Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

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

18 April 2023

Contents

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 June 2023 meetings of the Advisory Committees on Medicines and Chemicals Scheduling. Submissions must be received by close of business **17 May 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 17 May 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 #42

1.1 Bisacodyl

Proposal

The applicant has proposed the creation of a new Schedule 2 entry for bisacodyl for oral use except in divided preparations in packs containing 20 tablets or less. Bisacodyl is a laxative that is not currently scheduled. The proposed amendment would restrict all oral preparations of bisacodyl to pharmacy sale, except packs of 20 tablets or less which would still be available for purchase from supermarkets and convenience stores.

CAS number

603-50-9

Alternative names

4,4′-(2-Pyridylmethylene)bisphenol 1,1′-diacetate; Bis(p-acetoxyphenyl)-2-pyridylmethane; (4,4′-diacetoxydiphenyl)(2-pyridyl)methane; 2-(4,4′-diacetoxydiphenylmethyl)pyridine

Applicant

Private applicant

Proposed Scheduling

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

Schedule 2 – New entry

BISACODYL for oral use **except** in divided preparations in packs containing 20 tablets or less.

Index – New entry

BISACODYL

Schedule 2

Background

Bisacodyl is a stimulant laxative intended for the relief of episodic and chronic constipation. Bisacodyl is presently not scheduled and is available in 5 mg tablets in packs ranging up to 240 doses.

Summary of applicant's reasons for the proposal

- Bisacodyl is being misused for weight loss. This proposed amendment of the Poisons Standard would help minimise the risk of intentional or unintentional misuse of this substance by vulnerable populations, such as older adults, children and those with eating disorders or other mental health concerns.

[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.

- Australia's access controls over bisacodyl are not consistent with comparable jurisdictions such as New Zealand and the UK. Stimulant laxatives and their accessibility have been the subject of recent reviews in the UK (MHRA) in 2020 and by New Zealand (Medsafe) in 2021, both of which recommended tighter control of these substances than is presently the case in Australia.
- Reassigning bisacodyl to Schedule 2 will not unduly impair access for its intended use, as access under supervision of health care professionals will remain unchanged for these patients. A scheduling change will assist in ensuring the safe and effective use of bisacodyl, and the minimisation of harm to the public from intentional or unintentional misuse.

Key uses / expected use

Medicine (laxative)

Australian regulations

- According to the TGA Ingredient Database,[2] bisacodyl 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 therapeutic good.
- As of March 2023, there were 20 medicines currently active on the Australian Register of Therapeutic Goods (ARTG)[3] that contain bisacodyl as an active ingredient. All are non-prescription medicines.
- Bisacodyl is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination[4] No.1 of 2023.
- The TGA prescribing medicines in pregnancy database[5] classifies bisacodyl as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Bisacodyl	A	Alimentary System	Laxatives	
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 bisacodyl in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021[6]
- Since January 2013, there have been 23 reports of adverse events for products containing bisacodyl as an active ingredient on the Database of Adverse Event Notifications (DAEN),[7] with 17 reports where bisacodyl was the single suspected medicine. The majority of reports related to gastrointestinal disorders such as diarrhoea and abdominal pain.

[2] TGA Ingredient Database https://www.ebs.tga.gov.au/

[3] ARTG database https://www.tga.gov.au/artg

[4] Therapeutic Goods (Permissible Ingredients) Determination https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LBPermissible%20IngredientsRB%20Determination

[5] TGA prescribing medicines in pregnancy database https://www.tga.gov.au/prescribing-medicines-pregnancy-database

[6] Therapeutic Goods (Medicines Advisory Statements) Specification 2021 https://www.legislation.gov.au/Details/F2021L01888

[7] Database of Adverse Event Notifications (DAEN) https://apps.tga.gov.au/Prod/daen/daen-entry.aspx

- As of March 2023, there were no products containing bisacodyl as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS).[8]

International regulations

- Ireland's Health Products Regulatory Authority[9] lists suppositories and gastro-resistant tablets containing bisacodyl as pharmacy-only medicines.
- The Health Canada Drug Product Database[10] lists 16 marketed products containing bisacodyl, including tablets, suppositories and enemas. All are listed as OTC medicines except enemas which are categorised as 'ethical' medicines.
- New Zealand Medsafe's[11] Medicines Classification Database lists bisacodyl as a pharmacy only medicine.
- The United States Food and Drug Administration[12] database does not include any approved products containing bisacodyl.
- In the United Kingdom[13] the sale of stimulant laxatives such as bisacodyl is restricted in retail outlets to patients over the age of 18, in packs containing not more than 20 standard-strength tablets. Pharmacists are permitted to sell stimulant laxatives for use in children aged 12 and over.

1.2 Olopatadine

Proposal

The applicant has proposed the creation of a new Schedule 2 entry for olopatadine when combined with mometasone in aqueous nasal sprays with limitations on dose per actuation and maximum recommended daily dose, for the short-term treatment of allergy conditions in patients aged 12 and over. Olopatadine is an anti-histamine that is currently available by prescription only (Schedule 4).

CAS number

113806-05-6

140462-76-6 (as hydrochloride)

Alternative names

(11*Z*)-11-[3-(Dimethylamino)propylidene]-6,11-dihydrodibenz[*b,e*]oxepin-2-acetic acid

Applicant

Private applicant

[8] Public Chemical Registration Information System Search (PubCRIS) https://portal.apvma.gov.au/pubcris

[9] HPRA www.hpra.ie/homepage/medicines/medicines-information/find-a-medicine/results/item?compare=PA23180/018/003,PA23180/018/002

[10] Health Canada health-products.canada.ca/dpd-bdpp/dispatch-repartition

[11] NZ Medsafe http://www.medsafe.govt.nz/profs/class/classintro.asp

[12] Drugs@FDA www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process

[13] UK Govt statement on laxatives www.gov.uk/drug-safety-update/stimulant-laxatives-bisacodyl-senna-and-sennosides-sodium-picosulfate-available-over-the-counter-new-measures-to-support-safe-use

Proposed Scheduling

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

Schedule 4 – Amend entry

OLOPATADINE **except** when included in Schedule 2.

Schedule 2 – New entry

OLOPATADINE when combined with mometasone in a single aqueous nasal spray delivering 600 micrograms or less of olopatadine per actuation when the maximum recommended daily dose is no greater than 4800 micrograms for the treatment of allergic rhinitis and rhino-conjunctivitis for up to six months in adults and children 12 years of age and over.

Index – Amend entry

OLOPATADINE

Schedule 4
Schedule 2

Appendix F, Clause 4 – Amend entry

ANTIHISTAMINES not separately specified in this Appendix except the following:

a) dermal, ocular, parenteral and paediatric preparations;

b) oral preparations of astemizole, azelastine, bilastine, desloratadine, fexofenadine, loratadine, terfenadine or cetirizine;

c) nasal preparations of azelastine or olopatadine;

d) preparations for the treatment of animals.

Background

Olopatadine is an antihistamine with mast cell-stabilising properties that is used to reduce the allergic response in conditions such as allergic rhinitis and allergic conjunctivitis. The substance is used in an aqueous nasal spray in combination with the corticosteroid mometasone, which is a Schedule 2 medicine for this presentation and purpose. The combination product is currently a prescription-only medicine due to the presence of olopatadine.

Summary of applicant's reasons for the proposal

- Allergic rhinitis is among the most common chronic diseases, affecting approximately 4.7 million Australians, and has a major negative impact on the quality of life of patients living in Australia.
- People with allergic rhinitis have a higher chance of going on to develop asthma as well as other chronic complications including sinusitis, hearing impairment and other allergy-related conditions. Uncontrolled seasonal allergic rhinitis is a condition that can place a substantial burden on patients and society but can be effectively managed through appropriate use of medications.
- Combination antihistamine and corticosteroid nasal sprays are recommended by the Australasian Society of Clinical Immunology and Allergy (ASCIA) as one of the first line treatment options, providing both rapid symptomatic relief and anti-inflammatory effects.
- Olopatadine is a Schedule 4 medicine that has previously been evaluated by the TGA, however meets the scheduling factors for Schedule 2 due to ready identification of the symptoms of the conditions for which is it used to treat, with low potential for harm from inappropriate use and low

[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.

likelihood of producing dependency. These assessments are backed by data already available from the evaluation of the prescription-only fixed dose combination product.

Key uses / expected use

Medicines

Australian regulations

- As of March 2023, there were 5 medicines currently active on the Australian Register of Therapeutic Goods (ARTG)[15] that contain olopatadine (as hydrochloride) as an active ingredient. All are prescription medicines. Of the 5 medicines, only one product, RYALTRIS, meets the requirements of the proposed Schedule 2 entry. RYALTRIS is an olopatadine 600 microgram/actuation and mometasone furoate 25 microgram/actuation nasal spray for the treatment of symptoms associated with allergic rhinitis and rhinoconjunctivitis in patients 6 years of age and older, with a recommended dosage of 2 sprays in each nostril twice daily for adults and adolescents (4800 microgram daily dose). The other 4 medicines are eye drop formulations for treatment of the signs and symptoms of seasonal allergic conjunctivitis. However, the proposal is not congruent with the age indication for the product.
- According to the TGA Ingredient Database,[16] olopatadine hydrochloride 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 therapeutic good.
  - Olopatadine (not as hydrochloride) is available for use Active Ingredient in Biologicals and Prescription Medicines; not available as an Excipient Ingredient in any application; and available for use as an Equivalent Ingredient in Prescription Medicines.
- Olopatadine is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination[17] No.1 of 2023.
- The TGA prescribing medicines in pregnancy database[18] classifies olopatadine as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Olopatadine	B1	Ophthalmic Drugs	-	-
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.				

- There are no warning statements pertaining to olopatadine in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.[19]
- Between January 2013 and March 2023, there were 10 reports of adverse events for products containing olopatadine as an active ingredient on the Database of Adverse Event Notifications

[15] ARTG database https://www.tga.gov.au/artg

[16] TGA Ingredient Database https://www.ebs.tga.gov.au/

[17] Therapeutic Goods (Permissible Ingredients) Determination https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LBPermissible%20IngredientsRB%20Determination

[18] TGA prescribing medicines in pregnancy database https://www.tga.gov.au/prescribing-medicines-pregnancy-database

[19] Therapeutic Goods (Medicines Advisory Statements) Specification 2021 https://www.legislation.gov.au/Details/F2021L01888

(DAEN),[20] with 7 reports where olopatadine was the single suspected medicine. The reported reactions were diverse in nature and affected organ class.

- As of March 2023, there were no products containing olopatadine as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS).[21]

International regulations

- The United States Food and Drug Administration[22] database lists 20 approved products containing olopatadine hydrochloride. Fourteen of these are over-the-counter solutions/drops for ophthalmic use and 6 are nasal spray preparations which are all available by prescription-only, including the fixed dose combination product containing mometasone.
- New Zealand Medsafe's Medicine Classification Database[23] lists olopatadine as a prescription only medicine.
- Health Canada's Drug Product Database[24] lists 10 marketed products containing olopatadine. All are ophthalmic solutions and listed as prescription-only medicines.

2 Proposed amendments referred for scheduling advice to the Joint ACMS-ACCS meeting #34

2.1 Lead (anti-fouling paints)

Proposal

The applicant proposes an amendment to the limit of lead in anti-fouling paints, which is due to come into effect on 1 October 2023 pursuant to a final decision to amend the Poisons Standard published in September 2021. That decision included a maximum permissible level of 90 mg/kg (equivalent to 90 ppm or 0.009%) of lead in anti-fouling and anti-corrosive paints. The applicant is seeking to amend this limit to 600 mg/kg (equivalent to 600 ppm or 0.06%). The applicant is not proposing a change to the limit for anti-corrosive paints.

CAS Number

7439-92-1 (metallic lead)

Applicant

Private applicant

[20] Database of Adverse Event Notifications (DAEN) https://apps.tga.gov.au/Prod/daen/daen-entry.aspx
[21] Public Chemical Registration Information System Search (PubCRIS) https://portal.apvma.gov.au/pubcris
[22] Drugs@FDA www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process
[23] Medsafe www.medsafe.govt.nz/profs/class/classintro.asp
[24] Health Canada health-products.canada.ca/dpd-bdpp/dispatch-repartition#results

Current Scheduling

PART 2, DIVISION 9 - General requirements

(2) An anti-fouling or anti-corrosive paint containing more than 0.1% lead (the proportion of lead for the purposes of this section is calculated as a percentage of the element present in the non-volatile content of the paint) must not be manufactured, supplied or used.

(3) A paint (other than an anti-fouling or anti-corrosive paint) or tinter containing more than 0.009% lead (calculated as a percentage of the element present in the non-volatile content of the paint) must not be manufactured, supplied or used.

Schedule 10

LEAD COMPOUNDS:

a) in anti-fouling or anti-corrosive paints **except** in preparations containing 0.1% or less of lead calculated on the non-volatile content of the paint; or

b) in paints (other than anti-fouling or anti-corrosive paints), tinters, inks or ink additives **except** in preparations containing 0.009% or less of lead calculated on the non-volatile content of the paint, tinter, ink or ink additive.

Schedule 6

LEAD COMPOUNDS **except**:

a) when included in Schedule 4; or

b) in paints, tinters, inks or ink additives; or

c) in preparations for cosmetic use containing 100 mg/kg or less of lead; or

d) in pencil cores, finger colours, showcard colours, pastels, crayons, poster paints/colours or coloured chalks containing 100 mg/kg or less of lead; or

e) in ceramic glazes when labelled with the warning statement:

CAUTION – Harmful if swallowed. Do not use on surfaces which contact food or drink written in letters not less than 1.5 mm in height.

Schedule 4

LEAD for human therapeutic use.

Appendix B, Clause 3

SUBSTANCE	DATE OF ENTRY	REASON FOR LISTING	AREA OF USE
LEAD METALLIC	-	a – Low Toxicity	7.1 – Any use

Appendix E, Clause 3

POISON	STANDARD STATEMENTS
LEAD COMPOUNDS	
• in hair cosmetics	**A** – For advice, contact a Poisons Information Centre (e.g. phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor (at once).
• in other preparations	**A** – For advice, contact a Poisons Information Centre (e.g. phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor (at once). **S1** – If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water.

Appendix F, Clause 4

POISON	WARNING STATEMENTS	SAFETY DIRECTION
Glazing preparations containing LEAD COMPOUNDS.	**50** - Unless adequately fired, utensils glazed with this preparation must not be used as containers for food or beverages; to do so may cause lead poisoning.	
LEAD COMPOUNDS		
a) in hair cosmetics.	**25** - Do not use on broken skin. Wash hands thoroughly after use.	
b) when in Schedule 6.		**1** - Avoid contact with eyes. **4** - Avoid contact with skin. **8** - Avoid breathing dust (or) vapour (or) spray mist.

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LEAD
cross reference: GLAZING PREPARATIONS, PRINTING INKS or INK ADDITIVES, SELENIUM
Schedule 4

LEAD COMPOUNDS
cross reference: GLAZING PREPARATIONS, PRINTING INKS or INK ADDITIVES, SELENIUM
Schedule 10
Schedule 6
Appendix E, Clause 3
Appendix F, Clause 4 (in glazing preparations)
Appendix F, Clause 4

LEAD METALLIC

Appendix B, Clause 3

Future scheduling and proposed changes

Note: the proposal is to amend entries that have not yet been introduced into the Poisons Standard pursuant to the final decision to amend the Poisons Standard published in September 2021. For clarity, the applicant's proposed amendments are shown below as changes compared to the future entries for lead as they are anticipated to appear in the Poisons Standard from 1 October 2023.

The applicant's proposed amendments to the Poisons Standard are:[25]

PART 2, DIVISION 9 - General requirements

(2) An ~~anti-fouling or~~ anti-corrosive paint containing more than 0.009% lead (the proportion of lead for the purposes of this section is calculated as a percentage of the element present in the non-volatile content of the paint) must not be manufactured, supplied or used.

[25] Proposed additions are shown in green underlined font, proposed deletions are shown in red strikethrough font, and text without this formatting represents the text in the Poisons Standard as it is currently due to appear from 1 October 2023. Only parts or schedules of the Poisons Standard that are proposed to be amended by the current applicant are depicted—refer to 'Current Scheduling' for a comprehensive view of entries for lead in the Poisons Standard.

(3) An anti-fouling paint containing more than 0.06% lead (the proportion of lead for the purposes of this section is calculated as a percentage of the element present in the non-volatile content of the paint) must not be manufactured, supplied or used.

(~~3~~4) A paint (other than an anti-fouling or anti-corrosive paint) or tinter containing more than 0.009% lead (calculated as a percentage of the element present in the non-volatile content of the paint) must not be manufactured, supplied or used.

Schedule 10

LEAD COMPOUNDS:

a) in ~~anti-fouling or~~ anti-corrosive paints **except** in preparations containing 0.009% or less of lead calculated on the non-volatile content of the paint; or

b) in anti-fouling paints **except** in preparations containing 0.06% or less of lead calculated on the non-volatile content of the paint; or

c) in paints (other than anti-fouling or anti-corrosive paints), tinters, inks or ink additives **except** in preparations containing 0.009% or less of lead calculated on the non-volatile content of the paint, tinter, ink or ink additive.

Background

Anti-fouling paints are applied to the hulls of water vessels to prevent biofouling, which reduces streamlining and increases fuel consumption, as well as increasing the risk of introduction of invasive species. Anti-fouling paints most commonly used in Australia presently are based on recycled copper, which contains lead as an impurity.

The permissible level of lead in anti-fouling paints is due to be reduced to 90 mg/kg (equivalent to 90 ppm or 0.009%) in the Therapeutic Goods (Poisons Standard - October 2023) Instrument 2023 pursuant to a final decision of the chemicals scheduling delegate on September 2021. The decision was made due to the public health concerns pertaining to lead, being a substance with known cumulative toxicity to humans. There is no regulatory threshold for human exposure, below which is considered safe. Instead, international standards highlight the need to reduce exposure to lead from various sources to as low as possible or eliminated altogether. In a similar manner, the United Nations Environment Program has endorsed lower limits for the presence of lead in paint, with the 90 mg/kg limit being adopted by several countries for some or all types of paints and coatings.

Summary of applicant's reasons for the proposal

- Lead is an impurity in the zinc and copper used in a range of specialty paints – anti-fouling and anti-corrosive paints.
- Achieving a 90 ppm lead limit is possible for anti-corrosive paints containing zinc. However, it is not currently feasible for anti-fouling paints based on cuprous oxide. This is recognised by other governments, including the European Union, Singapore and United States. It is also recognised by the UNEP, the agency promoting the adoption of the 90 ppm limit.
- Australia is alone in applying the 90 ppm limit to anti-fouling paints.
- Australia's failure to align its anti-fouling paint standards with those applying in other jurisdictions will have significant impact on the cost and availability of anti-fouling paints in Australia. This will have flow-on implications for the Australian industries that rely on copper-based anti-fouling paints, including ship building and repairs, maritime transportation, maritime tourism, maritime infrastructure and the commercial fishing fleet. It will also have impacts for leisure craft and vessels.
- Human exposure to anti-fouling paints is extremely limited. Once applied, anti-fouling sits below the waterline on the vessel's hull. Most Australians will never be exposed to anti-fouling paints.

Hence, the public health risk from exposure to the low levels of lead in anti-fouling paints is extremely low, particularly at the 600 ppm level.

Key uses / expected use

Industrial and commercial use – water vessels including yachts, boats and ships.

Australian regulations

- According to the TGA Ingredient Database,[26] lead 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 and Prescription Medicines;
  - Available for use as an Equivalent Ingredient in Listed Medicines.
- As of March 2023, there were no medicines currently active on the Australian Register of Therapeutic Goods (ARTG)[27] that contain lead as an active ingredient.
- According to the Therapeutic Goods (Permissible Ingredients) Determination[28] No.1 of 2023, lead is permitted to be included in listed medicines as follows:

Item	Ingredient name	Purpose	Specific requirements
2981	LEAD	H	Only for use as an active homeopathic ingredient. The concentration in the medicine must be no more than 0.001%.
H = homoeopathic preparation ingredient meaning an ingredient that is a constituent of a homoeopathic preparation			

- Lead is not included in the TGA prescribing medicines in pregnancy database.[29]
- There are no warning statements pertaining to lead in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.[30]
- As of March 2023, there were no reports of adverse events for products containing lead as an active ingredient on the Database of Adverse Event Notifications (DAEN).[31]
- As of March 2023, there was one product containing lead (as lead acetate) listed on the Public Chemical Registration Information System Search (PubCRIS).[32] The product is a dermatological antiseptic lotion.
- In 2009-2019 there were no adverse experiences recorded for lead in the APVMA Adverse Experience Reporting Program database (AERP).[33]

[26] TGA Ingredient Database https://www.ebs.tga.gov.au/
[27] ARTG database https://www.tga.gov.au/artg
[28] Therapeutic Goods (Permissible Ingredients) Determination https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LBPermissible%20IngredientsRB%20Determination
[29] TGA prescribing medicines in pregnancy database https://www.tga.gov.au/prescribing-medicines-pregnancy-database
[30] Therapeutic Goods (Medicines Advisory Statements) Specification 2021 https://www.legislation.gov.au/Details/F2021L01888
[31] Database of Adverse Event Notifications (DAEN) https://apps.tga.gov.au/Prod/daen/daen-entry.aspx
[32] Public Chemical Registration Information System Search (PubCRIS) https://portal.apvma.gov.au/pubcris
[33] APVMA Adverse Experience Reporting Program database (AERP) https://apvma.gov.au/node/10946

International regulations

The regulations cited below pertain only to lead in anti-fouling paints.

- The United Nations Environment Programme[34] statement on the regulation of lead paint indicates that due to the presence of lead impurity in recycled copper, copper-based marine anti-fouling coatings would not be able to consistently meet a 90 ppm lead limit at this time.
- The Performance Specification on Paint System, Anticorrosive and Antifouling, Ship Hull 2013,[35] as approved for use by all Departments and Agencies of the United States Department of Defence, limits lead levels in anti-fouling topcoat paints to 600 mg/L of soluble lead and/or its compounds and less than 0.06 weight percent total lead and/or its compounds.
- The European Union (EU) evaluated and approved a limit of 1200 ppm residual lead contamination in cuprous oxide which often comprises less than 50% by weight in marine antifouling coatings, generally resulting in less than 600 ppm lead in the marine anti-fouling coating.[36]
- The Environmental Protection And Management Act (Amendment Of Second Schedule) Order 2021, implemented by the Ministry of Sustainability and the Environment, Singapore, excludes anti-fouling and anti-corrosive paints from the provisions on lead compounds in paint in Part I "Toxic Substances" of Appendix 2 of the Environmental Protection Administration Law (90-ppm limit). [37]
- The Vietnam Chemical Agency (Vinachemia) has a 600 ppm limit for all paints from March 2021, with a 90 ppm limit of 5 years post-implementation. However, anti-foulings are exempt, classified under a different HS code prescribed in the National Technical Regulations. [38,39]

Information sought by the delegate

Information is sought in relation to any matter that is required to be taken into account by the decision-maker (where relevant) to protect public health in accordance with subsection 52E(1) of the *Therapeutic Goods Act 1989*. However, the decision maker is particularly seeking information regarding the risks when applying or removing lead-containing anti-fouling paints from objects such as marine vessels undergoing maintenance. This includes the current risk mitigation practices of persons within the industry using and disposing of anti-fouling paints.

2.2 Ibotenic acid

Proposal

The applicant has proposed the creation of new entries in Schedule 4 and Schedule 7 for ibotenic acid. The Schedule 4 entry is intended to capture therapeutic use, while the Schedule 7 entry will cover all other uses of the substance.

[34] www.unep.org/explore-topics/chemicals-waste/what-we-do/emerging-issues/global-alliance-eliminate-lead-paint/faq

[35] everyspec.com/MIL-PRF/MIL-PRF-010000-29999/MIL-PRF-24647D_8111/

[36] This statement was accepted and supported by the United Nations Environment Programme (UNEP) and the UN Lead Paint Alliance. It is available on the UNEP website under "Answers to Questions about Lead Paint and Lead Paint Laws (FAQs)."

[37] Environmental Protection And Management Act (Amendment Of Second Schedule) Order 2021 - https://sso.agc.gov.sg/SL-Supp/S365-2021/Published/20210603?DocDate=20210603&ViewType=Pdf&_=20210604054914

[38] National technical regulation on the limits of total lead in paints - https://images.chemycal.com/Media/Files/TBT/20_5970_00_x.pdf

[39] Lead paint in Vietnam, October 2021 IPEN https://ipen.org/sites/default/files/documents/ipen-2021-lead-paint-vietnam_v1_5-en.pdf

CAS number:

2552-55-8

Alternative names

α-amino-2,3-dihydro-3-oxo-5-isoxazoleacetic acid; α-amino-3-hydroxy-5-isoxazoleacetic acid; amino-(3-hydroxy-5-isoxazolyl)acetic acid

Applicant

Private applicant

Proposed Scheduling

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

The applicant's proposed amendments to the Poisons Standard are:[40]

Schedule 4 – New Entry

IBOTENIC ACID for therapeutic use in preparations included in the Australian Register of Therapeutic Goods.

Schedule 7 – New Entry

IBOTENIC ACID **except** when included in Schedule 4.

Index – New Entry

IBOTENIC ACID

Schedule 7
Schedule 4

Background

Ibotenic acid is a psychoactive constituent of *Amarita spp*. mushrooms with a history of use in indigenous cultural ceremonies. Ibotenic acid is a prodrug, as after ingestion it is partially metabolised into the pharmacologically active substance muscimol, which is currently included in Schedule 9 of the Poisons Standard. Ibotenic acid and muscimol are isoxazole derivatives that resemble the neurotransmitters glutamate and GABA, respectively, having central nervous system (CNS) effects such as euphoria, disorientation, agitation, and occasionally seizures.

Summary of applicant's reasons for the proposal

- Ibotenic acid is a hazardous psychedelic neurotoxin that should be in Schedule 7 according to the toxicity of the substance. However, ibotenic acid is approved by the Therapeutic Good Administration to be used as an ingredient in therapeutic biological devices.
- Due to the severe neurotoxic nature of ibotenic acid, therapeutic use of the substance should have overview and responsibility of a medical practitioner as a Schedule 4 poison.

Key uses / expected use

Medicines, medical research

[40] 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.

Australian regulations

- According to the TGA Ingredient Database,[41] ibotenic acid is:
  - Not available as an Active Ingredient in any therapeutic good;
  - Available for use as an Excipient Ingredient in Devices;
  - Not available as an Equivalent Ingredient in any therapeutic good.
- As of March 2023, there were no medicines currently active on the Australian Register of Therapeutic Goods (ARTG)[42] that contain ibotenic acid as an active ingredient.
- Ibotenic acid is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination[43] No.1 of 2023.
- Ibotenic acid is not included in the TGA prescribing medicines in pregnancy database.[44]
- There are no warning statements pertaining to ibotenic acid in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.[45]
- As of March 2023, there were no reports of adverse events for products containing ibotenic acid as an active ingredient on the Database of Adverse Event Notifications (DAEN).[46]
- As of March 2023, there were no products containing ibotenic acid as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS).[47]

International regulations

- According to the European Chemicals Agency (ECHA),[48] ibotenic acid is toxic if swallowed.
- Ibotenic acid is not included in the databases of the European Commission for cosmetic ingredients (CosIng),[49] the New Zealand Inventory of Chemicals (NZIoC)[50] or Medsafe Medicines Classification Database,[51] the United States Food and Drug Administration[52] or the Health Canada Drug Product Database.[53]

2.3 Amygdalin and hydrocyanic acid

Proposal

The applicant has proposed amendment of the Poisons Standard to exclude, from the Schedule 10 entry for amygdalin and the Schedule 4 entry for hydrocyanic acid, preparations of Wild Cherry Bark

[41] TGA Ingredient Database https://www.ebs.tga.gov.au/
[42] ARTG database https://www.tga.gov.au/artg
[43] Therapeutic Goods (Permissible Ingredients) Determination https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LBPermissible%20IngredientsRB%20Determination
[44] TGA prescribing medicines in pregnancy database https://www.tga.gov.au/prescribing-medicines-pregnancy-database
[45] Therapeutic Goods (Medicines Advisory Statements) Specification 2021 https://www.legislation.gov.au/Details/F2021L01888
[46] Database of Adverse Event Notifications (DAEN) https://apps.tga.gov.au/Prod/daen/daen-entry.aspx
[47] Public Chemical Registration Information System Search (PubCRIS) https://portal.apvma.gov.au/pubcris
[48] ECHA echa.europa.eu/substance-information/-/substanceinfo/100.165.123
[49] CosIng ec.europa.eu/growth/tools-databases/cosing/index.cfm?fuseaction=search.results
[50] NZIoC www.epa.govt.nz/database-search/new-zealand-inventory-of-chemicals-nzioc/DatabaseSearchForm/?SiteDatabaseSearchFilters=36&Keyword=ibotenic&DatabaseType=NZIOC
[51] Medsafe www.medsafe.govt.nz/profs/class/classintro.asp
[52] Drugs@FDA www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process
[53] Health Canada health-products.canada.ca/dpd-bdpp/dispatch-repartition

containing these substances. The exclusion is subject to additional labelling requirements and the maximum recommended daily dose being less than 5 mg of amygdalin or 0.3 mg of hydrocyanic acid.

CAS number:

29883-15-6 (amygdalin)

74-90-8 (hydrocyanic acid)

Alternative names

AMYGDALIN: amygdaloside; mandelonitrile-β-gentiobioside; D-mandelonitrile-β-D-glucosido-6-β-D-glucoside;
(α*R*)-α-[(6-*O*-β-D-Glucopyranosyl-β-D-glucopyranosyl)oxy]benzeneacetonitrile; laetrile

HYDROCYANIC ACID: hydrogen cyanide; formonitrile; prussic acid; AC

Applicant

Private applicant

Proposed Scheduling

The applicant's proposed amendments to the Poisons Standard are:[54]

Schedule 10 – Amend Entry

AMYGDALIN for therapeutic use, **except**:

(a) in preparations entered on the ARTG containing Wild Cherry Bark (Prunus serotina) containing amygdalin as a naturally occurring constituent; and
(b) where the preparation is labelled, in bold face letters not less than 1.5 mm high:
    a. for adult use
    b. not for use in pregnancy
    c. if symptoms persist, seek professional advice
(c) the maximum recommended daily dose of the preparation provides less than 5 mg of amygdalin.

Schedule 7

HYDROCYANIC ACID **except**:

(a) when included in Schedule 4; or
(b) its salts and derivatives other than cyanides separately specified in this Schedule.

Schedule 4 – Amend entry

HYDROCYANIC ACID for therapeutic use, **except**:

(a) in preparations entered on the ARTG containing Wild Cherry Bark (Prunus serotina) containing hydrocyanic acid and/or amygdalin as naturally occurring constituents; and
(b) where the preparation is labelled, in bold face letters not less than 1.5 mm high:
    a. for adult use
    b. not for use in pregnancy
    c. if symptoms persist, seek professional advice

[54] 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.

(c) the maximum recommended daily dose of the preparation provides less than 0.3 mg of hydrocyanic acid (including the theoretical yield from the complete hydrolysis of any amygdalin present).

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AMYGDALIN
cross reference: APRICOT KERNELS

Schedule 10

HYDROCYANIC ACID
cross reference: CYANIDES, APRICOT KERNELS

Schedule 7
Schedule 4
Appendix F, clause 4
Appendix G, clause 1
Appendix J, clause 1

Secretariat note: the proposed scheduling as shown above would cause the relevant Wild Cherry Bark preparations containing hydrocyanic acid to be in Schedule 7, rather than not be scheduled. To give effect to the applicant's intent, an amendment (not depicted above) to the Schedule 7 (Dangerous Poisons) entry for hydrocyanic acid would be required to exclude all therapeutic uses that are proposed by the applicant to be excluded from Schedule 4.

Background

Amygdalin is a cyanogenic glycoside found naturally in many plants including cassava, sorghum, lima beans, bitter almonds, apricot kernels and seeds of other plants in the Prunus genus. Amygdalin hydrolyses to hydrocyanic acid, a highly poisonous compound, through beta-glucoside enzymes in human digestive tract. Plants containing amygdalin and hydrocyanic acid are used in traditional Chinese medicines for the treatment of a variety of indications. Amygdalin has previously been, and to a certain extent continues to be, promoted as an alternative treatment for cancer.

Summary of applicant's reasons for the proposal

- PRUNUS SEROTINA (Wild Cherry Bark) is included in the *Therapeutic Goods (Permissible Ingredients) Determination (No. 5) 2022* (entry 4208) as an Active, Excipient or Homeopathic ingredient. Amygdalin and hydrocyanic acid are mandatory components of the ingredient: the concentration of amygdalin must be 0% and the concentration of hydrocyanic acid must be no more than 1 microgram/kg or 1 microgram/L.
- It is not possible to achieve an amygdalin concentration of 0% in crude Wild Cherry Bark material. The current scheduling of amygdalin thus effectively bans Wild Cherry Bark from use in therapeutic goods. This applies to listed complementary medicines on the ARTG as well as raw materials used by herbal medicine practitioners to compound extemporaneous medicines that are exempt from inclusion on the ARTG.
- The Scheduling Policy Framework for Medicines and Chemicals allows for a cut-off from scheduling where the substance no longer meets the factors for inclusion in the Schedule or in any other Schedule in the Poisons Standard. Amygdalin at less than 5 mg per daily dose in adults and hydrocyanic acid at less than 0.3 mg per daily dose each meet this criterion.

Key uses / expected use

Medicines

Australian regulations

- According to the TGA Ingredient Database,[55] amygdalin is:
  - Not available as an Active Ingredient in any therapeutic good;
  - Not available as an Excipient Ingredient in any therapeutic good;
  - Available for use as an Equivalent Ingredient in Export Only and Listed Medicines.

  Hydrocyanic acid (as hydrogen cyanide) 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 and Prescription Medicines.
- As of March 2023, there were no medicines currently active on the Australian Register of Therapeutic Goods (ARTG)[56] that contain amygdalin or hydrocyanic acid as an active ingredient.
- Amygdalin is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination[57] No.1 of 2023.
- According to the Therapeutic Goods (Permissible Ingredients) Determination[58] No.1 of 2023, hydrocyanic acid (as hydrogen cyanide) is permitted to be included in listed medicines as follows:

Item	Ingredient name	Purpose	Specific requirements
2602	HYDROGEN CYANIDE	H	Only for use as an active homeopathic ingredient
H = homoeopathic preparation ingredient meaning an ingredient that is a constituent of a homoeopathic preparation			

- Neither amygdalin nor hydrocyanic acid are included in the TGA prescribing medicines in pregnancy database.[59]
- There are no warning statements pertaining to amygdalin or hydrocyanic acid in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.[60]
- As of March 2023, there were no reports of adverse events for products containing amygdalin or hydrocyanic acid as an active ingredient on the Database of Adverse Event Notifications (DAEN).[61]
- As of March 2023, there were 2 products containing hydrocyanic acid (as hydrogen cyanide) as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS).[62] Both products are mixed function pesticides.

[55] TGA Ingredient Database https://www.ebs.tga.gov.au/
[56] ARTG database https://www.tga.gov.au/artg
[57] Therapeutic Goods (Permissible Ingredients) Determination https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LBPermissible%20IngredientsRB%20Determination
[58] Therapeutic Goods (Permissible Ingredients) Determination https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LBPermissible%20IngredientsRB%20Determination
[59] TGA prescribing medicines in pregnancy database https://www.tga.gov.au/prescribing-medicines-pregnancy-database
[60] Therapeutic Goods (Medicines Advisory Statements) Specification 2021 https://www.legislation.gov.au/Details/F2021L01888
[61] Database of Adverse Event Notifications (DAEN) https://apps.tga.gov.au/Prod/daen/daen-entry.aspx
[62] Public Chemical Registration Information System Search (PubCRIS) https://portal.apvma.gov.au/pubcris

- In 2009-2019 there were no adverse experiences recorded for hydrocyanic acid in the APVMA Adverse Experience Reporting Program database (AERP).[63]

International regulations

- New Zealand Medsafe's Medicines Classification Database[64] lists amygdalin as a prescription medicine at all strengths. Hydrocyanic acid is included in the same database as follows:

Ingredient	Conditions (if any)	Classification
Hydrocyanic acid	**except** when specified elsewhere in this schedule; **except** in medicines containing 1 microgram or less per litre or per kilogram	Prescription
Hydrocyanic acid	for oral use in packs containing 5 milligrams or less and more than 0.5 milligrams; **except** in medicines containing 1 microgram or less per litre or per kilogram	Pharmacy Only
Hydrocyanic acid	for oral use in packs containing 0.5 milligrams or less; in medicines containing 1 microgram or less per litre or per kilogram	General Sale

- The United States Food and Drug Administration[65] database does not include any products containing amygdalin or hydrocyanic acid.
- Health Canada's Drug Product Database[66] does include any marketed products that contain amygdalin or hydrocyanic acid as an active ingredient.

How to respond

Submissions must be provided by the closing date of **15 May 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 committee/s, 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 **September 2023**.

[63] APVMA Adverse Experience Reporting Program database (AERP) https://apvma.gov.au/node/10946

[64] Medsafe www.medsafe.govt.nz/profs/class/classintro.asp

[65] Drugs@FDA www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process

[66] Health Canada health-products.canada.ca/dpd-bdpp/dispatch-repartition

Version history

Version	Description of change	Author	Effective date
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