Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

Consultation: Proposed amendments to the Poisons Standard – ACMS #45, ACCS #39 and Joint ACMS-ACCS #37 meetings, June 2024

23 April 2024

Confidentiality

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

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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 **June 2024** meetings of the Advisory Committee on Medicines Scheduling (**ACMS**), Advisory Committee on Chemicals Scheduling (**ACCS**) and Advisory Committees on Medicines and Chemicals Scheduling in joint session (**Joint ACMS-ACCS**). Submissions must be received by close of business **22 May 2024.**

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 **22 May 2024**.

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 amendment referred for scheduling advice to ACMS meeting #45

1.1 Sildenafil

Proposal

The applicant proposed to create a new Schedule 3 (Pharmacist only) entry for sildenafil. The proposed amendment would include divided preparations containing 50 mg of sildenafil for oral use, in packs of 4 or fewer dosage units, in Schedule 3 and a new entry for sildenafil in Appendix H to permit advertising of Schedule 3 preparations. Sildenafil is currently included in Schedule 4 (Prescription-only medicines).

CAS number

139755-83-2 (base), 171599-83-0 (as citrate)

Alternative names

Viagra

5-[2-Ethoxy-5-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-1,6-dihydro-1-methyl-3-propyl-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one (CAS name)

Applicant

Private applicant

Proposed Scheduling

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

Schedule 4 – Amend Entry

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

Schedule 3 – New Entry

SILDENAFIL in divided preparations for oral use containing 50 mg of sildenafil per dosage unit in packs of not more than 4 dosage units.

Index – Amend Entry

SILDENAFIL

Schedule 4
Schedule 3
Appendix H, clause 1

Appendix H – New Entry

SILDENAFIL

[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.

Background

Sildenafil, usually presented as the citrate salt, is a well-established first-line therapy for the treatment of erectile dysfunction in adult males. Sildenafil is a phosphodiesterase-5 inhibitor and has been available as a prescription-only medicine in Australia since 1998. Applications for creation of a new Schedule 3 entry for Sildenafil were also considered by the ACMS in July 2017, June 2018 and June 2020.

Summary of applicant's reasons for the proposal

- The availability of sildenafil preparations under the proposed scheduling changes will assist men who may be reluctant to use physician-based health services for the treatment of erectile disfunction.
- Down-scheduling of sildenafil provides a safer route for the treatment of erectile dysfunction and discourages the use of unregulated internet-based sources for advice and treatment.
- The pharmacy model for sildenafil preparations still allows the pharmacist to refer identified patients to their doctor should it be deemed appropriate.

Key uses / expected use

Medicines

Australian regulations

- According to the TGA Ingredient Database, sildenafil (as citrate) 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 April 2024, there were 115 medicines currently active on the Australian Register of Therapeutic Goods (ARTG) that contain sildenafil as an active ingredient. All are prescription-only medicines.
- Sildenafil is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination (No.1) 2024.
- The TGA prescribing medicines in pregnancy database classifies sildenafil (as citrate) as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Sildenafil citrate	B1	Cardiovascular System	Vasodilators	
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 sildenafil in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.
- Since sildenafil was approved for use in Australia in 1998, there have been 1,305 reports of adverse events for products containing sildenafil as an active ingredient on the Database of Adverse Event Notifications (DAEN), with 1,012 reports where sildenafil was the single suspected

medicine. More than half of the total reports (682) were received in the first 2 years after the medicine's approval (1998 and 1999).

- As of April 2024, there were no products containing sildenafil as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS).

International regulations

- The Health Canada Drug Product Database includes 39 marketed products containing sildenafil. All are prescription-only medicines.
- The New Zealand Medsafe Medicines Classification Database lists sildenafil as follows:

Ingredient	Conditions (if any)	Classification
Sildenafil and its structural analogues	Except sildenafil in medicines for oral use containing 100 milligrams or less per dose unit when sold in the manufacturer's original pack containing not more than 12 solid dosage units for the treatment of erectile dysfunction in males aged 35-70 years by a registered pharmacist who has successfully completed a training programme endorsed by the Pharmaceutical Society of New Zealand.	Prescription

- The US Food and Drug Administration's Orange Book includes 89 approved products containing sildenafil. All are prescription-only medicines, including oral suspensions, powders, solutions and tablets.
- Ireland's Health Products Regulatory Authority regulates 46 products containing sildenafil. Three of these products (all tablets containing 50 mg sildenafil) are available without a prescription and can be advertised to the public. The remainder are prescription-only medicines.
- The United Kingdom's electronic medicines compendium (emc) lists 33 active products that contain sildenafil. This includes 5 products (all are tablets containing 50 mg sildenafil) that are available as Pharmacy medicines, i.e., without a prescription.

2 Proposed amendments referred for scheduling advice to ACCS meeting #39

2.1 Allyl esters

Proposal

The Department of Health and Aged Care has proposed amendments to the current Schedule 6 entry for allyl esters to include four additional esters. These four esters are currently captured in Schedule 7 as derivatives of allyl alcohol. The proposal follows a referral from the Australian Industrial Chemicals Introduction Scheme (AICIS; formerly National Industrial Chemicals Notification and Assessment Scheme) assessment of allyl esters of acetic acid ethers published in June 2019.

CAS number

7493-74-5 (allyl phenoxyacetate)

67634-00-8 (allyl (3-methylbutoxy)acetate)

67634-01-9 (allyl (2-methylbutoxy)acetate)

68901-15-5 (allyl (cyclohexyloxy)acetate)

Alternative names

Acetic acid, phenoxy-, 2-propenyl ester

Acetic acid, (3-methylbutoxy)-, 2-propenyl ester; allyl amyl glycolate

Acetic acid, 2-(2-methylbutoxy)-, 2-propenyl ester

Acetic acid, (cyclohexyloxy)-, 2-propenyl ester

Proposed Scheduling

These four substances are not currently explicitly listed in the Poisons Standard, but are captured in Schedule 7 as derivatives of ALLYL ALCOHOL:

Schedule 7

ALLYL ALCOHOL **except**:

(a) in preparations containing 5% or less of allyl esters with 0.1% or less of free allyl alcohol by weight of allyl ester; or

(b) when separately specified in these Schedules.

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ALLYL ALCOHOL

Schedule 7
Appendix J, clause 1

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

Schedule 6 – Amend Entry

ALLYL ESTERS (excluding derivatives) being:

(a) ALLYL CYCLOHEXANEACETATE (CAS No. 4728-82-9); or

(b) ALLYL CYCLOHEXANEPROPIONATE (CAS No. 2705-87-5); or

(c) ALLYL HEPTANOATE/ALLYL HEPTYLATE (CAS No. 142-19-8); or

(d) ALLYL HEXANOATE (CAS No. 123-68-2); or

(e) ALLYL ISOVALERATE (CAS No. 2835-39-4); or

(f) ALLYL NONANOATE (CAS No. 7493-72-3); or

(g) ALLYL OCTANOATE (CAS No. 4230-97-1); or

(h) ALLYL PHENYLACETATE (CAS No. 1797-74-6); or

(i) ALLYL TRIMETHYLHEXANOATE (CAS No. 68132-80-9); or

(j) ALLYL PHENOXYACETATE (CAS No. 7493-74-5); or

(k) ALLYL AMYL GLYCOLATE (CAS No. 67634-00-8); or

(l) ALLYL (2-METHYLBUTOXY)ACETATE (CAS No. 67634-01-9); or

(m) ALLYL (CYCLOHEXYLOXY)ACETATE (CAS No. 68901-15-5);

in preparations containing 0.1% or less of free allyl alcohol by weight of allyl ester **except** in preparations containing 5% or less of allyl esters with 0.1% or less of free allyl alcohol by weight of allyl esters.

Background

The 4 substances that are the subject of this proposal are esters of allyl alcohol and an alkoxycarboxylic acid. They are all used in food flavourings or as fragrance components.

Summary of reasons for the proposal

- The acute toxicity data relating to the four allyl esters in the AICIS referral are consistent with that of the substances already included in the Schedule 6 entry for allyl esters. The data is also consistent with the Scheduling Policy Framework factors for Schedule 6.
- The 4 substances already have reported use in a range of domestic products, including air fresheners, surface wipes, cleaning products, cosmetics and as food additives. There is minimal/no information indicating hazards to human health resulting from use in these products.
- The substances are metabolised in the liver similar to the other scheduled allyl esters.

[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.

Key uses / expected use

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

Australian regulations

- According to the TGA Ingredient Database, allyl phenoxyacetate and allyl amyl glycolate are:
  - Available for use as an Active Ingredient in Biologicals and Prescription Medicines
  - 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.
  - The other two allyl esters are not included in the database.
- As of April 2024, there were 2 medicines currently active on the Australian Register of Therapeutic Goods (ARTG) that contain only one of the specified allyl esters (allyl cyclohexyloxyacetate or allyl amyl glycolate) as an excipient ingredient. Both are non-prescription medicines.
- According to the Therapeutic Goods (Permissible Ingredients) Determination No.1 of 2024, these allyl esters are permitted to be included in listed medicines as follows (allyl (2-methoxybutoxy) acetate is not included in the Determination):

Item	Ingredient name	Purpose	Specific requirements
464	ALLYL AMYL GLYCOLATE	E	Permitted for use only in combination with other permitted ingredients as a flavour or a fragrance. If used in a fragrance the total fragrance concentration in a medicine must be no more than 1%.
467	ALLYL CYCLOHEXYLOXYACETATE	E	Permitted for use only in combination with other permitted ingredients as a fragrance. If used in a flavour the total flavour concentration in a medicine must be no more than 5% If used in a fragrance the total fragrance concentration in a medicine must be no more than 1%.
472	ALLYL PHENOXYACETATE	E	Permitted for use only in combination with other permitted ingredients as a fragrance. If used in a flavour the total flavour concentration in a medicine must be no more than 5% If used in a fragrance the total fragrance concentration in a medicine must be no more than 1%.
E = excipient for a medicine meaning an ingredient that is not an active ingredient or a homoeopathic preparation ingredient			

- There are no entries relating to any of the four allyl esters in the proposal in the TGA prescribing medicines in pregnancy database.
- There are no warning statements pertaining to any of the four allyl esters in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.
- As of April 2024, there were no reports of adverse events for products containing any of the four allyl esters in the proposal as an active ingredient on the Database of Adverse Event Notifications (DAEN).

- As of April 2024, there were no products containing any of the four allyl esters in the proposal as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS).
- All four allyl esters in the proposal are listed on the Australian Industrial Chemicals Introduction Scheme's industrial chemicals inventory.

International regulations

- The European Commission database on cosmetic substances and ingredients (CosIng) includes all four allyl esters in the proposal. All are listed in Annex III of Regulation (EC) No 1223/2009, which permits use of the substances in cosmetics subject to restrictions (level of free allyl alcohol in the ester shall be less than 0.1%).
- The New Zealand Inventory of Chemicals (NZIoC) lists allyl (2-methylbutoxy)acetate as "does not have an individual approval but may be used as a component in a product covered by a group standard. It is not approved for use as a chemical in its own right". The other three allyl esters in the proposal are listed on the NZIoC as "does not have an individual approval but may be used under an appropriate group standard".
- None of the four allyl esters are included on New Zealand Medsafe's Medicines Classification Database or Health Canada's Drug Product Database.

2.2 Glyoxylic acid

Proposal

The Department of Health and Aged Care has proposed the creation of a Schedule 6 entry for glyoxylic acid. The proposal is intended to mitigate the risks arising from dermal and ocular exposure to these chemicals, particularly among workers and end users. The proposal follows a referral from the Australian Industrial Chemicals Introduction Scheme (AICIS) evaluation of glyoxylic acid published in December 2022.

CAS number

298-12-4 (Acetic acid, oxo-)

563-96-2 (Acetic acid, dihydroxy-)

Alternative names

Acetic acid, oxo-

Acetic acid, dihydroxy-

Formylformic acid

Oxoethanoic acid

Proposed Scheduling

Glyoxylic acid is not currently listed in the Poisons Standard. The proposal is to amend the Poisons Standard as follows[3]:

Schedule 6 – New Entry

GLYOXYLIC ACID (including its salts and esters) in cosmetic products or when packed and labelled for use as an agricultural chemical **except** in cosmetic preparations containing up to 12% w/v of glyoxylic acid for salon use only, when labelled in accordance with requirements under applicable jurisdictional Work Health and Safety laws, as amended from time to time.

Appendix E, clause 3 (First aid instructions for poisons) – New Entry

Item	Poison	Statement code (and statement)
138a	GLYOXYLIC ACID	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).) G3 (If swallowed, do NOT induce vomiting.) E2 (If in eyes, hold eyelids apart and flush the eye continuously with running water. Continue flushing until advised to stop by a Poisons Information Centre (e.g. phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor, or for at least 15 minutes.)

Appendix F, clause 4 (Poisons that must be labelled with warning statements and safety directions) – New Entry

Item	Poison	Warning statement item number (and statement)	Safety direction item number (and statement)
160a	GLYOXYLIC ACID	79 (Will irritate eyes)	1 (Avoid contact with eyes) 5 (Wear protective gloves when mixing or using) 6 (Wash hands after use) 31 (Do not use on broken skin)

Index – New Entry

GLYOXYLIC ACID

Schedule 6
Appendix E, clause 3
Appendix F, clause 4

Background

An evaluation statement of glyoxylic acid the Australian Industrial Chemicals Introduction Scheme (AICIS) recommended an amendment to the Poisons Standard with respect to glyoxylic acid to restrict the exemptible concentration in cosmetics and provide warning statements and safety directions relating to skin sensitisation and eye irritation.

Summary of reasons for the proposal

- Glyoxylic acid has a potential to cause sensitisation effects at low pH. Inhalation of aerosols/vapours is expected when the substance is applied onto hair (often added as a pH adjuster in hair products) and subsequently heated during hair straightening/styling process.

[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.

- Additional control measures are required to manage the risk arising from dermal and ocular exposure to these chemicals, particularly among workers and end users.

Key uses / expected use

Cosmetic, domestic, industrial use, pesticide formulations.

Australian regulations

- According to the TGA Ingredient Database, glyoxylic acid is not an approved therapeutic ingredient.
- As of April 2024, there were no medicines currently active on the Australian Register of Therapeutic Goods (ARTG) that contain glyoxylic acid as an active ingredient.
- Glyoxylic acid is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination No.1 of 2024 .
- The TGA prescribing medicines in pregnancy database does not classify glyoxylic acid.
- The Therapeutic Goods (Medicines Advisory Statements) Specification 2019 does not require any warning statements pertaining to glyoxylic acid to be included on the labelling.
- As of April 2024, there were no reports of adverse events for products containing glyoxylic acid as an active ingredient on the Database of Adverse Event Notifications (DAEN).
- Between 2014 and 2020 no adverse experiences were recorded for glyoxylic acid in the APVMA Adverse Experience Reporting Program database (AERP).
- Glyoxylic acid is listed on the Australian Industrial Chemicals Introduction Scheme's industrial chemicals inventory.

International regulations

- Glyoxylic acid is listed on the European Chemicals Agency (ECHA) with the hazard classification of GHS05 – 'Corrosive' and GHS07 – 'Health Hazard.' According to the harmonised classification and labelling (ATP15) approved by the European Union, this substance causes serious eye damage and may cause an allergic skin reaction. Skin sensitising is noted as a property of a concern for glyoxylic acid.
- The European Commission database for information on cosmetic substances and ingredients database (CosIng) lists glyoxylic acid as an antistatic, buffering and hair-waving or straightening agent.
- The New Zealand Inventory of Chemicals (NZIoC) does not list an individual approval for glyoxylic acid but it may be used under an appropriate group standard.

3 Proposed amendments referred for scheduling advice to the Joint ACMS-ACCS meeting #37

3.1 Intravenous potassium salts

Proposal

The applicant has proposed a new Schedule 4 entry for preparations of potassium salts for injection or infusion. Potassium salts for intravenous administration are currently unscheduled.

CAS number

7447-40-7 (potassium chloride)

7778-77-0 (potassium dihydrogen phosphate)

127-08-2 (potassium acetate)

Alternative names

Potassium phosphate, monobasic; phosphoric acid potassium salt 1:1 (CAS name)

Acetic acid potassium salt 1:1 (CAS name)

Applicant

Private applicant

Proposed Scheduling

The applicant's proposed amendments to the Poisons Standard are[4]:

Schedule 4 – New Entry

POTASSIUM SALTS, being the chloride, phosphate or acetate salts of potassium alone or in any combination, in preparations for human therapeutic use for injection or infusion **except** those containing less than 10 mmol/100mL of potassium.

Index – New Entry

POTASSIUM SALTS
cross reference: POTASSIUM CHLORIDE, POTASSIUM PHOSPHATE, POTASSIUM DIHYDROGEN PHOSPHATE, POTASSIUM ACETATE

Schedule 4

Background

Intravenous preparations of potassium are used for the prevention and treatment of moderate to severe potassium deficiency (hypokalaemia) in cases where oral therapy is not possible or appropriate. Intravenous potassium replacement carries risks of inadvertent hyperkalaemia (excessive

[4] 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.

potassium), fluid overload, and peripheral vein extravasation/thrombophlebitis. Rapid administration may cause cardiac arrest. Potassium chloride is the most commonly used potassium salt for injection or infusion, with potassium phosphate and potassium acetate used less often.

Summary of applicant's reasons for the proposal

- The prescription and administration of intravenous potassium should be the responsibility of a qualified medical practitioner due to the risk associated with inadvertent use of these medicines. These risks can include cardiac arrest and death if the medicine is not administered correctly using a rate limiting device. Risks are also associated with the preparation of potassium chloride concentrates prior to administration. While hospitals have independently developed high-risk medicine policies that control the availability and administration of intravenous potassium products, the Poisons Standard should be amended to reflect the risks associated with these products.
- International jurisdictions, including the United Kingdom and United States, already regulate intravenous potassium as a prescription-only medicine.

Key uses / expected use

Medicines

Australian regulations

Note: as potassium chloride is the commonly used potassium salt in therapeutic products, this section focuses on the regulation of this substance.

- According to the TGA Ingredient Database, potassium chloride is:
  - Available for use as an Active Ingredient in Biologicals, Export Only, Listed Medicines, Over the Counter and Prescription Medicines
  - Available for use as a Homeopathic Ingredient in Listed Medicines
  - Available for use as an Excipient Ingredient in Biologicals, Devices, Export Only, Listed Medicines, Over the Counter and Prescription Medicines
  - Available for use as an Equivalent Ingredient in Listed Medicines
- As of April 2024, there were 453 medicines currently active on the Australian Register of Therapeutic Goods (ARTG) that contain potassium chloride as an active ingredient. These include 80 products for injection and infusion.

- According to the Therapeutic Goods (Permissible Ingredients) Determination No.1 of 2024, potassium chloride is permitted to be included in listed medicines as follows:

Item	Ingredient name	Purpose	Specific requirements
4078	POTASSIUM CHLORIDE	A, E, H	When for oral use: (a) potassium is a mandatory component of potassium chloride; (b) the medicine requires the following warning statement on the medicine label: - (POTAS1) 'If you have kidney disease or are taking heart or blood pressure medicines - consult your doctor or pharmacist before use. Keep out of reach of children.'; and (c) except when the medicine is for use as oral rehydration therapy, the amount of potassium chloride per dosage unit must not be more than 550 mg. Medicines containing potassium chloride for use as oral rehydration therapy, are subject to the following conditions: (a) the medicine complies with the requirements specified in the British Pharmacopoeia, as in force or existing from time to time, for Oral Rehydration Salts; (b) the sodium, potassium and glucose content, and total osmolarity of the solution after it has been prepared according to the instructions on the packet are consistent with the criteria specified by the World Health Organisation (WHO) and the United Nations Children's Fund (UNICEF) in the document 'Expert consultation on oral rehydration salts formulation' 18 July 2001; and (c) the following warning statements are required on the medicine label: - (UOAD) 'Use only as directed' - (DIAR3) 'If diarrhoea persists, seek medical advice.' When for dental use, the concentration of potassium chloride in the medicine must not be more than 3.75%.
A = active ingredient for a medicine has the same meaning as in the Regulations 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			

- Potassium chloride is not included in the TGA prescribing medicines in pregnancy database.
- There are no warning statements pertaining to potassium chloride in the Therapeutic Goods (Medicines Advisory Statements) Specification 2021.
- As of April 2024, there were 1,106 reports of adverse events for products containing potassium chloride as an active ingredient on the Database of Adverse Event Notifications (DAEN), with 339 reports where potassium chloride was the single suspected medicine. There were 70 reports of deaths associated with potassium chloride use. The most common reported events were associated with site of administration and included symptoms such as rash and pruritis.
- As of April 2024, there were 19 products containing potassium chloride as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS). Most of these products contain potassium chloride as a component of an electrolyte supplement for livestock.

- In 2015-2020 there were no adverse experiences recorded for potassium chloride in the APVMA Adverse Experience Reporting Program database (AERP).

International regulations

- The Health Canada Drug Product Database includes 163 marketed products containing potassium chloride. Most are classified as ethical medicines that do not require a prescription but are generally provided under the guidance of a medical practitioner.
- The New Zealand Medsafe Medicines Classification Database lists potassium as a general sale substance in medicines for oral rehydration therapy, parenteral nutrition replacement or dialysis.
- The US Food and Drug Administration's Orange Book includes 334 approved products containing potassium chloride as an active ingredient. All are listed as prescription-only medicines, including oral preparations, emulsions and injectable preparations.
- The United Kingdom's electronic medicines compendium (emc) lists 51 active products that contain potassium chloride for infusion. All are listed as prescription-only medicines.

3.2 Sulfonamides

Proposal

The Department of Health and Aged Care has proposed amendments to the current Schedule 4 entry for sulfonamides. The proposal is intended to clarify the status of sulfonamides when used in a variety of settings, including therapeutically and industrially. The proposal follows a referral from the Australian Industrial Chemicals Introduction Scheme (AICIS) evaluation of sulfonamides published in January 2022.

CAS number

Sulfonamides are a large class of substances with a variety of applications. The most common sulfonamides for therapeutic use are:

Sulfamethoxazole (732-46-6)

Sulfasalazine (599-79-1)

Sulfadiazine (68-35-9)

Proposed Scheduling

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

Schedule 4 – Amend Entry

SULFONAMIDES in preparations for therapeutic use **except**:

(a) when separately specified in ~~this~~these Schedules; or

(b) ~~when included in Schedule 3, 5 or 6; or~~ when used as an excipient.

(c) ~~when packed and labelled solely for use as a herbicide~~.

[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.

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SULFONAMIDES
cross reference: SULFACETAMIDE, SULPHANILAMIDE

Schedule 4

Background

The current Schedule 4 entry for sulfonamides is not specific to therapeutic use and captures all uses of these substances, such as industrial use in manufacturing. The AICIS evaluation recommended a review to ensure that is the current entry is fit for purpose and accurately reflects the hazards associated with these substances.

Summary of reasons for the proposal

- Sulfonamides are a wide-ranging class of substances whose applications extend well beyond therapeutic use. The original intent of the Schedule 4 group entry was only to capture substances with antimicrobial activity.
- Some chemicals in the class have industrial use, such as in manufacturing, and are not suitable for access by prescription only. It is suspected that those importing, handling and using these substances are unaware of the restrictions imposed by the current scheduling.

Key uses / expected use

Medicines, veterinary, agriculture, industrial use, pesticide formulations, foods (artificial sweeteners).

Australian regulations

- According to the TGA Ingredient Database, most of the sulfonamide medicines included in the Poisons Standard are available for use as active ingredients or excipients in Biologicals and Prescription Medicines, and not available for use as Equivalent Ingredients in any application.
- In addition, the following are available for use in Export Only medicines: sulfadiazine, sulfadoxine, sulfamethoxazole, and sulfasalazine.
- As of April 2024, there were 17 medicines currently active on the Australian Register of Therapeutic Goods (ARTG) that contain a scheduled sulfonamide as an active ingredient (namely, sulfamethoxazole, sulfasalazine or sulfadiazine). All products are prescription medicines.
- Sulfonamide antimicrobial substances are not permitted to be included in listed medicines as none are included in the Therapeutic Goods (Permissible Ingredients) Determination No.4 of 2023.
- The TGA prescribing medicines in pregnancy database includes several sulfonamides as follows:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
sulfacetamide	C	Ophthalmic Drugs		
sulfadiazine	C	Antimicrobials	Antibiotics	Sulfonamides
sulfadoxine	C	Antimicrobials	Antibiotics	Sulfonamides
sulfamethizole	C	Antimicrobials	Antibiotics	Sulfonamides
sulfamethoxazole	C	Antimicrobials	Antibiotics	Sulfonamides
sulfasalazine	A	Alimentary system	Antidiarrhoeals	

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. 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.

- The Therapeutic Goods (Medicines Advisory Statements) Specification 2021 requires the following warning statements pertaining to sulfacetamide to be included on the labelling:

Substance	Conditions	Required Statement(s)
Sulfacetamide	In medicines for ophthalmic use	Contact lens wearers should not use this product except on the advice of a doctor or optometrist. If your eye infection does not improve within 48 hours, seek immediate medical advice.

- Between January 2014 and April 2024, on the Database of Adverse Event Notifications (DAEN) there were:
  - 15 reports of adverse events for products containing sulfadiazine as an active ingredient, with 7 reports where sulfadiazine was the single suspected medicine. The reported events were diverse in nature and affected organ class, and
  - 208 reports of adverse events for products containing sulfasalazine as an active ingredient, with 125 reports where sulfasalazine was the single suspected medicine. The reported events were predominantly related to skin disorders and administration site conditions.
- As of April 2024, there were 64 products containing various sulfonamides as an active ingredient/constituent or scheduled substance listed on the Public Chemical Registration Information System Search (PubCRIS). Sulfonamide active ingredients included sulfacetamide, sulfadiazine, sulfadimidine and sulfadoxine.
- Between 2014 and 2020 there were 10 adverse experiences recorded for sulfonamides in the APVMA Adverse Experience Reporting Program database (AERP). Substances involved included mafenide, sulfacetamide, sulfadiazine and sulfadimidine.
- There are at least 155 sulfonamides listed on the Australian Industrial Chemicals Introduction Scheme's industrial chemicals inventory.

International regulations

- Several products containing sulfonamides including sulfacetamide, sulfadiazine, sulfamethoxazole, and sulfasalazine are classified as prescription-only medicines in the United States FDA's Approved Drug Products Database.
- According to Medsafe's Medicines Classification Database, most sulfonamides for therapeutic use are regulated as prescription only medicines in New Zealand. The exceptions are silver sulfadiazine (pharmacy only for packs of 50 grams or less) and sulfacetamide (restricted medicine for ophthalmic use containing 10% or less).
- Under Annex II of Regulation (EC) No 1223/2009, sulphonamides (defined as sulphanilamide and its derivatives obtained by substitution of one or more H-atoms of the -NH2 groups) and their salts are prohibited in cosmetic products. Similar restrictions are included in Canada's Cosmetic Ingredient Hotlist.

How to respond

Submissions must be provided by the closing date of **22 May 2024** 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 and further comments will be sought.

Therapeutic Goods Administration

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