



Australian Government

Department of Health

Therapeutic Goods Administration

Consultation: Proposed amendments to the Poisons Standard – ACCS, ACMS and joint ACCS/ACMS meetings, November 2022

1 September 2022

TGA Health Safety
Regulation

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1 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 2022 meetings of the Advisory Committees on Medicines and Chemicals Scheduling. Submissions must be received by close of business **29 September 2022**.

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 2022.

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

2 Proposed amendments referred for scheduling advice to ACMS meeting #40, November 2022

Ivermectin

Proposal

The applicant has proposed deletion of the Appendix D entry relating to ivermectin. This will remove the restrictions on the prescription of ivermectin, which is currently limited to approved indications by medical specialists in nominated fields. The restrictions were originally implemented due to concerns regarding the significant increase in off-label prescribing of ivermectin for the prevention and treatment of COVID-19.

CAS number:

70288-86-7

Alternative names

22,23-Dihydroabamectin; 22,23-dihydroavermectin B₁; 22,23-dihydro C-076B₁

Applicant

Private applicant

Current scheduling

Ivermectin is currently listed in Schedules 4, 5 and 7 of the Poisons Standard as follows:

Schedule 4

IVERMECTIN:

- a) for human use; or
- b) for the treatment of mange in dogs.

Schedule 7

IVERMECTIN **except** when included in Schedule 4 or 5.

Schedule 5

IVERMECTIN for use in animals:

- a) in preparations for the prophylaxis of heartworm in cats and dogs;
- b) in intraruminal implants containing 160 mg or less of ivermectin;
- c) in preparations containing 3.5 per cent or less of ivermectin when packed in child-resistant packaging or in packaging approved by the relevant registration authority;
or
- d) in other preparations containing 2 per cent or less of ivermectin.

Index

IVERMECTIN

Schedule 7

Schedule 5

Schedule 4

Appendix D, Item 10

It is also included in Appendix D as follows:

10.	Poisons available only when prescribed or authorised for:	
	(1)	<p>an indication that is accepted by the Secretary of the Australian Government Department of Health in relation to the inclusion of ivermectin in tablet dosage form in the Australian Register of Therapeutic Goods (an <i>approved indication</i>); or</p> <p>Note: Approved indications are shown in the public summary of the Australian Register of Therapeutic Goods on the Therapeutic Goods Administration website at www.tga.gov.au.</p>
	(2)	<p>an indication that is not an approved indication, when the preparation is prescribed or authorised by a medical practitioner registered under State or Territory legislation that forms part of the Health Practitioner Regulation National Law, as a specialist in any of the following specialties or fields of specialty practices:</p> <p>(a) dermatology;</p> <p>(b) gastroenterology and hepatology;</p> <p>(c) infectious diseases;</p> <p>(d) paediatric gastroenterology and hepatology;</p> <p>(e) paediatric infectious diseases; or</p>
	(3)	use in a clinical trial that is approved by, or notified to, the Secretary of the Australian Government Department of Health under the Therapeutic Goods Act 1989.
		IVERMECTIN in preparations for oral administration for human use.

Proposed scheduling

No changes are proposed for the entries for ivermectin in Schedules 4, 5 or 7.

Index – Amend Entry

IVERMECTIN

Schedule 7

Schedule 5

Schedule 4

Appendix D, Item 10

Appendix D – Delete Entry

10.	Poisons available only when prescribed or authorised for:	
(1)	<p>an indication that is accepted by the Secretary of the Australian Government Department of Health in relation to the inclusion of ivermectin in tablet dosage form in the Australian Register of Therapeutic Goods (an <i>approved indication</i>); or</p> <p>Note: Approved indications are shown in the public summary of the Australian Register of Therapeutic Goods on the Therapeutic Goods Administration website at www.tga.gov.au.</p>	
(2)	<p>an indication that is not an approved indication, when the preparation is prescribed or authorised by a medical practitioner registered under State or Territory legislation that forms part of the Health Practitioner Regulation National Law, as a specialist in any of the following specialties or fields of specialty practices:</p> <p>(a) dermatology;</p> <p>(b) gastroenterology and hepatology;</p> <p>(c) infectious diseases;</p> <p>(d) paediatric gastroenterology and hepatology;</p> <p>(e) paediatric infectious diseases; or</p>	
(3)	<p>use in a clinical trial that is approved by, or notified to, the Secretary of the Australian Government Department of Health under the Therapeutic Goods Act 1989.</p>	
	IVERMECTIN in preparations for oral administration for human use.	

Background

Ivermectin is an antiparasitic drug that is indicated in tablet form for the treatment of conditions such as strongyloidiasis and scabies. Concerns regarding the increase in off-label prescribing of oral ivermectin as a potential therapy for prophylaxis or treatment of COVID-19 led to the creation of the existing Appendix D entry in September 2021, on the advice of the ACMS. The Appendix D entry restricts off-label prescribing of ivermectin to dermatologists, gastroenterologists, hepatologists, and specialists in infectious diseases. The [National COVID-19 Clinical Evidence Taskforce](#)¹ does not recommend the use of ivermectin for the treatment of COVID-19.

Summary of applicant's reasons for the proposal

- The listing of ivermectin in Appendix D of the Poisons Standard is irrational, irresponsible, reckless, negligent, and possibly criminal. It poses a serious threat to public safety and may

¹ <https://app.magicapp.org/#/guideline/6624/section/113367>

have caused the unnecessary deaths of thousands of Australians by preventing general practitioners from effectively treating their patients.

- Ivermectin is a safe, cheap, and effective medication [that may prevent 44 per cent of COVID-19 infections](#)² and may prevent serious illness and death caused by COVID-19 infections. Ivermectin is well tolerated at doses well beyond those that are typically prescribed for approved indications, which is at odds with the reasoning provided for the Appendix D entry. The [AusPAR for ivermectin](#)³ cites good tolerability and no safety concerns at doses ranging from 30 mg to 120 mg, which is up to 10 times the typical dose for the treatment of scabies.
- The Appendix D listing removes patient choice, and forces patients to access ivermectin on the black market or to use veterinary preparations of ivermectin. This unsupervised use of ivermectin is unsafe, caused by an undue change to the Poisons Standard which has the opposite effect to that which was intended.
- There is no evidence that general practitioners had been prescribing ivermectin unsafely or that this prescribing was undesirable prior to the inclusion of the Appendix D entry for ivermectin. Further, there is no evidence that ivermectin is unsafe when prescribed by doctors and dispensed by pharmacists.
- Vaccines against COVID-19 have not been completely effective and there is an unmet demand for an effective alternative treatment. Rising infection rates could also be ameliorated by the prophylactic use of ivermectin. The use of ivermectin in African countries and the corresponding relatively low rate of COVID-19 infection in these countries supports claims of the efficacy of ivermectin for this purpose, and is supported by a considerable volume of published literature.
- The original decision to place ivermectin into Appendix D was based on research indicating that ivermectin is ineffective in preventing or treating COVID-19. There was a failure to consider if counterfeit ivermectin could explain some or all of the negative research upon which the decision was based.

Key uses / expected use

Medicines (for the purposes of this application)

Australian regulations

- According to the [TGA Ingredient Database](#),⁴ ivermectin 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.

² [Cureus | Ivermectin Prophylaxis Used for COVID-19: A Citywide, Prospective, Observational Study of 223,128 Subjects Using Propensity Score Matching](#)

³ Ivermectin AusPAR <https://www.tga.gov.au/sites/default/files/auspar-ivermectin-131030.pdf>

⁴ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

- As of August 2022, there were three medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)⁵ that contain ivermectin as an active ingredient, all available as prescription-only medicines. This includes one oral dosage form (STROMEKTOL 3 mg tablets).
- Ivermectin is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)⁶ No.4 of 2022.
- The [TGA prescribing medicines in pregnancy database](#)⁷ classifies ivermectin as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Ivermectin	B3	Antimicrobials	Anthelmintics	
<p>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.</p> <p>Studies in animals have shown evidence of an increased occurrence of foetal damage, the significance of which is considered uncertain in humans.</p>				

- There are no warning statements pertaining to ivermectin in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#).⁸
- As of August 2022, there were 32 reports of adverse events for products containing ivermectin as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#),⁹ with 23 reports where ivermectin was the single suspected medicine. There were 5 reports of deaths associated with ivermectin use. The recorded adverse events were widely varied in nature.
- As of August 2022, there were 184 products containing ivermectin as an active ingredient/constituent or scheduled substance listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#).¹⁰
- In 2015-2020 there were 15 adverse experiences recorded for ivermectin in the [APVMA Adverse Experience Reporting Program database \(AERP\)](#).¹¹ [These included 11](#) incidents classified as related to animal health and one related to human health.

⁵ ARTG database <https://www.tga.gov.au/artg>

⁶ Therapeutic Goods (Permissible Ingredients) Determination <https://www.legislation.gov.au/Search/Therapeutic%20Goods%20SLBSPermissible%20IngredientsSRBS%20Determination>

⁷ TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

⁸ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

⁹ Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

¹⁰ Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

¹¹ APVMA Adverse Experience Reporting Program database (AERP) <https://apvma.gov.au/node/10946>

International regulations

- The [Health Canada Drug Product Database](#)¹² lists 20 marketed products containing ivermectin, including 2 prescription-only medicines for human use (one oral tablet and one topical cream).
- The [Medsafe \(New Zealand Medicines and Medical Devices Safety Authority\) Medicines Classification Database](#)¹³ lists ivermectin as a prescription-only medicine.
- [The United States Food and Drug Administration Orange Book](#)¹⁴ lists 8 products containing ivermectin, including two prescription-only oral dosage forms (tablets).
- [The European Commission lists 95 products containing ivermectin in the Union Register of medicinal products.](#)¹⁵ [All products listed are for veterinary use.](#)
- [The Health Products Regulatory Authority of Ireland](#)¹⁶ regulates two products containing ivermectin. Both are topical creams that are available by prescription-only.

International advice and recommendations

- The [World Health Organization](#)¹⁷ recommends not to use ivermectin in patients with COVID-19 except in the context of a clinical trial.
- The [United States National Institutes of Health](#)¹⁸ recommends against the use of ivermectin for the treatment of COVID-19, except in clinical trials.
- Ivermectin is not approved by the [US Food and Drug Administration](#)¹⁹ for the treatment or prevention of COVID-19.
- The [European Medicines Agency](#)²⁰ advises against the use of ivermectin for the prevention or treatment of COVID-19 outside randomised clinical trials.

¹² Health Canada Drug Product Database <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>

¹³ Medsafe Medicines Classification Database <https://www.medsafe.govt.nz/profs/class/classintro.asp>

¹⁴ US FDA Orange Book https://www.accessdata.fda.gov/scripts/cder/ob/search_product.cfm

¹⁵ European Commission Union Register of medicinal products https://ec.europa.eu/health/documents/community-register/html/reg_index_inn.htm

¹⁶ HPRA <https://www.hpra.ie/homepage/medicines/medicines-information/find-a-medicine/results/item?compare=PA22743/015/001.PPA23176/014/001>

¹⁷ WHO Therapeutic and COVID-19: living guideline <https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2022.4>

¹⁸ NIH COVID-19 Treatment Guidelines https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ivermectin/?ACSTrackingID=USCDC_1052-DM74752&ACSTrackingLabel=Ivermectin%20Products%20are%20Not%20Approved%20by%20FDA%20to%20Prevent%20or%20Treat%20COVID-19&deliveryName=USCDC_1052-DM74752

¹⁹ US FDA: Why you should not use ivermectin to treat or prevent COVID 19 <https://www.fda.gov/consumers/consumer-updates/why-you-should-not-use-ivermectin-treat-or-prevent-covid-19>

²⁰ EMA advice on ivermectin for COVID-19 <https://www.ema.europa.eu/en/news/ema-advises-against-use-ivermectin-prevention-treatment-covid-19-outside-randomised-clinical-trials>

Brimonidine

Proposal

The applicant has proposed the creation of a new Schedule 2 entry for ophthalmic preparations containing not more than 0.025 per cent of brimonidine for adult use. The new entry would provide pharmacy access to certain ophthalmic products for the treatment of eye redness and minor irritations in adults aged 18 years and over.

CAS number

59803-98-4

Alternative names

5-Bromo-N-(4,5-dihydro-1H-imidazol-2-yl)-6-quinoxalinamine; 5-bromo-6-(2-imidazolin-2-ylamino)quinoxaline.

Applicant

Private applicant

Current scheduling

Brimonidine is currently listed in Schedule 4 of the Poisons Standard as follows:

Schedule 4

BRIMONIDINE

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BRIMONIDINE

Schedule 4

Proposed scheduling

Schedule 4 – Amend Entry

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

Schedule 2 – Create entry

BRIMONIDINE in ophthalmic preparations for adult use containing not more than 0.025 per cent of brimonidine.

Index – Amend Entry

BRIMONIDINE

Schedule 4

Schedule 2

Background

Brimonidine (used as the tartrate salt) is an alpha-2 selective adrenergic agonist, a class of medicines known for vasoconstrictive properties. Ophthalmic preparations containing 0.025 per cent of brimonidine are used to relieve redness of the eye due to minor irritations such as environmental allergies, dryness and fatigue in adults. Higher strengths are used for lowering elevated intraocular pressure and the treatment of glaucoma. Topical preparations can be used for the treatment of rosacea. All preparations of brimonidine for human therapeutic use are currently Schedule 4 medicines.

Summary of applicant's reasons for the proposal

- Brimonidine tartrate 0.025 per cent w/v is already available and approved as over the counter (OTC) medicines both in the USA for use in children and adults aged 5 and over, and Canada for use in adults 18 and over. It is currently classified as a Schedule 4 prescription only medicine in Australia, however at the 0.025 per cent concentration, the substance meets Schedule 2 scheduling factors.
- Brimonidine at the concentration in the proposal is intended to treat eye redness, itching or irritation, which is easily diagnosed and can be self-managed by the individual, consistent with a Schedule 2 medicine. The substance has no observed potential of misuse or abuse, and at the proposed concentration accidental ingestion is unlikely to have any significant adverse effects in children.
- Brimonidine tartrate has reported some minor side effects such as pain at the application site, nasopharyngitis and headaches. However, all potential side effects reported were mild and temporary. Studies using brimonidine tartrate 0.025 per cent have shown low toxicity and no systemic absorption of the substance.
- Brimonidine tartrate 0.025 per cent is not proposed for use in children under 18 years of age, consistent with Health Canada's recommendation.

Key uses / expected use

Medicines

Australian regulations

- According to the [TGA Ingredient Database](#),²¹ brimonidine 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 2022, there were 7 medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)²² that contain brimonidine (as tartrate) as an active ingredient. All are prescription-only medicines in the form of eye drops or gels, including two dual-active preparations.

²¹ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

²² ARTG database <https://www.tga.gov.au/artg>

- Brimonidine is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)²³ No.4 of 2022.
- The [TGA prescribing medicines in pregnancy database](#)²⁴ classifies brimonidine as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
brimonidine/brinzolamide	B3	Ophthalmic drugs		
brimonidine/timolol	C	Ophthalmic drugs		
brimonidine tartrate	B3	Ophthalmic drugs		

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.

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 brimonidine in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#).²⁵
- Since January 2012, there have been 82 reports of adverse events for products containing brimonidine as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#),²⁶ with 63 reports where brimonidine was the single suspected medicine. The majority of reported incidents related to eye disorders, including iridocyclitis, increased intraocular pressure and conjunctivitis.
- As of August 2022, there were no products containing brimonidine as an active ingredient/constituent or scheduled substance listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#).²⁷

International regulations

- Brimonidine tartrate is listed on the [Food and Drug Administration Approved Drugs Database](#)²⁸ with 16 products, all prescription-only medicines except one with brimonidine tartrate concentration of 0.025 per cent w/v which is available as an OTC medicine.

²³ Therapeutic Goods (Permissible Ingredients) Determination [https://www.legislation.gov.au/Search/Therapeutic per cent20Goods per cent20SLBSPermissible per cent20IngredientsSRBS per cent20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20SLBSPermissible%20IngredientsSRBS%20Determination)

²⁴ TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

²⁵ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

²⁶ Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

²⁷ Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

²⁸ Food and Drug Administration Database <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process>

- [The Health Canada Drug Product Database](#)²⁹ has 19 products listed with brimonidine tartrate as an active ingredient, all of which are prescription-only medicines except one OTC at a concentration of 0.025 per cent w/v.
- The UK's [electronic medicines compendium](#) lists brimonidine tartrate 0.2 per cent w/v eye drops as a prescription only medicine.
- The [Health Products Regulatory Authority of Ireland](#) regulates brimonidine tartrate as a prescription-only medicine.
- New Zealand [Medsafe's Medicines Classification Database](#)³⁰ regulates brimonidine as a prescription-only medicine.

Fexofenadine

Proposal

The applicant has proposed an amendment to the Schedule 2 entry for fexofenadine to increase the pack size available for general sale from 5 dosage units to 10 dosage units, when labelled for the treatment of seasonal allergic rhinitis in adults and children aged 12 years and above.

CAS number

83799-24-0

Alternative names

4-[1-Hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]- α,α -dimethylbenzeneacetic acid; carboxyterfenadine; terfenadine carboxylate

Applicant

Private applicant

Current scheduling

Fexofenadine is currently listed in Schedules 2 and 4 of the Poisons Standard as follows:

Schedule 4

FEXOFENADINE **except:**

- e) when included in Schedule 2;
- f) in divided preparations for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:
 - i) in a primary pack containing 20 dosage units or less and not more than 10 days' supply; and

²⁹ Health Canada Drug Product Database <https://health-products.canada.ca/dpd-bdpp/dispatch-repartition.do>

³⁰ Medsafe Medicines Classification Database <https://www.medsafe.govt.nz/profs/class/classintro.asp>

- ii) labelled with a recommended daily dose not exceeding 120 mg of fexofenadine;
- g) for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:
 - i) in a primary pack containing 5 dosage units or less and not more than 5 days' supply; and
 - ii) labelled with a recommended daily dose not exceeding 180 mg of fexofenadine; or
- h) for the treatment of seasonal allergic rhinitis and children 6 years of age and over when:
 - i) in a primary pack containing 20 dosage units or less and not more than 10 days' supply; and
 - ii) labelled with a recommended daily dose not exceeding 60 mg of fexofenadine.

Schedule 2

FEXOFENADINE in preparations for oral use **except** in divided preparations:

- a) for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:
 - i) in a primary pack containing 20 dosage units or less and not more than 10 days' supply; and
 - ii) labelled with a recommended daily dose not exceeding 120 mg of fexofenadine;
- b) for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:
 - i) in a primary pack containing 5 dosage units or less and not more than 5 days' supply; and
 - ii) labelled with a recommended daily dose not exceeding 180 mg of fexofenadine; or
- c) for the treatment of seasonal allergic rhinitis and children 6 years of age and over when:
 - i) in a primary pack containing 20 dosage units or less and not more than 10 days' supply; and
 - ii) labelled with a recommended daily dose not exceeding 60 mg of fexofenadine.

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FEXOFENADINE

Schedule 4

Schedule 2

Fexofenadine is excluded under the entry for ANTIHISTAMINES in Appendix F, and does not require the specified warning statements as follows:

Warning Statements 39 (This medication may cause drowsiness. If affected do not drive a vehicle or operate machinery. Avoid alcohol.) and 40 (This medication may cause drowsiness and may increase the effects of alcohol. If affected do not drive a motor vehicle or operate machinery.)

ANTIISTAMINES not separately specified in this Appendix **except**:

- 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
- d) preparations for the treatment of animals.

Proposed scheduling

Schedule 4

FEXOFENADINE **except**:

- a) when included in Schedule 2;
- b) in divided preparations for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:
 - i) in a primary pack containing 20 dosage units or less and not more than 10 days' supply; and
 - ii) labelled with a recommended daily dose not exceeding 120 mg of fexofenadine;
- c) for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:
 - i) in a primary pack containing ~~105~~ dosage units or less and not more than ~~105~~ days' supply; and
 - ii) labelled with a recommended daily dose not exceeding 180 mg of fexofenadine; or
- d) for the treatment of seasonal allergic rhinitis and children 6 years of age and over when:
 - i) in a primary pack containing 20 dosage units or less and not more than 10 days' supply; and
 - ii) labelled with a recommended daily dose not exceeding 60 mg of fexofenadine.

Schedule 2

FEXOFENADINE in preparations for oral use **except** in divided preparations:

- a) for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:

- i) in a primary pack containing 20 dosage units or less and not more than 10 days' supply; and
 - ii) labelled with a recommended daily dose not exceeding 120 mg of fexofenadine;
- b) for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:
- i) in a primary pack containing ~~10~~ 5 dosage units or less and not more than ~~10~~ 5 days' supply; and
 - ii) labelled with a recommended daily dose not exceeding 180 mg of fexofenadine; or
- c) for the treatment of seasonal allergic rhinitis and children 6 years of age and over when:
- i) in a primary pack containing 20 dosage units or less and not more than 10 days' supply; and
 - ii) labelled with a recommended daily dose not exceeding 60 mg of fexofenadine.

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FEXOFENADINE

Schedule 4

Schedule 2

Background

Products containing fexofenadine hydrochloride are currently approved by the TGA for providing temporary relief of seasonal allergic rhinitis (SAR) in children and adults aged 12 years and over. Since being placed into Schedule 2 of the Poisons Standard in 1999, a number of amendments have been made to progressively enable general sale of oral preparations of fexofenadine in specified pack sizes and dosages and to particular age groups.

Summary of applicant's reasons for the proposal

- Fexofenadine is non-sedating and well tolerated for up to 24 hours of therapeutic effect from one 120 mg or 180 mg dose, indicating the safety associated with normal use of the medicine that is compatible with sale outside of a pharmacy.
- A larger pack size would be more convenient for consumers to purchase outside a pharmacy setting. The user can have greater certainty of having a ready supply to relieve symptoms immediately after exposure to a trigger without the need to purchase multiple packs. A larger pack can also support the treatment for multiple family members, or for those sufferers experiencing intermittent episodes over a longer period in parts of Australia where the distance or duration of travel to a pharmacy during their opening hours may not be convenient.
- There is already precedence in the Australian market for general sale access to larger pack sizes of comparable medicines. For example, loratadine 10 mg is available for general sale in divided preparations for the treatment of SAR, in a primary pack containing 10 dosage units or less for adults and children aged 6 years and over.

- Sufferers of SAR are capable of self-diagnosis due to the distinctive seasonal onset which differentiates it from other types of rhinitis. Access to immediate relief of SAR is integral to self-management of the condition, which aligns with making the medicine more widely available for general sale.
- First registered in the United Kingdom in 1996, fexofenadine is now approved in over 100 countries for the same indication. In Australia, the substance has been approved since 1997. Fexofenadine is accessible via supermarkets in several countries including Australia, USA and NZ and has been available at this level for over a decade.

Key uses / expected use

Medicines

Australian regulations

- According to the [TGA Ingredient Database](#),³¹ fexofenadine (as hydrochloride) 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 August 2022, there were 50 medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)³² that contain fexofenadine as an active ingredient. All are non-prescription medicines in tablet or oral suspension dosage forms.
- Fexofenadine is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)³³ No.4 of 2022.

³¹ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

³² ARTG database <https://www.tga.gov.au/artg>

³³ Therapeutic Goods (Permissible Ingredients) Determination [https://www.legislation.gov.au/Search/Therapeutic per cent20Goods per cent20SLBS/Permissible per cent20Ingredients/SRBS per cent20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20SLBS/Permissible%20Ingredients/SRBS%20Determination)

- The [TGA prescribing medicines in pregnancy database](#)³⁴ classifies fexofenadine as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Fexofenadine	B2	Allergy and Immune System	Antihistamines	
<p>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.</p> <p>Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of foetal damage.</p>				

- The [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)³⁵ requires the following warning statements pertaining to fexofenadine to be included on the labelling:

Substance	Conditions	Required Statement(s)
Fexofenadine	In medicines for oral use	If you are pregnant or breastfeeding, check with your doctor or pharmacist before using this medicine.

- Since January 2012, there have been 96 reports of adverse events for products containing fexofenadine as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#),³⁶ with 52 reports where fexofenadine was the single suspected medicine. The reported adverse reactions were diverse in nature with no clear pattern to the affected organs.
- As of August 2022, there were no products containing fexofenadine as an active ingredient/constituent or scheduled substance listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#).³⁷

International regulations

- Fexofenadine is listed on the [Food and Drugs Administration Approved Drugs Database](#)³⁸ in over the counter and prescription-only products and the [Health Canada Drug Product Database](#)³⁹ with 4 OTC listings.

³⁴ TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

³⁵ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

³⁶ Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

³⁷ Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

³⁸ Drugs@FDA <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm>

³⁹ Health Canada Drug Product Database <https://health-products.canada.ca/dpd-bdpp/dispatch-repartition.do>

- The [Health Products Regulatory Authority of Ireland⁴⁰](#) has several listings for fexofenadine, all of which are prescription-only except for one 120 mg tablet product which is available without a prescription.
- [New Zealand Medicines and Medical Devices Safety Authority \(MedSafe\)](#) regulates fexofenadine as follows:

Ingredient	Conditions	Classification
Fexofenadine	except for oral use	Prescription
Fexofenadine	for oral use except for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when in capsules containing 60 milligrams or less of fexofenadine hydrochloride or in tablets containing 120 milligrams or less of fexofenadine hydrochloride with a maximum daily dose of 120 milligrams when sold in the manufacturer's original pack containing 10 dosage units or less and not more than 5 days' supply	Pharmacy Only
Fexofenadine	for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when in capsules containing 60 milligrams or less of fexofenadine hydrochloride or in tablets containing 120 milligrams or less of fexofenadine hydrochloride with a maximum daily dose of 120 milligrams when sold in the manufacturer's original pack containing 20 dosage units or less and not more than 10 days' supply	General Sale
Fexofenadine	for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when in tablets containing 180mg or less of fexofenadine hydrochloride with maximum daily dose of 180mg when sold in the manufacturer's original pack containing 5 dosage units or less and not more than 5 days' supply.	General Sale

Ibuprofen

Proposal

The applicant has proposed the rescheduling of modified release ibuprofen from Schedule 3 to Schedule 2. The change would apply to divided preparations containing 300 mg or less of ibuprofen, in a primary pack containing not more than 12 dosage units, when labelled with a recommended daily dose of 1200 mg or less of ibuprofen. This will enable patients over 12 years

⁴⁰ HPRA of Ireland <https://www.hpra.ie/homepage/medicines/medicines-information/find-a-medicine/results?query=fexofenadine&field=>

of age to access some preparations of modified release ibuprofen without prior consultation with a pharmacist.

CAS number

15687-27-1

Alternative names

α -Methyl-4-(2-methylpropyl)benzeneacetic acid

p-Isobutylhydratropic acid

Applicant

Private applicant

Current scheduling

IBUPROFEN is currently listed in Schedules 2, 3 and 4 of the Poisons Standard as follows:

Schedule 4

IBUPROFEN **except**:

- a) when included in or expressly excluded from Schedule 2 or 3; or
- b) in preparations for dermal use.

Schedule 3

IBUPROFEN:

- a) in divided preparations, each containing 400 mg or less of ibuprofen in a primary pack containing not more than 50 dosage units, when labelled:
 - i) with a recommended daily dose of 1200 mg or less of ibuprofen; and
 - ii) not for the treatment of children under 12 years of age; or
- b) in a modified release dosage form, each containing 600 mg of ibuprofen in a primary pack containing not more than 32 dosage units, when labelled:
 - i) with a recommended daily dose of 1200 mg or less of ibuprofen; and
 - ii) not for the treatment of children under 12 years of age;

except when included in or expressly excluded from Schedule 2.

Schedule 2

IBUPROFEN in preparations for oral use when labelled with a recommended daily dose of 1200 mg or less of ibuprofen:

- a) in liquid preparations when sold in the manufacturer's original pack containing 8 g or less of ibuprofen; or
- b) in divided preparations, each containing 200 mg or less of ibuprofen, in packs of not more than 100 dosage units **except** when:
 - i) as the only therapeutically active constituent (other than phenylephrine or when combined with an effervescent agent);
 - ii) packed in blister or strip packaging or in a container with a child-resistant closure;
 - iii) in a primary pack containing not more than 25 dosage units;
 - iv) compliant with the requirements of the Required Advisory Statements for Medicine Labels;
 - v) not labelled for the treatment of children 6 years of age or less; and
 - vi) not labelled for the treatment of children under 12 years of age when combined with phenylephrine; or
- c) in divided immediate release preparations, each containing 400 mg or less of ibuprofen in a primary pack containing not more than 12 dosage units, when labelled not for the treatment of children under 12 years of age.

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IBUPROFEN

cross reference: PARACETAMOL

Schedule 4

Schedule 3

Schedule 2

Appendix F, Part 3

Appendix H

It is also included under the entry IBUPROFEN in Appendix F, part 3 as follows:

Warning statements

101. Don't use [this product/name of the product]:

If you have a stomach ulcer.

In the last 3 months of pregnancy. [This statement may be omitted in preparations used exclusively for the treatment of dysmenorrhoea.]

If you are allergic to (name of substance) or anti-inflammatory medicines.

104. Unless a doctor has told you to, don't use [this product/name of the product]:

For more than a few days at a time.

With other medicines containing (name of substance) or other anti-inflammatory medicines.

If you have asthma.

If you are pregnant. [This statement may be omitted in preparations used exclusively for the treatment of dysmenorrhoea.]

Proposed scheduling

Schedule 4

IBUPROFEN **except**:

- a) when included in or expressly excluded from Schedule 2 or 3; or
- b) in preparations for dermal use.

Schedule 3

IBUPROFEN:

- a) in divided preparations, each containing 400 mg or less of ibuprofen in a primary pack containing not more than 50 dosage units, when labelled:
 - i) with a recommended daily dose of 1200 mg or less of ibuprofen; and
 - ii) not for the treatment of children under 12 years of age; or
- b) in a modified release dosage form, each containing 600 mg of ibuprofen in a primary pack containing not more than 32 dosage units, when labelled:
 - i) with a recommended daily dose of 1200 mg or less of ibuprofen; and
 - ii) not for the treatment of children under 12 years of age;

except when included in or expressly excluded from Schedule 2.

Schedule 2 – Amend entry

IBUPROFEN in preparations for oral use when labelled with a recommended daily dose of 1200 mg or less of ibuprofen:

- a) in liquid preparations when sold in the manufacturer's original pack containing 8 g or less of ibuprofen; or
- b) in divided preparations, each containing 200 mg or less of ibuprofen, in packs of not more than 100 dosage units **except** when:
 - i) as the only therapeutically active constituent (other than phenylephrine or when combined with an effervescent agent);
 - ii) packed in blister or strip packaging or in a container with a child-resistant closure;
 - iii) in a primary pack containing not more than 25 dosage units;
 - iv) compliant with the requirements of the Required Advisory Statements for Medicine Labels;
 - v) not labelled for the treatment of children 6 years of age or less; and

- vi) not labelled for the treatment of children under 12 years of age when combined with phenylephrine; or
- c) in divided **immediate-release** preparations, each containing 400 mg or less of ibuprofen in a primary pack containing not more than 12 dosage units, when labelled not for the treatment of children under 12 years of age.

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IBUPROFEN

cross reference: PARACETAMOL

Schedule 4

Schedule 3

Schedule 2

Appendix F, Part 3

Appendix H

No changes are proposed to Appendix F, Part 3 or Appendix H.

Background

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID). It works by inhibiting the enzyme cyclooxygenase (COX), to reduce inflammation, relieve pain and reduce fever. Modified release ibuprofen tablets provide a longer duration of pain relief than immediate release. Current modified release ibuprofen products that are registered on the ARTG are approved for relief for up to 12 hours duration.

At the 34th meeting of the Advisory Committee on Medicines Scheduling (ACMS) in June 2021, an application was considered to move modified release ibuprofen 600 mg in a primary pack containing not more than 16 dosage units to Schedule 2. The final decision was to maintain the current scheduling due to:

- the risk posed by dosing errors,
- inconsistencies with minor short term, self-diagnosable conditions that are normally treated by Schedule 2 medicines, and
- agreement that pharmacist oversight was deemed necessary for safe use of these preparations.

Summary of applicant's reasons for the proposal

- Ibuprofen has a wide therapeutic index and this has been demonstrated to also apply to 300 mg modified release preparations.
- Commonly occurring short-term pain that persists for more than 6 hours can be appropriately managed with self-selected Schedule 2 medicines. However, modified release ibuprofen is not for the treatment of chronic pain and this is made clear in the labelling as well as the indications it aims to relieve.
- There are multiple health benefits for managing persistent pain with modified release medications. These include:
 - Longer duration of relief, leading to more consistent pain control and the convenience of less frequent dosing;

- Less interference with sleep from night-time pain and decreased need for medicinal sleep aids, which are associated with adverse effects and the potential for misuse;
- Reduction in GP consultations for the management of acute pain conditions that can be managed by modified release ibuprofen, such as acute back pain.
- It has been demonstrated that consumers can determine the likely duration of their pain, making modified release ibuprofen suitable for Schedule 2.
- The safety profile of ibuprofen at doses of 1200 mg/day has been presented and evaluated in the previous scheduling applications for ibuprofen. Ibuprofen has an excellent safety profile that is at least equivalent to paracetamol and better than other NSAIDs including aspirin. The NDPSC and ACMS have previously accepted and provided recommendations on the basis that ibuprofen has a lower risk of adverse events and serious effects after overdose than over-the-counter aspirin and paracetamol.
- Modified release 300 mg ibuprofen preparations are already available for sale in pharmacies in many international jurisdictions, including the United Kingdom.

Key uses / expected use

Medicines

Australian regulations

- According to the [TGA Ingredient Database](#),⁴¹ ibuprofen is:
 - Available for use as an Active Ingredient in Biologicals, Export Only, Over the Counter, Prescription Medicines
 - Available for use as an Excipient Ingredient in Biologicals, Devices, Prescription Medicines
 - Available for use as an Equivalent Ingredient in Biologicals, Export Only, Prescription Medicines
- As of August 2022, there were 250 medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)⁴² that contain ibuprofen (as the base) as an active ingredient. This includes 230 non-prescription medicines, 15 prescription, 3 for export only and 2 in medical devices. Preparations include tablets, capsules, gels, suspensions, oral liquids, and solutions for injection.
- Ibuprofen is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)⁴³ No.4 of 2022.

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 per cent20Goods per cent20SLBS/Permissible per cent20Ingredients/SRBS per cent20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20SLBS/Permissible%20Ingredients/SRBS%20Determination)

- The [TGA prescribing medicines in pregnancy database](#)⁴⁴ classifies IBUPROFEN as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Ibuprofen	C	Musculoskeletal System	Non-steroidal anti-inflammatory drugs (NSAIDS)	
<p>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.</p>				

- The [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)⁴⁵ requires the following warning statements pertaining to ibuprofen to be included on the labelling:

Substance	Conditions	Required Statement(s)
Ibuprofen (Entry 1 of 6)	For the purpose of exclusion from the schedules to the SUSMP, when the preparation is for oral use in adults and children aged 12 years and over.	<ul style="list-style-type: none"> Do not use if you have a stomach ulcer. Do not use if you have impaired kidney function. Do not use if you have heart failure. Do not use if you are allergic to ibuprofen or other anti-inflammatory medicines. If you get an allergic reaction, stop taking and see your doctor immediately. Unless a doctor has told you to, do not use if you have asthma. Unless advised by your doctor or pharmacist, do not use with products containing ibuprofen, aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly. Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage. Do not use if trying to become pregnant, or during the first 6 months of pregnancy, except on doctor's advice. Do not use at all during the last 3 months of pregnancy. Unless a doctor has told you to, do not use if you are aged 65 years or over.

⁴⁴ TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

⁴⁵ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

<p>Ibuprofen (Entry 2 of 6)</p>	<p>When included in a schedule to the SUSMP for oral use in adults and children aged 12 years and over</p>	<ul style="list-style-type: none"> · Do not use if you have a stomach ulcer. · Do not use if you have impaired kidney function. · Do not use if you have heart failure. · Do not use if you are allergic to ibuprofen or other anti-inflammatory medicines. · If you get an allergic reaction, stop taking and see your doctor immediately. · Unless a doctor has told you to, do not use if you have asthma. · Unless advised by your doctor or pharmacist, do not use with products containing ibuprofen, aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly. · Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage. · Do not use if trying to become pregnant, or during the first 6 months of pregnancy, except on doctor's advice. Do not use at all during the last 3 months of pregnancy.
<p>Ibuprofen (Entry 3 of 6)</p>	<p>For the purpose of exclusion from the schedules to the SUSMP, for oral use in children under 12 years of age</p>	<ul style="list-style-type: none"> · Do not use if you have a stomach ulcer. · Do not use if you have impaired kidney function. · Do not use if you have heart failure. · Do not use if you are allergic to ibuprofen or other anti-inflammatory medicines. · If you get an allergic reaction, stop taking and see your doctor immediately. · Unless a doctor has told you to, do not use if you have asthma. · Unless advised by your doctor or pharmacist, do not use with products containing ibuprofen, aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly. · Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage. · Do not use if trying to become pregnant, or during the first 6 months of pregnancy, except on doctor's advice. Do not use at all during the last 3 months of pregnancy. · Ask your doctor or pharmacist before use of the medicine in children suffering from dehydration through diarrhoea and/or vomiting. · Unless a doctor has told you to, do not use if you are aged 65 years or over. · Unless a doctor has told you to, do not use in children 6 years of age or less.

<p>Ibuprofen (Entry 4 of 6)</p>	<p>When included in a schedule to the SUSMP for oral use in children under 12 years of age</p>	<ul style="list-style-type: none"> · Do not use if you have a stomach ulcer. · Do not use if you have impaired kidney function. · Do not use if you have heart failure. · Do not use if you are allergic to ibuprofen or other anti-inflammatory medicines. · If you get an allergic reaction, stop taking and see your doctor immediately. · Unless a doctor has told you to, do not use if you have asthma. · Unless advised by your doctor or pharmacist, do not use with products containing ibuprofen, aspirin or other anti-inflammatory medicines or with medicines that you are taking regularly. · Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage. · Do not use if trying to become pregnant, or during the first 6 months of pregnancy, except on doctor's advice. Do not use at all during the last 3 months of pregnancy. · Ask your doctor or pharmacist before use of the medicine in children suffering from dehydration through diarrhoea and/or vomiting.
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<p>Ibuprofen (Entry 5 of 6)</p>	<p>In combination with paracetamol, in medicines for oral use</p>	<ul style="list-style-type: none"> · 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.
<p>Ibuprofen (Entry 6 of 6)</p>	<p>In preparations for dermal use</p>	<ul style="list-style-type: none"> · Do not use [this product/<i>insert name of product</i>] 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 or pharmacist has told you to, do not use [this product/<i>insert name of product</i>] with other medicines that you are taking regularly.

- Since January 2012, there have been 701 reports of adverse events for products containing ibuprofen as an active ingredient (including multiactive preparations) on the [Database of Adverse Event Notifications \(DAEN\)](#),⁴⁶ with 436 reports where ibuprofen was the single suspected medicine. The most common adverse effects reported pertained to skin and subcutaneous tissue reactions and gastrointestinal disorders.

⁴⁶ Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

- As of August 2022, there were no products containing ibuprofen as an active ingredient/constituent or scheduled substance listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#).⁴⁷

International regulations

- Ibuprofen is listed on the [Food and Drugs Administration Approved Drugs Database](#) as a prescription-only and OTC medicine in several different dosage forms.
- [The Health Canada Drug Product Database](#) lists ibuprofen as a prescription-only and OTC medicine.
- The UK's [electronic medicines compendium](#) lists ibuprofen as a prescription-only and OTC medicine.
- The [Health Products Regulatory Authority of Ireland](#) regulates ibuprofen as a prescription-only and OTC medicine.
- Ibuprofen is currently listed in the [New Zealand Medicines and Medical Devices Safety Authority \(MedSafe\)](#) with the specifications below:

Ingredient	Conditions (if any)	Classification
Ibuprofen	except when specified elsewhere in this schedule	Prescription
Ibuprofen	for oral use in tablets or capsules containing up to 400 milligrams per dose form and in packs containing not more than 50 dose units and that have received the consent of the Minister or the Director-General to their distribution as restricted medicines and that are sold in the manufacturer's original pack labelled for use by adults and children over 12 years of age	Restricted
Ibuprofen	for oral use in liquid form with a recommended daily dose of not more than 1.2 grams for the relief of pain and reduction of fever or inflammation when sold in the manufacturer's original pack containing not more than 8 grams; for oral use in solid dose form containing not more than 200 milligrams per dose form and with a recommended daily dose of not more than 1.2 grams when sold in the manufacturer's original pack containing not more than 100 dose units; except in divided solid dosage forms for oral use containing 200 milligrams or less per dose form with a recommended daily dose of not more than 1.2 grams and when sold in the manufacturer's original pack containing not more than 25 dose units	Pharmacy Only

⁴⁷ Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

Ibuprofen	for external use; in divided solid dosage forms for oral use containing 200 milligrams or less per dose form with a recommended daily dose of not more than 1.2 grams and when sold in the manufacturer's original pack containing not more than 25 dose units per pack	General Sale
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Melatonin

Proposal

The applicant has proposed the rescheduling of immediate release melatonin from Schedule 4 to Schedule 3 for the treatment of jetlag. The rescheduling would apply to divided preparations containing 5 mg or less of melatonin, in packs of no more than 10 dosage units, for adults aged 18 and over. This will allow access to melatonin for this indication, without a prescription, after consulting with a pharmacist.

CAS number

73-31-4

Alternative names

N-acetyl-5-methoxytryptamine

N-[2-(5-Methoxy-1H-indol-3-yl)ethyl]acetamide

Applicant

Private applicant

Current scheduling

MELATONIN is currently listed in Schedules 3 and 4 of the Poisons Standard as follows:

Schedule 4

MELATONIN for human use **except** when included in Schedule 3.

Schedule 3

MELATONIN in modified release tablets containing 2 mg or less of melatonin for monotherapy for the short-term treatment of primary insomnia characterised by poor quality of sleep for adults aged 55 or over, in packs containing not more than 30 tablets.

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Proposed scheduling

Schedule 4

MELATONIN for human use **except** when included in Schedule 3

Schedule 3 – Amend Entry

MELATONIN in:

- a) modified release tablets containing 2 mg or less of melatonin for monotherapy for the short-term treatment of primary insomnia characterised by poor quality of sleep for adults aged 55 or over, in packs containing not more than 30 tablets; **or**
- b) **immediate release preparations containing 5 mg or less of melatonin for the treatment of jet lag in adults aged 18 or over, in a primary pack containing no more than 10 dosage units.**

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Background

Melatonin is produced naturally by the body in the pineal gland. The hormone plays a part in regulating the circadian rhythm or the body's natural sleep cycles through the release of the hormone from the suprachiasmatic nucleus of the hypothalamus when exposed to a dim or dark environment. Melatonin products are used to stimulate production when the sleep cycle has been disrupted. Melatonin has the potential to be used as an effective treatment for jet lag due to its ability to reset the 'body clock'.

Summary of applicant's reasons for the proposal

- Previous applications for the rescheduling of melatonin have established that the substance has a good safety profile, and noted that the risk of toxicity in acute use of the substance is low. There is no new evidence to show that the toxicity risks have changed. The substance is well absorbed with the rate of adverse events reported in clinical trials being lower in the melatonin group than the placebo group.
- No immediate release products containing melatonin as the active ingredient are approved or registered for use in Australia. The access pathways for these products currently consist of homeopathic formulations or through the Special Access Scheme (SAS). Homeopathic formulations are largely ineffective and not recommended by Australian guidelines, and the SAS places undue burden on doctors, patients and regulators to access a safe and effective medication for treatment of a short-term condition.

- Information taken from the [Australian Therapeutic Guidelines](#)⁴⁸ stipulates that immediate release melatonin at 0.5-5 mg dosage has evidence of benefit to prevent or reduce the effects of jet lag in adults.
- The symptoms of jet lag are transient (4-6 days), and it is expected that treatment using melatonin would therefore be short-term. This is consistent with the proposed pack size (10 units) for a Schedule 3 melatonin product. Jet lag is therefore a condition suitable for self-management and treatment with melatonin as proposed.
- A Schedule 3 listing provides consumers with the benefits of increased access to this therapy. However, it also provides the safeguards of pharmacist oversight until sufficient local experience is obtained with immediate release melatonin for the management of jet lag in adults. In combination with appropriate labelling, the risk of this medication being used for other indications or in children is sufficiently mitigated.

Key uses / expected use

Medicines

Australian regulations

- According to the [TGA Ingredient Database](#),⁴⁹ melatonin is:
 - Available for use as an Active Ingredient in Biologicals, Export Only, Over the Counter, 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 2022, there were 21 medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)⁵⁰ that contain melatonin as an active ingredient. These include 10 prescription, 6 non-prescription medicines and 5 medicines for export only. All registered melatonin products available in Australia are modified or prolonged release preparations.
- Melatonin is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)⁵¹ No.4 of 2022.

⁴⁸ Australian Therapeutic Guidelines

https://tgldcdp.tg.org.au/viewTopic?etgAccess=true&guidelinePage=Psychotropic&topicfile=jet-lag&guidelinename=Psychotropic§ionId=toc_d1e69#toc_d1e69

⁴⁹ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

⁵⁰ ARTG database <https://www.tga.gov.au/artg>

⁵¹ Therapeutic Goods (Permissible Ingredients) Determination https://www.legislation.gov.au/Search/Therapeutic_per_cent20Goods_per_cent20SLBSPermissible_per_cent20IngredientsSRBS_per_cent20Determination

- The [TGA prescribing medicines in pregnancy database](#)⁵² classifies melatonin as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Melatonin	B3	Central nervous system	Hypnotics and sedatives	
<p>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.</p> <p>Studies in animals have shown evidence of an increased occurrence of foetal damage, the significance of which is considered uncertain in humans.</p>				

- There are no warning statements pertaining to melatonin in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#).⁵³
- As of August 2022, there were 119 reports of adverse events for products containing melatonin as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#),⁵⁴ with 87 reports where melatonin was the single suspected medicine. The most commonly reported adverse events were dizziness and insomnia.
- As of August 2022, there was one product containing melatonin as an active ingredient/constituent or scheduled substance listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#),⁵⁵ a parenteral implant for sheep and goats.
- In 2012-2022 no adverse experiences were recorded for melatonin in the [APVMA Adverse Experience Reporting Program database \(AERP\)](#).⁵⁶

International regulations

- [European Commission database \(cosmetics and ingredients\)](#)⁵⁷ lists melatonin with its function as an antioxidant.
- [European Medicines Agency](#)⁵⁸ lists prolonged-release melatonin, for the short-term treatment of primary insomnia in patients aged 55 and over, as a prescription-only medicine.
- [New Zealand Medicines and Medical Devices Safety Authority \(MedSafe\)](#)⁵⁹ regulates melatonin with the below conditions:

⁵² TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

⁵³ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

⁵⁴ Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

⁵⁵ Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

⁵⁶ APVMA Adverse Experience Reporting Program database (AERP) <https://apvma.gov.au/node/10946>

⁵⁷ [European Commission database for information on cosmetic substances and ingredients database](https://ec.europa.eu/growth/tools-databases/cosing/) <https://ec.europa.eu/growth/tools-databases/cosing/>

⁵⁸ European Medicines Agency <https://www.ema.europa.eu/en/medicines/human/EPAR/circadin>

⁵⁹ New Zealand Medicines and Medical Devices Safety Authority (MedSafe) <https://www.medsafe.govt.nz/profs/class/classintro.asp>

Ingredient	Conditions (if any)	Classification
Melatonin	except when supplied in medicines for oral use containing 3mg or less per immediate release dose unit, or 2mg or less per modified release dose unit, when sold in the manufacturers original pack that has received consent from the Minister of Health or the Director General for the treatment of primary insomnia for adults aged 55 years or older for up to 13 weeks by a registered pharmacist.	Prescription

- [The Health Products Regulation Agency of Ireland](#)⁶⁰ lists 4 medicines with melatonin as active ingredient on their database. All are prescription-only medicines - three modified or prolonged release products, and one immediate release.
- [Health Products Canada database](#)⁶¹ includes one product containing melatonin which is available OTC for veterinary use only. However, on a [MedEffect](#)⁶² safety review for melatonin it states that it is used in adults, adolescents, and children with sleep problems as an OTC natural health product, but recommends seeking health professional advice before giving it to children. Over 500 natural health products that include melatonin have been licenced by Health Canada available in a variety of forms including, capsules, sublingual, liquids, and gums.

⁶⁰Health Product Regulatory Authority <https://www.hpra.ie/homepage/medicines/medicines-information/find-a-medicine/results?query=Melatonin&field=ACTIVESUBSTANCES>

⁶¹ <https://health-products.canada.ca/dpd-bdpp/dispatch-repartition.do>

⁶² Health Canada database <https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/safety-reviews/summary-safety-review-melatonin-acetyl-methoxytryptamine-review-safety-melatonin-children-adolescents.html>

3 Proposed amendments referred for scheduling advice to the Joint ACMS-ACCS meeting #32

Green tea extract

Proposal

The applicant has proposed that a new Schedule 2 entry for green tea extract be included in the Poisons Standard in preparations for internal use, unless they are labelled with specified warning statements. This amendment would remove green tea products not bearing the specified warning labels from general sale.

CAS Number

N/A

Alternative names

Camellia sinensis

Thea sinensis

Common tea

Green tea

Camellia thea

Applicant

The Department of Health and Aged Care

Current scheduling

Green tea extract is not specifically scheduled in the current Poisons Standard.

Proposed scheduling

Schedule 2 – Proposed New Entry

GREEN TEA EXTRACT (*Camellia sinensis*) for internal use except

- a) when present as an excipient in preparations containing 5 per cent or less of green tea extract; or
- b) when labelled with the warnings:

“Take with food.”; and

“WARNING: Green tea extract (*Camellia sinensis*) may harm the liver in some people. If you experience yellowing of the skin/eyes, dark urine, discoloured stool, nausea, vomiting, unusual tiredness,

weakness, abdominal pain, and/or loss of appetite, stop using this product and see your doctor.”

Index – New Entry

GREEN TEA EXTRACT

cross reference: CAMELLIA SINENSIS

Schedule 2

Background

The fermentation of *Camellia sinensis* results in the oxidation of catechins into condensed polymeric compounds, which can be purified and concentrated to be used as green tea extracts. The two key bioactive molecules in green tea are methylxanthines alkaloids and polyphenols, of which epigallocatechin-3-gallate (EGCG) is the most abundant, holds the highest antioxidant potential, and is therefore considered the most biologically active antioxidant constituent of tea. In products that are currently available in Australia, extract levels of EGCG have been reported at levels of 50 per cent and 98 per cent. The constituents of materials referred to as “green tea extracts” can vary considerably, and often can be related to whether the substance is to be used as an active ingredient or an excipient.

Green tea extract is found in different types of therapeutic goods and foods, in particular products broadly characterised as sports supplements. Food Standards Australia New Zealand (FSANZ) currently allows tea as the product made from the leaves and buds of *Camellia sinensis* (of a single type or several varieties), however green tea extracts are not permitted to be used in foods.

In 2018 the Department of Health (now the Department of Health and Aged Care) conducted a review to ascertain the association of hepatotoxicity in adverse events reported following the use of Australian medicines that contained green tea extract. This review was supported by an earlier review conducted by Health Canada regarding Canadian medicines in 2017.⁶³ Following the evaluation from the Department of Health, the European Food Safety Authority (EFSA) published a review that established EGCG’s capability of inducing dose-dependent liver-associated injuries.

Summary of applicant’s reasons for the proposal

- Reviews have found evidence that green tea extracts in products such as sports supplements (some of which may in law be medicines despite not being included in the Australian Register of Therapeutic Goods (ARTG)) pose a risk for hepatotoxicity in consumers.
- The proposed Poisons Standard amendment will raise awareness of early warning signs for liver damage to mitigate the hepatotoxicity risk for certain preparations purchased by general sale. The warning statements included in the proposal are to be included in the Poisons Standard rather than the Required Advisory Statements of Medicines Labels (RASML). This is to ensure clarity that the warning statements will capture all products for internal use containing this substance (except products that are, in law, food) whether or not they are entered in the ARTG.
- If the proposal is to be accepted and green tea extract were to be included in the Poisons Standard, several supplements would subsequently be regulated as therapeutic goods as per

⁶³ www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/safety-reviews/green-tea-extract-containing-natural-health-products-assessing-potential-risk-liver-injury.html

the Therapeutic Goods (Declared Goods) Order 2019 Schedule 1, part 2. Products containing green tea extract usually make low-level claims and risks of overuse can be mitigated with the relevant labels and safety warnings. The label statements proposed alerts consumers to the early warning signs of hepatotoxicity and can reduce the risk and severity of potential harm, which is usually reversible with early cessation of use or medical intervention.

Key uses / expected use

Medicines, cosmetics, sports supplements, foods, flavours, and antioxidants.

Australian regulations

- According to the [TGA Ingredient Database](#),⁶⁴ Green tea is:
 - Available for use as an Active Ingredient in Export Only, Listed Medicines, Over the Counter, Prescription Medicines
 - Also available for use as a Homoeopathic Ingredient in Listed Medicines
 - Available for use as an Excipient Ingredient in Devices, Export Only, Listed Medicines, Over the Counter, Prescription Medicines
 - Not available as an Equivalent Ingredient in any application
- As of August 2022, there were 256 medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)⁶⁵ that contain green tea as an active ingredient. 233 of these products were listed medicines, with 23 for export only.
- *Camellia sinensis* is permitted to be included in listed medicines as it is included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)⁶⁶ No.4 of 2022.

⁶⁴ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

⁶⁵ ARTG database <https://www.tga.gov.au/artg>

⁶⁶ Therapeutic Goods (Permissible Ingredients) Determination [https://www.legislation.gov.au/Search/Therapeutic per cent20Goods per cent20SLBSPermissible per cent20IngredientsSRBS per cent20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20SLBSPermissible%20IngredientsSRBS%20Determination)

Item	Ingredient name	Purpose	Specific requirements
1136	CAMELLIA SINENSIS	A,E,H	<p>Caffeine is a mandatory component of Camellia sinensis.</p> <p>When the medicine is packaged for supply as a divided preparation and is for internal use or oral application, the medicine must not contain a concentration of total caffeine greater than 33 per cent.</p> <p>When for internal use or oral application, the maximum recommended daily dose of the medicine must provide no more than 400 mg of total caffeine.</p> <p>When the medicine is packaged for supply as an undivided preparation and is for internal use or oral application, the medicine must not contain a concentration of total caffeine greater than 1 per cent.</p> <p>When the medicine is for internal use or oral application, a maximum recommended dose of the medicine must not provide more than 100 mg of total caffeine within a 3 hour period.</p> <p>When the maximum recommended daily dose of the medicine provides greater than 10 mg of total caffeine and the medicine is for internal use or oral application, the following warning statements are required on the label:</p> <ul style="list-style-type: none"> - (ADULT) 'Adults only' (or words to that effect). - (CAFF) 'Contains [state quantity per dosage unit or per mL or per gram of product] total caffeine [per dosage unit or per mL or per gram]. A cup of instant coffee contains approximately 80mg of caffeine.' - (CAFFPREG) 'Caffeine intake more than 200 mg per day is not recommended during pregnancy or breastfeeding.' <p>When the maximum recommended daily dose of the medicine provides greater than 80 mg of total caffeine and the medicines is for internal use or oral application, the following warning statements are required on the label:</p> <ul style="list-style-type: none"> - (CAFFLMT) 'Limit the use of caffeine-containing products (including tea and coffee) when taking this product.' - (CAFFCYP) 'Caffeine interacts with enzyme CYP1A2 in the liver. Consult your health professional before taking with other medicines' (or words to that effect).
<p>A = active ingredient for a medicine has the same meaning as in the Regulations</p> <p>E = excipient for a medicine meaning an ingredient that is not an active ingredient or a homoeopathic preparation ingredient</p> <p>H = homoeopathic preparation ingredient meaning an ingredient that is a constituent of a homoeopathic preparation</p>			

- The [TGA prescribing medicines in pregnancy database](#)⁶⁷ does not include green tea extract.
- There are no warning statements pertaining to green tea extract in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)⁶⁸
- As of July 2022, there were 255 reports of adverse events for products containing green tea (or *Camellia sinensis*) as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#),⁶⁹ with 214 reports where green tea extract was the single suspected medicine. Adverse events were most commonly related to gastrointestinal disorders (nausea and vomiting) or nervous system disorders (dizziness and headaches).
- As of August 2022, there were no products containing green tea extract listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#).⁷⁰

International regulations

- [The Health Products Regulatory Authority of Ireland](#)⁷¹ lists one product (ointment) with green tea extract as an active ingredient which is regulated as a prescription medicine.
- The [European Commission](#)⁷² has recently proposed putting restrictions on the use of green-tea extracts on the basis that catechins in green-tea extracts have the potential to cause liver injury.

⁶⁷ TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

⁶⁸ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

⁶⁹ Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

⁷⁰ Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

⁷¹ Health Products Regulation Authority [https://www.hpra.ie/homepage/medicines/medicines-information/find-a-medicine/results/item?pano=PA1748/003/001&t=Catephen per cent2010 per cent20 per cent per cent20ointment](https://www.hpra.ie/homepage/medicines/medicines-information/find-a-medicine/results/item?pano=PA1748/003/001&t=Catephen%20per%20cent20per%20cent20ointment)

⁷² European Commission Food Safety green-tea initiative https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12572-Food-safety-restricting-the-use-of-green-tea-catechins-in-foods_en

4 Proposed amendments referred for scheduling advice to ACCS meeting #35

Ethalfluralin

Proposal

The applicant is requesting new entries in Schedule 6 and Schedule 7 of the Poisons Standard for ethalfluralin. The Schedule 6 entry is for preparations containing ethalfluralin that are packed in bulk containers for specific use in closed mixing and loading agricultural equipment with a nominal capacity of 400 L or more. The Schedule 7 entry is for all other preparations.

CAS Number

55283-68-6

Alternative names

N-Ethyl-N-(2-methyl-2-propen-1-yl)-2,6-dinitro-4-(trifluoromethyl)benzenamine

N-ethyl-N- α,α,α -trifluoro-N-(2-methylallyl)-2,6-dinitro-p-toluidine

N-ethyl-N-methylallyl-4-trifluoromethyl-2,6-dinitroaniline

Applicant

Australian Pesticides and Veterinary Medicines Authority (APVMA)

Current scheduling

Ethalfluralin is not specifically scheduled in the current Poisons Standard.

Proposed scheduling

Schedule 7 – New Entry

ETHALFLURALIN except when included in Schedule 6

Schedule 6 – New entry

ETHALFLURALIN in products packed in bulk containers with a nominal capacity of 400L or more, for specific use in closed mixing and loading agricultural equipment.

Background

Ethalfluralin is intended to be used as a pre-emergent herbicide on pulse crops such as mung beans, chickpeas, and lentils. The mechanism of action involves the inhibition of plant cell formation. Ethalfluralin has been found to be of low acute toxicity via the oral, dermal and inhalation routes but is a moderate to severe eye and skin irritant and skin sensitiser. The substance also has mutagenic potential and was found to be a developmental toxicant.

Summary of applicant's reasons for the proposal

- Ethalfluralin is intended to be used in crop resistance management in the form of pre-planting weed controls and is expected to be available as an alternative to Trifluralin, which is currently listed under Appendix B, Part 3 of the Poisons Standard. It is estimated that Australia grows around 2 million hectares of pulse crops including white lupins, chickpeas, field peas, lentils, faba, broad beans and mung beans. Ethalfluralin is intended to act as a herbicide to protect these pulse crops.
- Ethalfluralin has no other established purpose or use and therefore has no risk of dependency, abuse, misuse, or diversion into illicit use.
- Ethalfluralin was not found to be a reproductive toxicant but was found to be potentially mutagenic in vitro and a potential developmental toxicant. In acute and repeat-dose animal studies there was no evidence of neurotoxicity.
- Due to ethalfluralin being a potential carcinogenicity hazard from unprotected repeat use, the applicant indicates that it meets the Scheduling Policy Framework criteria for inclusion in Schedule 7. The risks of exposure to ethalfluralin can be mitigated by the use of specialised packaging and the use of bulk containers for specific use. Therefore a Schedule 6 entry that includes these conditions should be considered.

Key uses / expected use

Agricultural use – herbicide

Australian regulations

- Ethalfluralin does not appear in the [TGA Ingredient Database](#).⁷³
- There are no medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)⁷⁴ that contain ethalfluralin as an active ingredient.
- Ethalfluralin is not included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)⁷⁵ No. 4 of 2022.
- Ethalfluralin does not appear in the [TGA prescribing medicines in pregnancy database](#).⁷⁶
- Ethalfluralin does not appear in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2021](#).⁷⁷
- Ethalfluralin does not appear in the [Public Chemical Registration Information System Search \(PubCRIS\)](#).⁷⁸

⁷³ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

⁷⁴ ARTG database <https://www.tga.gov.au/artg>

⁷⁵ Therapeutic Goods (Permissible Ingredients) Determination [https://www.legislation.gov.au/Search/Therapeutic per cent20Goods per cent20SLBSPermissible per cent20IngredientsSRBS per cent20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20SLBSPermissible%20IngredientsSRBS%20Determination)

⁷⁶ TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

⁷⁷ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

⁷⁸ Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

International regulations

- As of March 2022, the [United States' Environmental Protection Agency \(EPA\)](#) has received an initial application to establish tolerances of ethalfluralin on stevia leaves.
- The [Canadian Pesticides and Pest Management database](#) indicates that there are 7 current applications and have been 37 historical applications for ethalfluralin.
- The [European Chemicals Agency \(ECHA\)](#) lists ethalfluralin with requirements for specific Hazard classification and labelling, and indicates that a majority of data submitters agree this substance is a skin sensitiser, toxic to aquatic life, an eye irritant, a suspected carcinogen, and harmful by inhalation.
- The [European Union Pesticides Database](#) states that ethalfluralin is not currently approved.

Tigolaner

Proposal

The applicant has proposed the creation of two new entries in the Poisons Standard for the new veterinary pest control agent tigolaner. A new Schedule 5 entry would be for preparations containing 10 per cent or less of tigolaner. A Schedule 6 entry would be for all other preparations.

CAS Number

1621436-41-6

Alternative names

2-Chloro-N-(1-cyanocyclopropyl)-5-[2'-methyl-5'-(pentafluoroethyl)-4'-(trifluoromethyl)-2'H-[1,3'-bipyrazol]-4-yl]benzamide

Applicant

Australian Pesticides and Veterinary Medicines Authority (APVMA)

Current scheduling

Tigolaner is not specifically scheduled in the current Poisons Standard.

Proposed scheduling

Schedule 6 – New Entry

TIGOLANER except when in Schedule 5.

Schedule 5 – New Entry

TIGOLANER in preparations containing 10 per cent or less of tigolaner.

Index – New Entry

TIGOLANER

Schedule 6
Schedule 5

Background

Tigolaner belongs to the chemical class of bispyrazoles. It is an acaricide and insecticide that acts by blocking gamma-aminobutyric acid (GABA) gated chloride channels in the nervous system. The proposed use of the substance is for the treatment and prevention of flea infestations, control of ticks and mites, and treatment and control of intestinal worms in cats and kittens in the form of a spot-on solution.

Summary of applicant's reasons for the proposal

- Studies indicate that tigolaner has low acute oral and dermal toxicity, is not mutagenic, is not a skin nor eye irritant, and is not a potential skin sensitiser in mice. However, adverse reproductive effects have been observed in tests on rats and rabbits, including birth defects such as increased incidence of cleft palate and non-adverse skeletal variations.
- The toxicology profile of tigolaner is considered to be consistent with the Scheduling Policy Framework criteria for inclusion in Schedule 6 of the Poisons Standard based on moderate health hazards, except for preparations containing 10 per cent or less of tigolaner which should be placed into Schedule 5.
- There is no risk of dependency, abuse, misuse, or diversion into illicit use.

Key uses / expected use

Veterinary medicines

Australian regulations

- Tigolaner does not appear in the [TGA Ingredient Database](#).⁷⁹
- There are no medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)⁸⁰ that contain tigolaner as an active ingredient.
- Tigolaner is not included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)⁸¹ No. 4 of 2022.
- Tigolaner does not appear in the [TGA prescribing medicines in pregnancy database](#).⁸²
- Tigolaner does not appear in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2021](#).⁸³

⁷⁹ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

⁸⁰ ARTG database <https://www.tga.gov.au/artg>

⁸¹ Therapeutic Goods (Permissible Ingredients) Determination [https://www.legislation.gov.au/Search/Therapeutic per cent20Goods per cent20SLBSPermissible per cent20IngredientsSRBS per cent20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20SLBSPermissible%20IngredientsSRBS%20Determination)

⁸² TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

⁸³ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

- Tigolaner does not appear in the [Public Chemical Registration Information System Search \(PubCRIS\)](#).⁸⁴

International regulations

- Tigolaner is listed as an active ingredient in a veterinary medicine to treat cats authorised for use by the [European Medicines Agency](#).⁸⁵

5 How to respond

Submissions must be provided by the closing date of **29 September 2022** 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.

6 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 February 2022

⁸⁴ Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

⁸⁵ European Medicines Agency <https://www.ema.europa.eu/en/medicines/veterinary/EPAR/felpreva>