum of 3% cholic acid, 21% deoxycholic acid, and 6% chenodeoxycholic acid.
- The product is classified as follows under the GHS:
  - H303: May be harmful if swallowed
  - H320: Causes eye irritation
  - H335: May cause respiratory irritation.
- Product toxicity is relatively low with a product oral LD50 of >5,000 mg/kg bw with an oral subchronic NOAEL of 3,000 mg/kg.
- The potential for misuse or abuse is very low as the proposed preparation is for an animal feed additive and feed pre-mix.
- The preparation and administration of animal feed containing bile acids does not require specialised handling.

Key uses / expected use

Agriculture

Australian regulations

- According to the TGA Ingredient Database, chenodeoxycholic acid, cholic acid, and deoxycholic acid are:
  - Available for use as an Active Ingredient in Biologicals, Prescription Medicines
  - Available for use as an Excipient Ingredient in Biologicals, Devices, Prescription Medicines
  - Not available as an Equivalent Ingredient in any application.
- As of August 2023, there was one medicine currently active on the Australian Register of Therapeutic Goods (ARTG) that contains deoxycholic acid as an active ingredient, which is a prescription medicine, and no medicines containing chenodeoxycholic acid or cholic acid.
- Chenodeoxycholic acid, cholic acid and deoxycholic acid are not permitted to be included in listed medicines as they are not included in the Therapeutic Goods (Permissible Ingredients) Determination No.3 of 2023.
- The TGA prescribing medicines in pregnancy database classifies chenodeoxycholic acid, cholic acid and deoxycholic acid as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Chenodeoxycholic acid	B3	Alimentary System	Cholelitholytics	
Cholic acid	B2	Alimentary System	Cholelitholytics	
Deoxycholic acid	B1	Drug Used in Dermatology		

Category B1 – Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed.

Studies in animals have not shown evidence of an increased occurrence of foetal damage.

Category B2 – Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed.

Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of foetal damage.

Category B3 – Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed.

Studies in animals have shown evidence of an increased occurrence of foetal damage, the significance of which is considered uncertain in humans.

- There are no warning statements for chenodeoxycholic acid, cholic acid or deoxycholic acid in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.
- As of July 2023, on the Database of Adverse Event Notifications (DAEN) there were:
  - 9 reports of adverse events for products containing chenodeoxycholic acid as an active ingredient, with 7 reports where chenodeoxycholic acid was the single suspected medicine.
  - 15 reports of adverse events for products containing deoxycholic acid (or sodium salt) as an active ingredient, with 11 reports where deoxycholic acid was the single suspected medicine.
  - No listed medicines containing cholic acid as an active ingredient.

The reported adverse events were diverse in nature.

- As of July 2023, there were no products containing chenodeoxycholic acid, cholic acid or deoxycholic acid as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS).

International regulations

- Chenodeoxycholic acid, cholic acid and deoxycholic acid are approved as prescription-only medicines in the United States. Two products containing chenodeoxycholic acid are approved by the United States' FDA, whilst 12 approved products contain cholic acid or a therapeutic equivalent (Obeticholic acid), with 2 products indicated as subcutaneous solutions. Deoxycholic acid is an active ingredient in 2 approved products within the United States.
- The European Chemicals Agency (ECHA)**Error! Bookmark not defined.**lists hazard classifications for these substances (from notifications under the Classification, Labelling and Packaging (CLP) Regulation) as follows:
  - Chenodeoxycholic acid: 'Danger… this substance causes serious eye irritation, is suspected of damaging fertility or the unborn child, is harmful if swallowed, is harmful in contact with skin, is harmful if inhaled, may cause long lasting harmful effects to aquatic life, causes skin irritation, may cause respiratory irritation, may cause an allergic skin reaction and may cause allergy or asthma symptoms or breathing difficulties if inhaled.'
  - Cholic acid: 'Warning… this substance is harmful in contact with skin and may cause an allergic skin reaction.'
  - Deoxycholic acid: 'Warning… this substance is harmful if swallowed, causes serious eye irritation, causes skin irritation and may cause respiratory irritation.'
- The European Union lists deoxycholic acid as a cosmetic ingredient with therapeutic functions as a skin emollient, humectant and condition agent. The EU Register of medicinal products[16] includes chenodeoxycholic acid and cholic acid products indicated for the treatment of inborn errors in primary bile acid synthesis and primary biliary cirrhosis.
- In New Zealand deoxycholic acid and cholic acid are listed on the Inventory of Chemicals without individual approval but may be used under an appropriate group standard. New Zealand MedSafe classifies chenodeoxycholic acid and cholic acid as prescription medicines. Deoxycholic acid is prescription-only when for injection, though is available for general sale in oral usage preparations.
- Deoxycholic acid is a prescription medicine in Canada and Ireland.

[16] European Commission https://ec.europa.eu/health/documents/community-register/html/reg_index_inn.htm

How to respond

Submissions must be provided by the closing date of **29 September 2023** through our consultation hub. Any submission about any of the proposals to amend the Poisons Standard will be considered at the next meeting of the Advisory Committee on Medicines Scheduling (ACMS), meeting of the Advisory Committee on Chemicals Scheduling (ACCS), or a joint meeting of these two committees.

What will happen

All public submissions will be published on the TGA website at Public submissions on scheduling matters, unless marked confidential or indicated otherwise in the submission coversheet (see Privacy information).

Following consideration of public submissions received before the closing date and advice from the expert advisory committees, decisions on the proposed amendments will be published as interim decisions on the TGA website: Scheduling delegate's interim decisions & invitations for further comment in **February 2024.**

Therapeutic Goods Administration

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