



Australian Government
Department of Health
Therapeutic Goods Administration

Consultation: Proposed amendments to the Poisons Standard – ACCS, ACMS and joint ACCS/ACMS meetings, November 2020

26 August 2020

TGA Health Safety
Regulation

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1 Proposed amendments referred for scheduling advice to ACMS #32

1.1 Amygdalin and hydrocyanic acid

CAS Number:

Amygdalin: 29883-15-6

Hydrocyanic acid: 74-90-8

Alternative names

Amygdalin: D-mandelonitrile- β -D-glucoside-6- β -glucoside; mandelonitrile- β -gentiobioside; Vitamin B17

Hydrocyanic acid: Hydrogen cyanide; formonitrile; prussic acid

Applicant

Private applicant

Current scheduling

Amygdalin

Schedule 10

AMYGDALIN for therapeutic use.

Index

AMYGDALIN

Schedule 10

Hydrocyanic acid

Schedule 7

HYDROCYANIC ACID **except:**

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

Schedule 4

HYDROCYANIC ACID for therapeutic use.

Appendix F, Part 3

Poison	Warning Statements	Safety Directions
HYDROCYANIC ACID when included in Schedule 7.	13 (May be fatal if inhaled, swallowed or absorbed through skin)	4 (Avoid contact with skin), 8 (Avoid breathing dust (or) vapour (or) spray mist)

Appendix G

Poison	Concentration (quantity per litre or kilogram)
HYDROCYANIC ACID	1 microgram

Appendix J, Part 2

Poisons	Authorisation Considerations
HYDROCYANIC ACID AND CYANIDES	P (additional restrictions on possession)

Index**HYDROCYANIC ACID**

cross reference: CYANIDES

Schedule 7

Schedule 4

Appendix F, Part 3

Appendix J, Part 2

Proposed scheduling

A request has been made to amend the Poisons Standard as follows:

Amygdalin**Schedule 10 – Amend Entry**AMYGDALIN for therapeutic use **except when included in or expressly excluded from Schedule 4.****Schedule 4 – New Entry****AMYGDALIN when included as a natural component in traditional Chinese medicines for oral use in adults except when the maximum recommended daily dose is equivalent to no greater than 5 mg of amygdalin.****Index****AMYGDALIN**

Schedule 10

Schedule 4

Hydrocyanic acid

Schedule 4 – Amend Entry

HYDROCYANIC ACID for therapeutic use **except when present as a natural component of amygdalin in traditional Chinese medicines for oral use in adults.**

Index – Amend Entry

HYDROCYANIC ACID

cross reference: CYANIDES

Schedule 7

Schedule 4

Appendix F, Part 3

Appendix G

Appendix J, Part 2

Key uses / expected use

Medicines

Reasons for proposal put forward by the applicant

- Amygdalin is a cyanogenic glycoside found naturally in many plants including cassava, sorghum, lima beans, bitter almonds, apricot kernels and seeds of other plants in the *Prunus* genus.
- Many traditional Chinese medicines are formulated to include one or more of these plant ingredients, usually in combination with other traditional Chinese herbs. Under the current scheduling arrangements, products that contain amygdalin in any quantity cannot be used in therapeutic goods, which means that many formulated TCM products that are freely available in other countries are not available to Australian TCM practitioners.
- This application proposes excluding amygdalin from Schedule 10 when included as a natural component in traditional Chinese medicines for oral use in adults and including it in Schedule 4 with a cut-off to unscheduled at a maximum daily adult dose of 5 mg or less.
- The selected cut-off of 5 mg per maximum daily dose is based on animal studies and assessment by a wide range of regulatory and expert committees that an oral intake of 5 to 20 µg/kg/d cyanide (equivalent to 5.1 to 20.3 mg/d amygdalin for a 60 kg adult) is considered to present no appreciable risk. It is substantially less than the legal limit in many foods for human consumption in Australia and New Zealand.
- By way of comparison 100 g of confectionary could legally contain more than 8 times this proposed maximum daily dose and one standard drink of red wine could legally contain more than 4 times this dose.
- An associated change to exclude hydrocyanic acid from Schedule 4 when present as a natural component of amygdalin in traditional Chinese medicines for oral use in adults is also proposed.
- The effect of the changes would be:
 - To make traditional Chinese medicine products containing very low doses of amygdalin available without prescription; and
 - To allow medically qualified traditional Chinese medicine practitioners to prescribe traditional Chinese medicines containing higher doses of amygdalin as Schedule 4

medicines (e.g. in registered complementary medicines or via the TGA's Special Access Scheme).

Australian regulations

- According to the [TGA Ingredient Database](#),¹ amygdalin and hydrocyanic acid are:
 - Not available for use as active ingredients in any application;
 - Not available for use as excipient ingredients in any application; and
 - Available for use as equivalent ingredients in export only and listed medicines.
- As of August 2020, there were no medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)² that contain amygdalin or hydrocyanic acid as an active ingredient.
- Amygdalin and hydrocyanic acid are not permitted to be included in listed medicines as they are not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)³ No.2 of 2020.
- There are no warning statements pertaining to amygdalin or hydrocyanic acid in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)⁴.
- As of August 2020, there were no reports of adverse events for products containing amygdalin or hydrocyanic acid as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#)⁵.

International regulations

- Amygdalin has not been approved for use by the U.S Food and Drugs Administration or the European Commission. Import of amygdalin is prohibited in the U.S, UK and Europe.
- In Canada, no health products containing B17 or amygdalin have been authorised to treat cancer or any other condition.
- Amygdalin was first entered in the [New Zealand Inventory of Chemicals \(NZIoC\)](#) on 1 December 2006. According to the [New Zealand Medicines and Medical Devices Safety Authority \(MedSafe\)](#) amygdalin is available as follows in New Zealand:

Ingredient	Conditions	Classification
Amygdalin	At all strengths	Prescription

¹ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

² ARTG database <https://www.tga.gov.au/artg>

³ Therapeutic Goods (Permissible Ingredients) Determination

[https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB\\$%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20IngredientsRB%20Determination)

⁴ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

⁵ Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

1.2 Cannabidiol

CAS Number:

13956-29-1

Alternative names

CBD; 2-(6-Isopropenyl-3-methyl-2-cyclohexen-1-yl)-5-pentyl-1,3-benzenediol

Applicant

Private applicant

Current scheduling

Schedule 4

CANNABIDIOL in preparations for therapeutic use where:

- a) cannabidiol comprises 98 per cent or more of the total cannabinoid content of the preparation; and
- b) any cannabinoids, other than cannabidiol, must be only those naturally found in cannabis and comprise 2 per cent or less of the total cannabinoid content of the preparation.

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CANNABIDIOL

cross reference: NABIXIMOLS, CANNABIS, TETRAHYDROCANNABINOLS

Schedule 4

Proposed scheduling

A request has been made to amend the Poisons Standard as follows:

Schedule 4 – Amend Entry

CANNABIDIOL in preparations for therapeutic use where:

- a) cannabidiol comprises 98 per cent or more of the total cannabinoid content of the preparation; and
- b) any cannabinoids, other than cannabidiol, must be only those naturally found in cannabis and comprise 2 per cent or less of the total cannabinoid content of the preparation; **or**
- c) **cannabidiol is a synthetic or semi-synthetic copy of the molecule and comprises 98 per cent or more of the total cannabinoid content of the preparation and any other synthetic or semi-synthetic cannabinoids; and**
- d) **any impurities in the synthesis of the cannabidiol, other than cannabidiol, must comprise 2 per cent or less of the total cannabinoid content of the preparation.**

Key uses / expected use

Medicines

Reasons for proposal put forward by the applicant

- CBD can be obtained from synthetic sources. There is no mention of CBD from synthetic sources in the Schedule 4 entry although the chemical structure is the same as that found naturally in the *Cannabis sativa* plant.
- Synthetic (-) CBD has a similar safety profile when compared with naturally derived CBD, related substances and impurities considered.
- Natural and synthetic (-) CBD show identical biological activities. The impurity profile and related substances were studied in detail before the release of 'Safety of low dose Cannabidiol' by TGA. We propose that the amended entry to Schedule 4 would benefit from having mention of other impurities.

Australian regulations

- According to the [TGA Ingredient Database](#),⁶ cannabidiol is:
 - Available for use as an active ingredient in export only and prescription medicines
 - Not available as an excipient ingredient in any application
 - Not available as an equivalent ingredient in any application
- As of August 2020, there were 8 medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)⁷ that contain cannabidiol (CBD) as an active ingredient. These are all export only medicines. Formulations include oral liquid preparations in the following dosages: CBD: 5 mg/mL and THC: 20 mg/mL, CBD: 10 mg/mL and THC: 10 mg/mL, CBD: 20 mg/mL and THC: 1 mg/mL, CBD: 25 mg/mL, CBD: 50mg/mL and CBD: 100 mg/mL.
- Cannabidiol is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)⁸ No.2 of 2020.
- Cannabidiol is not included in the [TGA prescribing medicines in pregnancy database](#)⁹.
- There are no warning statements pertaining to cannabidiol in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)¹⁰.
- As of August 2020, there were 2 reports of adverse events for products containing cannabidiol as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#)¹¹, with 1 report where cannabidiol was the single suspected medicine.
- According to the [Australia New Zealand Food Standards Code – Standard 1.4.4 – Prohibited and restricted plants and fungi](#)¹², cannabidiol must not be present in any food for sale at a level greater than 75 mg/kg.

⁶ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

⁷ ARTG database <https://www.tga.gov.au/artg>

⁸ Therapeutic Goods (Permissible Ingredients) Determination

[https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB\\$%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20IngredientsRB%20Determination)

⁹ TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

¹⁰ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

¹¹ Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

¹² ANZ Food Standards Code- Standard 1.4.4 – Prohibited and restricted substances

<https://www.legislation.gov.au/Details/F2017C01047>

- As of 12 August 2020, there were no products containing cannabidiol listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#)¹³.

International regulations

- In a letter dated 24 Jan 2019 from the Director General of the WHO to the Secretary General of the United Nations, on the basis of the 12 to 16 November 2018 reviews conducted by the WHO's Expert Committee on Drug Dependence (ECDD) on cannabis and cannabis related substances (including CBD), the WHO recommended that preparations containing predominantly CBD with not more than 0.2% THC should not be placed under international drug control (WHO 2019)¹⁴:

“To give effect to the recommendation of the fortieth meeting of the ECDD that preparations considered to be pure cannabidiol (CBD) should not be scheduled within the International Drug Control Conventions by adding a footnote to the entry for cannabis and cannabis resin in Schedule I of the Single Convention on Narcotic Drugs (1961) to read “Preparations containing predominantly cannabidiol and not more than 0.2 percent of delta-9-tetrahydrocannabinol are not under international control”.

- The [European Medicines Agency \(EMA\)](#)¹⁵ has authorised one prescription cannabidiol medicines for the treatment of Lennox-Gastaut syndrome and Dravet syndrome (two rare and severe forms of epilepsy) patients aged 2 years and older.
- The European Union guides all member states that hemp should not exceed a THC limit of 0.2%. In January 2019, European Union's Novel Food regime, led to the classification of all extracted cannabinoids as “novel”. Novel Food is defined as food that had not been used for human consumption to a significant degree in the European Union before 15th May 1997. According to this new classification, CBD products require pre-market authorisation¹⁶.
- In the United States (U.S.), the FDA has approved one CBD prescription product for the treatment of seizures associated with Lennox-Gastaut syndrome and Dravet syndrome in patients 2 years of age or older. It is currently illegal to market CBD by adding it to a food or labelling it as a dietary supplement. Some CBD products are being marketed with unproven medical claims and are of unknown quality. In 2018, the *Farm Bill*¹⁷ legalized the production and sale of hemp and its extracts. Hemp derived CBD containing less than 0.3 percent THC, is exempted under federal law, however some states still have legal restrictions on the possession of CBD.
- In Canada, there is one approved product containing a CBD/THC combination, available as a prescription medicine. Phytocannabinoids are regulated under the *Cannabis Act*¹⁸. Under the *Cannabis Act*, CBD products remain strictly regulated and are only legal when sold in compliance with the Act and its regulations. The provinces and territories are responsible for determining how cannabis is distributed and sold within their jurisdictions. CBD and products containing CBD, such as cannabis oil, may only be sold by a provincially or territorially-authorized cannabis retailer or a federally-licensed seller of cannabis for medical purposes.
- In the United Kingdom (U.K), CBD in its pure form is not classed as a controlled drug under the Misuse of Drugs Act (MDA) 1971/Misuse of Drugs Regulations (MDR) 2001. However, noting the difficulty to isolate pure CBD, based on the precautionary principles, a CBD containing product would be controlled under the MDA 1971/MDR 2001 as a result if it's

¹³ Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

¹⁴ WHO Cannabis recommendations <https://www.who.int/publications/m/item/ecdd-41-cannabis-recommendations>

¹⁵ EMA cannabidiol authorisation <https://www.ema.europa.eu/en/medicines/human/EPAR/epidvolex>

¹⁶ European Commission Novel Food https://ec.europa.eu/food/safety/novel_food/catalogue/search/public/index.cfm

¹⁷ USDA Farm Bill <https://www.usda.gov/farmbill>

¹⁸ Canadian Cannabis Act <https://laws-lois.justice.gc.ca/eng/acts/c-24.5/>

other cannabinoid content.¹⁹ The UK Food Standards Agency confirmed the novel food status of CBD extracts in January 2019 and has set a deadline of 31 March 2021 for companies marketing CBD extracts as foods or food supplements, to submit Novel Food approval applications.²⁰

- In New Zealand, cannabidiol is classified as a prescription only medicine, where the tetrahydrocannabinols (THCs) and specified substances within the product must not exceed 2 percent of the total CBD, tetrahydrocannabinol (THC) and other specified substances. If a product contains CBD but does not meet the definition of a CBD product, it is a 'controlled drug' and is subject to the regulatory requirements of the Misuse of Drugs Act.²¹

1.3 Bilastine

CAS Number:

202189-78-4

Alternative names

2-[4-(2-(4-(1-(2-ethoxyethyl)-1H-benzimidazol-2-yl)piperidin-1-yl)ethyl)phenyl]-2-methylpropionic acid; p-[2-[4-[1-(2-ethoxyethyl)-2-benzimidazolyl]piperidino]ethyl]- α -methylhydratropic acid

Benzeneacetic acid, 4-[2-[4-[1-(2-ethoxyethyl)-1H-benzimidazol-2-yl]-1-piperidinyl]ethyl]- α,α -dimethyl-

Applicant

Private applicant

Current scheduling

Bilastine is not specifically scheduled in the Poisons Standard. However, bilastine is captured by the current Schedule 4 and Appendix F, Part 3 entries for antihistamines as follows:

Schedule 4

ANTIHISTAMINES **except:**

- a) when included in Schedule 2 or 3; or
- b) when separately specified in this Schedule.

¹⁹ UK Government Factsheet – cannabis, CBD and other cannabinoids https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/825872/factsheet-cannabis-cbd-and-cannabinoids-2019.pdf

²⁰ UK Food Standards Agency CBD Guidance <https://www.food.gov.uk/business-guidance/cannabidiol-cbd>

²¹ NZ Ministry Of Health Medicinal Cannabis Agency – CBD products <https://www.health.govt.nz/our-work/regulation-health-and-disability-system/medicinal-cannabis-agency/medicinal-cannabis-agency-information-industry/medicinal-cannabis-agency-working-medicinal-cannabis/medicinal-cannabis-agency-cannabidiol-cbd-products>

Appendix F, Part 3

Poison	Warning Statements	Safety Directions
ANTIHISTAMINES not separately specified in this Appendix except: <ul style="list-style-type: none"> a) dermal, ocular, parenteral and paediatric preparations; b) oral preparations of astemizole, azelastine, desloratadine, fexafendadine, loratadine, terfenadine or cetirizine; or c) nasal preparations of azelastine; or d) preparations for the treatment of animals. 	39 (This medication may cause drowsiness. If affected do not drive a vehicle or operate machinery. Avoid alcohol) or 40 (This medication may cause drowsiness and may increase the effects of alcohol. If affected do not drive a motor vehicle or operate machinery).	

Index**ANTI-HISTAMINES**

cross reference: ASTEMIZOLE, AZELASTINE, DESLORATADINE, FEXOFENADINE, LORATADINE, TERFENADINE, CETIRIZINE

Schedule 4

Appendix F, Part 3

Proposed scheduling

A request has been made to amend the Poisons Standard as follows:

Schedule 2 - New Entry

BILASTINE in preparations for oral use.

Schedule 4 - New Entry

BILASTINE except when included in Schedule 2.

Appendix F, Part 3- Amend Entry

Poison	Warning Statements	Safety Directions
ANTIHISTAMINES not separately specified in this Appendix except: <ul style="list-style-type: none"> a) dermal, ocular, parenteral and paediatric preparations; b) oral preparations of astemizole, azelastine, desloratadine, fexafendadine, loratadine, terfenadine, bilastine or cetirizine; or c) nasal preparations of azelastine; or d) preparations for the treatment of animals. 	39 (This medication may cause drowsiness. If affected do not drive a vehicle or operate machinery. Avoid alcohol) or 40 (This medication may cause drowsiness and may increase the effects of alcohol. If affected do not drive a motor vehicle or operate machinery).	

Index – New Entry**BILASTINE**

Schedule 4

Schedule 2

Appendix F, Part 3

Index – Amend Entry**ANTIHISTAMINES**

cross reference: ASTEMIZOLE, AZELASTINE, **BILASTINE**, DESLORATADINE, FEXOFENADINE, LORATADINE, TERFENADINE, CETIRIZINE

Schedule 4

Appendix F, Part 3

Key uses / expected use

Medicine

Reasons for proposal put forward by the applicant

- This application seeks an amendment to the Poisons Standard to enable the supply of bilastine in oral preparations as Schedule 2 (Pharmacy Only) medicines.
- Bilastine is a new, second-generation non-sedating antihistamine (NSAH) molecule in Australia. It belongs to the same pharmacological class as fexofenadine, loratadine and cetirizine and is similarly used for the symptomatic treatment of allergic rhinitis (AR) and urticaria.
- NSAHS are very well-established OTC medicines in Australia and the availability of bilastine as a Schedule 2 medicine is considered appropriate given its risk-benefit and safety profiles are equivalent to existing Schedule 2 and unclassified molecules in its class.
- Bilastine has a well-defined safety and tolerability profile, with a wide therapeutic index. As bilastine is highly selective for peripheral H1-receptors and does not cross the blood-brain barrier, incidence of sedation is very low. At the therapeutic dose of 20 mg/day, bilastine does not impact psychomotor performance, enhance the depressant effect of alcohol or lorazepam, nor does it affect the ability to drive and/or operate machinery.
- The nature of the conditions bilastine is proposed to treat are generally intermittent and self-limiting, and the safe and effective use of second-generation NSAHS for such conditions with minimal instances of misuse and/or abuse has been widely established in Australia for over 20 years.
- Bilastine is regarded as having a very low risk of harm from inappropriate use and the availability of only a single strength and dosage form for use in all indications with no dose modification recommendations will assist in minimising risks associated with potential medication error.
- Given the nature of the condition (readily self-diagnosable, commonly intermittent) and the patient population (excellent awareness of their disease and expectations regarding symptomatic relief, rarely consult their doctor about their treatment), the availability of bilastine as a Schedule 2 medicine ensures that those patients who require assistance have access to an appropriately qualified and informed health professional.

Australian regulations

- According to the [TGA Ingredient Database](#)²², bilastine is:
 - Available for use as an active ingredient in export only and prescription medicines;
 - Not available as an excipient or an equivalent ingredient in any application.
- As of August 2020, there were no medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)²³ that contain bilastine as an active ingredient.
- Bilastine is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)²⁴ No.3 of 2020.
- Bilastine is not included in the [TGA prescribing medicines in pregnancy database](#)²⁵.
- While there are no warning statements pertaining specifically to bilastine in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)²⁶, the following warning statements pertaining to antihistamines are required to be included on the labelling:

Substance	Conditions	Required statement(s)
Antihistamines <i>(Entry 1 of 5)</i> including: <ul style="list-style-type: none"> • Alimemazine (trimeprazine) • Brompheniramine • Chlorphenamine • Dexchlorpheniramine • Diphenhydramine • Doxylamine • Pheniramine • Promethazine • Triprolidine when NOT separately specified in this table	In oral medicines that include dosage instructions for adults and children aged from 'x' years (where 'x' must not be less than 2) when NOT separately specified in this table	<i>either</i> <ul style="list-style-type: none"> – This medication may cause drowsiness. If affected do not drive a vehicle or operate machinery. Avoid alcohol. <i>or</i> <ul style="list-style-type: none"> – This medication may cause drowsiness and may increase the effects of alcohol. If affected do not drive a motor vehicle or operate machinery. • Do not give to children under 'x' years of age. • and (if 'x' < 12) <ul style="list-style-type: none"> – Do not give to children between 'x' and 11 years of age, except on the advice of a doctor, pharmacist or nurse practitioner.

²² TGA Ingredient Database <https://www.ebs.tga.gov.au/>

²³ ARTG database <https://www.tga.gov.au/artg>

²⁴ Therapeutic Goods (Permissible Ingredients) Determination

[https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB\\$%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20IngredientsRB%20Determination)

²⁵ TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

²⁶ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

Substance	Conditions	Required statement(s)
<p>Antihistamines (Entry 2 of 5) including:</p> <ul style="list-style-type: none"> • Alimemazine (trimeprazine) • Brompheniramine • Chlorphenamine • Dexchlorpheniramine • Diphenhydramine • Doxylamine • Pheniramine • Promethazine • Triprolidine <p>when NOT separately specified in this table</p>	<p>In oral medicines that ONLY include dosage instructions for CHILDREN aged between 'x' and 'y' years (where 'x' must not be less than 2, and 'y' must not be more than 11)</p> <p>when NOT separately specified in this table</p>	<ul style="list-style-type: none"> • This medication may cause drowsiness. • Do not give to children under 'x' years of age. • Do not give to children between 'x' and 'y' years of age, except on the advice of a doctor, pharmacist or nurse practitioner
<p>Antihistamines (Entry 3 of 5) including:</p> <ul style="list-style-type: none"> • Brompheniramine • Chlorphenamine • Dexchlorpheniramine • Diphenhydramine • Doxylamine • Pheniramine • Promethazine • Triprolidine <p>when NOT separately specified in this table</p>	<p>In oral preparations indicated for COUGH, COLD OR FLU:</p> <ul style="list-style-type: none"> • which include dosage instructions for adults and children aged from 'x' years (where 'x' must not be less than 6) 	<p><i>either</i></p> <ul style="list-style-type: none"> – This medication may cause drowsiness. If affected do not drive a vehicle or operate machinery. Avoid alcohol. <p><i>or</i></p> <ul style="list-style-type: none"> – This medication may cause drowsiness and may increase the effects of alcohol. If affected do not drive a motor vehicle or operate machinery. • Do not give to children under 'x' years of age. • and (if 'x' < 12) <ul style="list-style-type: none"> – Do not give to children between 'x' and 11 years of age, except on the advice of a doctor, pharmacist or nurse practitioner.

Substance	Conditions	Required statement(s)
<p>Antihistamines (Entry 4 of 5) including:</p> <ul style="list-style-type: none"> • Brompheniramine • Chlorphenamine • Dexchlorpheniramine • Diphenhydramine • Doxylamine • Pheniramine • Promethazine • Triprolidine <p>when NOT separately specified in this table</p>	<p>In oral preparations indicated for COUGH, COLD OR FLU:</p> <ul style="list-style-type: none"> • which ONLY include dosage instructions for CHILDREN aged between 'x' and 'y' years (where 'x' must not be less than 6 and 'y' must not be more than 11) 	<p>This medication may cause drowsiness.</p> <ul style="list-style-type: none"> • Do not give to children under 'x' years of age. • and (if 'x' < 12) <ul style="list-style-type: none"> – Do not give to children between 'x' and 11 years of age, except on the advice of a doctor, pharmacist or nurse practitioner.
<p>Antihistamines (Entry 5 of 5) including:</p> <ul style="list-style-type: none"> • Diphenhydramine • Doxylamine • Promethazine 	<p>In oral medicines indicated for SHORT TERM USE IN INSOMNIA:</p> <ul style="list-style-type: none"> • which include dosage instructions for adults and children aged from 'x' years (where 'x' must not be less than 2) <p><i>(Note: Antihistamine medicines indicated for sedation that only include dosage instructions for children aged < 12 years are subject to 'Antihistamines (Entry 2 of 5))</i></p>	<ul style="list-style-type: none"> • This product should be taken on medical or pharmacist advice. • Do not give to children under 'x' years of age. • either (if the substance is in pregnancy category B or C): <ul style="list-style-type: none"> – If pregnant or [likely/trying] to become pregnant, or if breastfeeding, consult a doctor or pharmacist before use. <p><i>or (if the substance is in pregnancy category A):</i></p> <p style="text-align: center;"><i>either</i></p> <ul style="list-style-type: none"> – Not recommended for use by pregnant or breastfeeding women. <p style="text-align: center;"><i>or</i></p> <ul style="list-style-type: none"> – If pregnant or breastfeeding, consult a doctor or pharmacist before use. • Do not take this medicine for more than a few days. • This preparation is to aid sleep. Drowsiness may continue the following day. If affected do not drive or operate machinery. Avoid alcohol.

- As of August 2020, there were no reports of adverse events for products containing bilastine as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#)²⁷,
- As of August 2020, there were no products containing bilastine listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#)²⁸.

International regulations

- Bilastine, 20 mg tablet is an authorised medicine in the [European Union](#)²⁹.
- According to the [Health Products Regulatory Authority of Ireland](#)³⁰, bilastine 2.5 mg oral solution, 10 mg orodispersible tablets are approved as a prescription medicine for children aged 6 to 11 years with a body weight of at least 20 kg to relieve symptoms of hayfever, other forms of allergic rhinitis and for the treatment of itchy skin rashes including urticaria. Bilastine 20 mg tablets are approved for use in adults and adolescents 12 years of age and older for the symptomatic treatment of seasonal and perennial allergic rhino-conjunctivitis and urticaria.
- In the [United Kingdom \(UK\)](#)³¹, bilastine 20 mg tablets is an approved prescription medicine for the symptomatic treatment of allergic rhino-conjunctivitis (seasonal and perennial) and urticaria in adults and in adolescents 12 years of age and over.
- While bilastine is included in the [United States Food and Drug Administration \(USFDA\) Substance Registration System](#)³² this does not imply any regulatory review or approval of the substance.
- According to [the Health Canada Drug Product database](#)³³, bilastine 20 mg tablets have been approved as a prescription antihistamine medicine since March 2016.
- The [New Zealand Medicines and Medical Devices Safety Authority \(MedSafe\)](#)³⁴ classifies bilastine as both a Prescription and Pharmacy only medicine. As a Pharmacy only medicine, bilastine is available in divided solid dosage forms for oral use containing 20 milligrams or less for the treatment of the symptoms of allergic rhino-conjunctivitis (seasonal and perennial) and urticaria. All other forms or strengths are prescription medicines.

1.4 Budesonide + formoterol

CAS Number:

Budesonide: 51333-22-3

Formoterol: 183814-30-4

Alternative names

Budesonide: 16 α , 17 α -22 R, S-propylmethylenedioxypregna-1, 4-diene-1 β , 21-diol-3, 20-dione

Formoterol: (R*R*)-(\pm)-N-[2-hydroxy-5-[1-hydroxy-2-[[2-(4-methoxyphenyl)-1-methylethyl]amino]ethyl]phenyl]formamide, (E)-2-butendioate(2:1), dihydrate

²⁷ Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

²⁸ Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

²⁹ EMA List of nationally authorised medicinal products https://www.ema.europa.eu/en/documents/psusa/bilastine-list-nationally-authorised-medicinal-products-psusa/00003163/201703_en.pdf

³⁰ Irish Health Products Regulatory Authority <http://www.hpra.ie/homepage/medicines/medicines-information/find-a-medicine>

³¹ Medicines UK <https://www.medicines.org.uk/emc/product/4551>

³² US FDA Substance Registration System – Unique Ingredient Identifier <https://fdasis.nlm.nih.gov/srs/unii/PA1123N395>

³³ Health Canada drug product database <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>

³⁴ New Zealand Medicines and Medical Devices Safety Authority (MedSafe) <https://www.medsafe.govt.nz/profs/class/classintro.asp>

Applicant

Private applicant

Current scheduling

Budesonide

Schedule 4

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

Schedule 2

BUDESONIDE in aqueous nasal sprays delivering 64 micrograms or less of budesonide per actuation when the maximum recommended daily dose is no greater than 400 micrograms, for the prophylaxis or treatment of allergic rhinitis for up to 6 months in adults and children 12 years of age and over.

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BUDESONIDE

Schedule 4

Schedule 2

Formoterol

Schedule 4

FORMOTEROL

Index

FORMOTEROL

Schedule 4

Proposed scheduling

A request has been made to amend the Poisons Standard as follows:

Budesonide

Schedule 4 – Amend Entry

BUDESONIDE **except** when included in Schedule 2 **or** Schedule 3.

Schedule 3 – New Entry

BUDESONIDE when combined with formoterol in a:

- a) dry powder inhaler delivering 160 micrograms budesonide and 4.5 micrograms formoterol fumarate dihydrate per inhalation (delivered dose) or less, when packed in a primary pack containing 60 inhalations or less; or
- b) pressurised metered dose inhaler delivering 80 micrograms budesonide and 2.25 micrograms formoterol fumarate dihydrate per actuation (delivered dose) or less, when packed in a primary pack containing 120 actuations or less; and

where supply is limited:

- a) to persons aged 12 years and over with evidence of medically diagnosed asthma; and
- b) for use as an anti-inflammatory reliever.

Appendix F, Part 3 – New Entry

Poison	Warning statements	Safety direction
Budesonide when included in Schedule 3.	32 (This preparation should be part of an overall treatment plan regularly assessed with your doctor.)	

Appendix M – New Entry

BUDESONIDE when combined with formoterol, where the pharmacist providing professional advice:

- Demonstrates competencies as outlined in the Pharmaceutical Society of Australia competency-based education framework relevant to the supply of budesonide/formoterol as a Pharmacist Only medicine; and
- Complies in all respects with the relevant professional practice standards, and the Pharmaceutical Society of Australia professional practice guidance for supply of budesonide/formoterol as a Pharmacist Only medicine; and
- Confirms the patient has a medical diagnosis of asthma; and
- Documents the supply of budesonide/formoterol in a clinical information system in accordance with professional practice guidance.

Index – Amend Entry

BUDESONIDE

Schedule 4

Schedule 3

Schedule 2

Appendix F, Part 3

Appendix M

Formoterol

Schedule 4 – Amend entry

FORMOTEROL except when included in Schedule 3.

Schedule 3 – New Entry

FORMOTEROL when combined with budesonide in a:

- a) dry powder inhaler delivering 160 micrograms budesonide and 4.5 micrograms formoterol fumarate dihydrate per inhalation (delivered dose) or less, when packed in a primary pack containing 60 inhalations or less; or

- b) pressurised metered dose inhaler delivering 80 micrograms budesonide and 2.25 micrograms formoterol fumarate dihydrate per actuation (delivered dose) or less, when packed in a primary pack containing 120 actuations or less; and

when supply is limited:

- a) to persons aged 12 years and over with evidence of medically diagnosed asthma; and
b) for use as an anti-inflammatory reliever.

Appendix F, Part 3 – New Entry

Poison	Warning statements	Safety direction
Formoterol when included in Schedule 3.	32 (This preparation should be part of an overall treatment plan regularly assessed with your doctor.)	

Appendix M – New Entry

Formoterol when combined with budesonide, where the pharmacist providing professional advice:

- Demonstrates competencies as outlined in the Pharmaceutical Society of Australia competency-based education framework relevant to the supply of budesonide/formoterol as a Pharmacist Only medicine; and
- Complies in all respects with the relevant professional practice standards, and the Pharmaceutical Society of Australia professional practice guidance for supply of budesonide/formoterol as a Pharmacist Only medicine; and
- Confirms the patient has a medical diagnosis of asthma; and
- Documents the supply of budesonide/formoterol in a clinical information system in accordance with professional practice guidance.

Index – Amend Entry

FORMOTEROL

Schedule 4

Schedule 3

Appendix F, Part 3

Appendix M

Key uses / expected use

Medicines

Reasons for proposal put forward by the applicant

Budesonide/formoterol fix dose combination (FDC) for 'as needed' use is well-established and is a recommended alternative reliever therapy option in the Australian asthma guidelines for Steps 2-4. Rescheduling to allow access to patients as a Pharmacist Only Medicine would provide the following benefits:

- Budesonide/formoterol FDC 'as needed' provides a more effective anti-inflammatory reliever alternative to the current OTC reliever which many patients now over rely on as their main treatment option thus helping to reshape behaviour learned over many years. In more recently diagnosed patients, this will also help to avoid the establishment of patient reliance on short acting β -agonist (SABA).
- OTC budesonide/formoterol FDC 'as needed' will provide patients with earlier inhaled corticosteroid (ICS) therapy helping to address the underlying inflammation to prevent exacerbations or asthma deterioration. ICS adherence is also not a concern with this therapy as the budesonide is provided in combination with the reliever.
- The benefits of reducing SABA overreliance and ICS under-utilisation would have indirect benefits with fewer patients with uncontrolled or poorly-controlled asthma, reduced urgent asthma-related healthcare visits and potentially less asthma-related deaths. Thus minimising cost and risk to the community.
- Consultations between pharmacists and patients with asthma will have an increased focus on the importance of reduction in underlying inflammation (in addition to symptom relief) to prevent exacerbations and maintain control. This has the potential to improve asthma outcomes for all patients, not only those who are recommended OTC budesonide/formoterol FDC.
- With patient consent and in accordance with professional practice guidance, pharmacists will follow up with the patient's medical practitioner as appropriate about the supply of OTC budesonide/formoterol FDC. This will facilitate best practice communication and collaboration between the pharmacist and medical practitioner about the patient's ongoing asthma management. This is especially important for patients with mild asthma.

Australian regulations

- According to the [TGA Ingredient Database](#)³⁵, budesonide 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.
- According to the [TGA Ingredient Database](#)³⁶, formoterol 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;

³⁵ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

³⁶ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

- Not available as an equivalent ingredient in any application.
- As of August 2020, there were 43 medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)³⁷ that contain budesonide as an active ingredient. These include 27 prescription medicines, 8 non-prescription medicines and 8 export only medicines.
- As of August 2020, there were 27 medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)³⁸ that contain formoterol as an active ingredient. These include 27 prescription medicines.
- As of August 2020, there were 14 medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)³⁹ that contain budesonide+formoterol as active ingredients. These include 14 prescription medicines.
- Budesonide and formoterol are not permitted to be included in listed medicines as they are not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)⁴⁰ No.2 of 2020.
- The [TGA prescribing medicines in pregnancy database](#)⁴¹ classifies budesonide and formoterol as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Budesonide	A	Endocrine system	Corticosteroids	Inhalation/intra nasal
Budesonide	A	Respiratory System	Inhalational agents	Preventative aerosols and inhalations
Budesonide (systemic)	B3	Alimentary System	Antidiarrhoeals	
Formoterol	B3	Respiratory System	Inhalational agents	Bronchospasm relaxants

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

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

- There are no warning statements pertaining to budesonide and formoterol in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)⁴².

³⁷ ARTG database <https://www.tga.gov.au/artg>

³⁸ ARTG database <https://www.tga.gov.au/artg>

³⁹ ARTG database <https://www.tga.gov.au/artg>

⁴⁰ Therapeutic Goods (Permissible Ingredients) Determination

[https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB\\$%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20IngredientsRB%20Determination)

⁴¹ TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

⁴² Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

- As of August 2020, there were 240 reports of adverse events for products containing budesonide+formoterol as active ingredients on the [Database of Adverse Event Notifications \(DAEN\)](#)⁴³, with 140 reports where budesonide+formoterol were the single suspected medicine.
- As of August 2020, there were three products containing budesonide listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#)⁴⁴.

International regulations

- Budesonide+formoterol is approved for use as a prescription medicine by the [United States Food and Drug Administration Approved Drug Products Database](#)⁴⁵.
- Budesonide+formoterol is approved for use as a prescription medicine according to the [Canadian \(Health Canada\) Drug Product Database](#)⁴⁶.
- Budesonide+formoterol is available in the United Kingdom as a prescription medicine.
- According to the [New Zealand Medicines and Medical Devices Safety Authority \(MedSafe\)](#)⁴⁷ budesonide and formoterol are available as follows in New Zealand:

Ingredient	Conditions	Classification
Budesonide	except when specified elsewhere in this schedule	Prescription
Budesonide	for the treatment or prophylaxis of allergic rhinitis in adults and children over 12 years of age in aqueous nasal sprays delivering up to 64 micrograms per actuation and when the maximum recommended daily dose is no greater than 400 micrograms (200 micrograms per nostril)	Pharmacy Only
Formoterol		Prescription

1.5 Psilocybin

CAS Number:

620-52-2

Alternative names

[3-(2-dimethylaminoethyl)-1H-indol-4-yl] dihydrogen phosphate

Applicant

Private applicant

⁴³ Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

⁴⁴ Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

⁴⁵ FDA-Approved Drugs <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=021929>

⁴⁶ Health Canada Drug Product Database <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>

⁴⁷ NZ MedSafe Classification Database <https://www.medsafe.govt.nz/profs/class/classintro.asp>

Current scheduling

Schedule 9

PSILOCYBINE.

Index

PSILOCYBINE

Schedule 9

Proposed scheduling

A request has been made to amend the Poisons Standard as follows:

Schedule 9 – Amend entry

PSILOCYBINE ~~E~~ **except when included in Schedule 8.**

Schedule 8 – New Entry

PSILOCYBIN for use in the treatment of medical conditions:

- a) **In preparation for oral use as part of psychotherapy under the authorisation of a treating psychiatrist or specialist addiction physician in a medically controlled environment;**
- b) **Manufactured in accordance with the *Narcotic Drugs Act 1967*; and/or**
- c) **Imported or manufactured in Australia as therapeutic goods, or for use in therapeutic goods, for supply, in accordance with the *Therapeutic Goods Act 1989*; and/or**
- d) **In therapeutic goods supplied in accordance with the *Therapeutic Goods Act 1989*.**

Index – Amend Entry

PSILOCYBINE

Schedule 9

Schedule 8

Key uses / expected use

Medicines

Reasons for proposal put forward by the applicant

- This application supports the opportunity to expand the paradigm for the treatment of mental illness to improve the mental health outcomes of suffering Australians. Psilocybin has been granted two Breakthrough Therapy Designations by the Food and Drug Administration (FDA) in the United States - the first to Compass Pathways Limited in 2018 for psilocybin as part of therapy for treatment resistant depression (COMPASS, 2018) and the second in 2019 to Usona Institute for psilocybin as part of therapy in the treatment of major depressive disorder (Businesswire, 2019). This designation from the FDA acknowledges both the unmet medical need in these broad populations and the potential for these therapies to offer significant improvements over existing therapies.

- In a medically controlled environment psilocybin-assisted therapy is safe, non-addictive, and there is no increase in risk for mental ill-health in a clinically controlled environment (Passie, 2008).
- Psilocybin-assisted therapy has yielded remarkable clinical results for depression and anxiety in numerous trials at leading universities internationally (Johnson & Griffiths, 2017).
- Psilocybin-assisted therapy can lead to remission in 60-80% of cases of anxiety and depression, whereas current existing treatments lead to remission in a maximum of 35-42% of cases (Griffiths et al., 2016; Ross, 2016; Carhart-Harris, 2016).
- The rescheduling of psilocybin from Schedule 9 to Schedule 8 will make it easier for Australians suffering from depression and anxiety disorders and substance abuse (and potentially other illnesses such as anorexia nervosa and OCD) to access psilocybin-assisted therapy through their psychiatrists and specialist addiction physicians (with supporting therapists) in strictly medically controlled environments. It will also increase the ease and reduce costs of clinical research.

Australian regulations

- Psilocybin is not listed as an ingredient on the [TGA Ingredient Database](#)⁴⁸.
- As of August 2020, there were no medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)⁴⁹ that contain psilocybin as an active ingredient.
- Psilocybin is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)⁵⁰ No.2 of 2020.
- There are no warning statements pertaining to psilocybin in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)⁵¹.
- As of August 2020, there were no reports of adverse events for products containing psilocybin as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#)⁵².
- As of August 2020, there were no products containing psilocybin listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#)⁵³.

International regulations

- Psilocybin is listed as a Schedule I drug under the [United Nations 1971 Convention on Psychotropic Substances](#)⁵⁴.
- Psilocybin is listed as a Schedule I (controlled substance) drug under the [U.S Psychotropic Substances Act](#)⁵⁵.
- Psilocin is listed as a controlled drug under the [U.K Misuse of Drugs Act 1971](#)⁵⁶.

⁴⁸ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

⁴⁹ ARTG database <https://www.tga.gov.au/artg>

⁵⁰ Therapeutic Goods (Permissible Ingredients) Determination

[https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB\\$%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20IngredientsRB%20Determination)

⁵¹ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

⁵² Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

⁵³ Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

⁵⁴ The International Drug Control Conventions – Schedules of the Convention on Psychotropic Substances of 1971, as at 3 November 2020 <https://undocs.org/ST/CND/1/Add.2/Rev.6>

⁵⁵ Drug Enforcement Agency Controlled substances https://www.deadiversion.usdoj.gov/schedules/orangebook/c_cs_alpha.pdf

⁵⁶ UK *Misuse of Drugs Act 1971* <https://www.legislation.gov.uk/ukpga/1971/38/schedule/2>

- Psilocybin is listed as a Schedule III (controlled substance) drug under the Canadian [Controlled Drugs and Substances Act](#)⁵⁷.
- According to the [New Zealand Medicines and Medical Devices Safety Authority \(MedSafe\)](#)⁵⁸ psilocybin is classified in New Zealand as a Class A controlled drug (i.e. is a drug that poses a very high risk of harm when misused)⁵⁹ and there are restrictions on its supply, prescribing or administration.

1.6 N, α -Dimethyl-3,4-(methylenedioxy)phenylethylamine (MDMA)

CAS Number:

42542-10-9

Alternative names

IUPAC Name: 1-(1,3-benzodioxol-5-yl)-N-methylpropan-2-amine

Methylenedioxyamphetamine

α -Dimethyl-3,4-(Methylenedioxy)Phenylethylamine

3,4-Methylenedioxy-N-A-Dimethylphenylethylamine

Applicant

Private applicant

Current scheduling

MDMA is currently in Schedule 9 of the Poisons Standard as follows:

Schedule 9

N, α -DIMETHYL-3,4-(METHYLENEDIOXY)PHENYLETHYLAMINE *(MDMA).

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N, α -DIMETHYL-3,4-(METHYLENEDIOXY)PHENYLETHYLAMINE

cross reference: 3,4-METHYLENEDIOXY-N- α -DIMETHYLPHENYLETHYLAMINE, MDMA

Proposed scheduling

A request has been made to amend the Poisons Standard as follows:

Schedule 9 – Amend Entry

N, α -DIMETHYL-3,4-(METHYLENEDIOXY)PHENYLETHYLAMINE *(MDMA) **except when in Schedule 8.**

⁵⁷ Canadian Controlled Drugs and Substances Act <https://laws-lois.justice.gc.ca/eng/acts/c-38.8/page-15.html#h-95603>

⁵⁸ NZ MedSafe Classification Database <https://www.medsafe.govt.nz/profs/class/classintro.asp>

⁵⁹ NZ Misuse of Drugs Act 1975 <http://www.legislation.govt.nz/act/public/1975/0116/latest/DLM436190.html>

Schedule 8 – New Entry

N, α -DIMETHYL-3,4-(METHYLENEDIOXY)PHENYLETHYLAMINE *(MDMA) for use in the treatment of medical conditions:

- a) In preparation for oral use under the authorisation of a treating psychiatrist or addiction specialist physician in a medically controlled environment;
- b) Manufactured in accordance with the *Narcotic Drugs Act 1967*; and/or
- c) Imported or manufactured in Australia as therapeutic goods, or for use in therapeutic goods, for supply, in accordance with the *Therapeutic Goods Act 1989*; and/or
- d) In therapeutic goods supplied in accordance with the *Therapeutic Goods Act 1989*.

Index- Amend Entry

N, α -DIMETHYL-3,4-(METHYLENEDIOXY)PHENYLETHYLAMINE

cross reference: 3,4-METHYLENEDIOXY-N- α -DIMETHYLPHENYLETHYLAMINE, MDMA

Schedule 9

Schedule 8

Key uses / expected use

Medicines

Reasons for proposal put forward by the applicant

- In a controlled setting, MDMA-assisted psychotherapy supports patients in reprocessing traumatic and painful memories, making MDMA efficacious for treating PTSD and addictions associated with trauma (Feduccia & Mithoefer, 2018)⁶⁰.
- There is strong evidence for the safety and efficacy of MDMA-assisted psychotherapy for the treatment of PTSD (Bahji et al, 2020)⁶¹. In controlled settings there have been no major adverse events and minor side effects related to MDMA resolve within a few days (MAPS, 2019)⁶². Further, medicinal MDMA does not produce dependence as defined in the contemporary versions of the Diagnostic and Statistical Manual of Mental Disorders or the International Statistical Classification of Diseases (Kalant, 2001)⁶³.
- MDMA-assisted therapy has been granted ‘Breakthrough Therapy’ status by the US Food and Drug Administration (FDA), expediting its transition to prescription medicines subject to positive outcomes from current Phase 3 trials (MAPS PR, 2017)⁶⁴. This designation highlights the FDA’s anticipation that MDMA-assisted therapies may offer substantial advantage over current treatments.

⁶⁰ Feduccia, A. A., & Mithoefer, M. C. (2018). MDMA-assisted psychotherapy for PTSD: are memory reconsolidation and fear extinction underlying mechanisms?. *Progress in neuro-psychopharmacology and biological psychiatry*, 84, 221-228. DOI: [10.1016/j.pnpbp.2018.03.003](https://doi.org/10.1016/j.pnpbp.2018.03.003)

⁶¹ Bahji et al. (2020) Efficacy of 3,4-methylenedioxyamphetamine (MDMA)-assisted psychotherapy for posttraumatic stress disorder: A systematic review and metaanalysis. *Progress in Neuropsychopharmacology and Biological Psychiatry* 96:1-15 DOI: [10.1016/j.pnpbp.2019.109735](https://doi.org/10.1016/j.pnpbp.2019.109735)

⁶² **Multidisciplinary Association for Psychedelic Studies (MAPS)**. (2019). MDMA Investigator’s Brochure. 11th Edition. <https://maps.org/research/mdma/mdma-research-timeline/104-other-mdma-resources/5400-mdma-investigator-s-brochure-and-fda-annual-report&Itemid=485>

⁶³ Kalant, H. 2001. The pharmacology and toxicology of “ecstasy” (MDMA) and related drugs. *CMAJ*, 165(7), pp. 917-928. PMID: 11599334 <https://pubmed.ncbi.nlm.nih.gov/11599334/>

⁶⁴ **Multidisciplinary Association for Psychedelic Studies (MAPS)**. 2017. FDA Grants Breakthrough Therapy Designation for MDMA-Assisted Psychotherapy for PTSD, Agrees on Special Protocol Assessment for Phase 3 Trials. Retrieved 19 May 2020 from, <https://maps.org/news/media/6786-press-release-fda-grants-breakthrough-therapy-designation-for-mdma-assisted-psychotherapy-for-ptsd.-agrees-on-special-protocol-assessment-for-phase-3-trials>

- The FDA has approved an “Expanded Access” or “Compassionate Use” scheme using MDMA for PTSD in patients who have limited treatment options (MAPS PR1, 2020)⁶⁵. Israel launched a Compassionate Use program for MDMA-assisted therapy for PTSD in 2019 (MAPS PR2, 2020)⁶⁶ and Switzerland also has a compassionate use program for MDMA with individual authorisations by the Federal Office of Public Health (Sessa et al, 2019)⁶⁷. Recently, the Australian Therapeutic Goods Administration (TGA) approved the first application for the use of MDMA-assisted therapy for the treatment of a patient with treatment resistant PTSD under the Special Access Scheme-B.
- MDMA treatment is only to be used in clinical settings according to the guidelines of a Schedule 8 controlled substance in the Poisons Standards and in accordance with strict safety protocols for supplying MDMA-assisted therapy through health care providers in a medically controlled environment.
- The current Schedule 9 classification of MDMA places hurdles on research (cost, stigma and ease of access) and on its use in a medically controlled environment as part of evidence-based treatment. Reclassifying MDMA as a Schedule 8 substance will reduce cost and improve ease of access for researchers and specialist medical practitioners for treatment of individuals seeking relief for treatment resistant conditions via the Special Access Scheme.
- Given the demonstrated therapeutic benefits for individuals suffering from PTSD whose condition has not improved after standard forms of treatment and, high remission rates shown in clinical trials, it is apparent that MDMA used in a medically controlled environment does not fit within the requirements of a Schedule 9 Substance and more closely reflects the requirements of Schedule 8.

Australian regulations

- MDMA is not listed as an ingredient on the [TGA Ingredient Database](#)⁶⁸.
- As of August 2020, there were no medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)⁶⁹ that contain MDMA as an active ingredient.
- MDMA is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)⁷⁰ No.2 of 2020.
- There are no warning statements pertaining to MDMA in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)⁷¹.
- As of August 2020, there were no reports of adverse events for products containing MDMA as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#)⁷².
- As of August 2020, there were no products containing MDMA listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#)⁷³.

⁶⁵ **Multidisciplinary Association for Psychedelic Studies (MAPS)**. 2020. PRESS RELEASE: FDA Agrees to Expanded Access Program for MDMA-Assisted Psychotherapy for PTSD. Retrieved 4 June 2020 from <https://maps.org/news/media/8008-press-release-fda-agrees-to-expanded-access-program-for-mdma-assisted-psychotherapy-for-ptsd>

⁶⁶ **Multidisciplinary Association for Psychedelic Studies (MAPS)**. 2020. PRESS RELEASE: Israel Embraces Research on MDMA-Assisted Psychotherapy for PTSD Retrieved 14 June 2020 <https://maps.org/news/media/8051-press-release-israel-embraces-research-on-mdma-assisted-psychotherapy-for-ptsd>

⁶⁷ **Sessa, B., Highted, L. & Nutt, D.** 2019. A Review of 3, 4- methylenedioxyamphetamine (MDMA)-Assisted Psychotherapy. *Frontiers in Psychiatry*, 10(138), pp. 1-7. DOI: [10.3389/fpsy.2019.00138](https://doi.org/10.3389/fpsy.2019.00138)

⁶⁸ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

⁶⁹ ARTG database <https://www.tga.gov.au/artg>

⁷⁰ Therapeutic Goods (Permissible Ingredients) Determination <https://www.legislation.gov.au/Search/Therapeutic%20Goods%20Permissible%20Ingredients%20Determination>

⁷¹ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

⁷² Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

⁷³ Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

International regulations

- MDMA is listed as a Schedule I drug under the [United Nations 971 Convention on Psychotropic Substances](#)⁷⁴.
- MDMA is listed as a Schedule I (controlled substance) drug under the [U.S Psychotropic Substances Act](#)⁷⁵.
- MDMA is listed as a controlled drug under the [U.K Misuse of Drugs Act 1971](#)⁷⁶.
- MDMA is listed as a Schedule III (controlled substance) drug under the Canadian [Controlled Drugs and Substances Act](#)⁷⁷.
- According to the [New Zealand Medicines and Medical Devices Safety Authority \(MedSafe\)](#)⁷⁸, in New Zealand, MDMA is classified as a class B1 controlled drug (i.e. a drug that poses a high risk of harm if misused)⁷⁹ and there are restrictions on prescribing.

2 Proposed amendments referred for scheduling advice to ACCS #29

2.1 Azoxystrobin

CAS Number:

131860-33-8

Alternative names

Methyl (E)-2-[2-[6-(2-cyanophenoxy)pyrimidin-4-yl]oxyphenyl]-3-methoxyprop-2-enoate (IUPAC name)

Applicant

Australian Pesticides and Veterinary Medicines Authority (APVMA)

Current scheduling

Substance is currently listed in Schedules 5 of the Poisons Standard as follows:

Schedule 5

AZOXYSTROBIN

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AZOXYSTROBIN

⁷⁴ International drug control conventions – Schedules of the Convention of psychotropic substances of 1972, as at 3 November 2020 <https://undocs.org/ST/CND/1/Add.2/Rev.6>

⁷⁵ US controlled substances orange book (Aug 2020) https://www.deadiversion.usdoj.gov/schedules/orangebook/c_cs_alpha.pdf

⁷⁶ UK *Misuse of drugs Act 1971* <https://www.legislation.gov.uk/ukpga/1971/38/schedule/2>

⁷⁷ Canadian Controlled Drugs and Substances ACT <https://laws-lois.justice.gc.ca/eng/acts/c-38.8/page-15.html#h-95603>

⁷⁸ NZ MedSafe <https://www.medsafe.govt.nz/profs/class/classintro.asp>

⁷⁹ *Misuse of Drugs Act 1975* <http://www.legislation.govt.nz/act/public/1975/0116/latest/DLM436190.html>

Proposed scheduling

Schedule 5 – Amend Entry

AZOXYSTROBIN **except in suspension concentrate preparations containing 10 per cent or less azoxystrobin.**

Key uses / expected use

Agriculture, pesticide formulations, to treat a variety of fungal diseases.

Reasons for proposal put forward by the applicant

- The proposal is to amend the Schedule 5 entry for azoxystrobin to include a cut-off for preparations containing 10 per cent or less of azoxystrobin, used for control of a variety of fungal diseases in turf.
- The applicant proposes that, the inclusion of an exemption to unscheduled formulations containing 10 per cent or less of azoxystrobin, will provide an additional choice of available products to consumers.
- In acute toxicity studies in rats, 10 per cent azoxystrobin was of low acute oral toxicity and dermal toxicity. Azoxystrobin was a slight skin and eye irritant in rabbits, but was not a skin sensitiser in guinea pigs (maximisation test).
- The cut off of 10 per cent or less is considered to be supported by the data evaluated by the APVMA, based on the testing results from formulations containing 96g/L of azoxystrobin and 194 g/L triticonazole.
- International restrictions.
 - EU acceptable minimum residue levels (MRL) in or on food and feed of plant and animal origin are between 1×10^{-7} to 0.007%⁸⁰.

Australian regulations

- According to the [TGA Ingredient Database](#)⁸¹, azoxystrobin is not listed as an ingredient in any application.
- As of 04 August 2020, there were no medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)⁸² that contain azoxystrobin as an active ingredient.
- Azoxystrobin is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)⁸³ No.2 of 2020.
- There are no warning statements pertaining to azoxystrobin in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)⁸⁴.
- As of 4 August 2020, there were no reports of adverse events for products containing azoxystrobin as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#)⁸⁵, with no reports where azoxystrobin was the single suspected medicine.

⁸⁰ EU Pesticides MRL <https://echa.europa.eu/legislation-obligation/-/obligations/100.127.964>

⁸¹ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

⁸² ARTG database <https://www.tga.gov.au/artg>

⁸³ Therapeutic Goods (Permissible Ingredients) Determination

[https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB\\$%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20IngredientsRB%20Determination)

⁸⁴ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

⁸⁵ Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

- As of August 2020, there were 92 products containing azoxystrobin listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#)⁸⁶.

International regulations

- Azoxystrobin was first approved by the [United States Environmental Protection Agency \(US EPA in May 1981\)](#)⁸⁷, for use as a pesticide.
- Azoxystrobin was approved for use as a pesticide in the [European Union in January 2012](#)⁸⁸. [The European Chemicals Agency \(ECHA\)](#)⁸⁹ hazard classification and labelling for azoxystrobin identifies it as “*this substance is toxic if inhaled, is very toxic to aquatic life with long lasting effects.*”
- Azoxystrobin is included in the New Zealand (NZ) Environmental Protection Authority’s (EPA) [Inventory of chemicals \(NZIoC\)](#)⁹⁰ with no restrictions.
- As of 5 August 2020, there are 41 insecticide products associated with azoxystrobin registered with [Health Canada](#)⁹¹.

2.2 Triticonazole

CAS Number:

131986-72-7

Alternative names

(RS)-(E)-5-(4-chlorobenzylidene)-2,2-dimethyl-1-(1H-1,2,4-triazol-1-ylmethyl) cyclopentanol (IUPAC name)

Applicant

Australian Pesticides and Veterinary Medicines Authority (APVMA)

Current scheduling

Substance is currently listed in Schedules 5 of the Poisons Standard as follows:

Schedule 5

TRITICONAZOLE

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TRITICONAZOLE

Schedule 5

⁸⁶ Public Chemical Registration Information System Search (PubCRIS) https://portal.apvma.gov.au/pubcris?p_auth=E74TsCid&p_p_id=pubcrisportlet_WAR_pubcrisportlet&p_p_lifecycle=1&p_p_state=normal&p_p_mode=view&p_p_col_id=column-1&p_p_col_pos=2&p_p_col_count=4&pubcrisportlet_WAR_pubcrisportlet_javax.portlet.action=search

⁸⁷ United States Environmental Protection Agency’s (US EPA) Office of Pesticides Programs https://iaspub.epa.gov/apex/pesticides/f?p=CHEMICALSEARCH:3::NO:1.3.31.7.12.25:P3_XCHEMICAL_ID:1282

⁸⁸ EU Pesticides database <https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=984>

⁸⁹ ECHA information card for Azoxystrobin <https://echa.europa.eu/substance-information/-/substanceinfo/100.127.964>

⁹⁰ NZ EPA, NZ Inventory of Chemicals <https://www.epa.govt.nz/database-search/new-zealand-inventory-of-chemicals-nzioc/DatabaseSearchForm/?SiteDatabaseSearchFilters=36&Keyword=azoxystrobin&DatabaseType=NZIOC>

⁹¹ Health Canada, product listings for Azoxystrobin: http://oasdmz01.hc-sc.gc.ca/pi-ip/rba-epa-eng.php?p_actv=AZOXYSTROBIN

Proposed scheduling

Schedule 5 – Amend Entry

TRITICONAZOLE **except** in suspension concentrate preparations containing 20 per cent or less triticonazole.

Key uses / expected use

Agriculture, pesticide formulations, to treat a variety of fungal diseases.

Reasons for proposal put forward by the applicant

- The proposal is to amend the Schedule 5 entry for triticonazole to include a cut-off for preparations containing 20 per cent or less of triticonazole used for control of a variety of fungal diseases in turf.
- The applicant proposes that, the inclusion of an exemption to unscheduled formulations containing 20 per cent or less of triticonazole, will provide an additional choice of available products to consumers.
- In acute toxicity studies in rats, 20 percent triticonazole was of low acute oral toxicity and dermal toxicity. Triticonazole was a slight skin and eye irritant in rabbits, but was not a skin sensitiser in guinea pigs (maximisation test).
- The cut off of 20 per cent or less is considered to be supported by the data evaluated by the APVMA, based on the testing results from formulations containing 96g/L of Azoxystrobin (~10 per cent) and 194 g/L Triticonazole (~20 per cent).
- International restrictions.
 - EU acceptable minimum residue levels (MRL) in or on food and feed of plant and animal origin is 1×10^{-7} %⁹².

Australian regulations

- According to the [TGA Ingredient Database](#),⁹³ triticonazole is not listed as ingredient in any application.
- As of 4 August 2020, there were no medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)⁹⁴ that contain triticonazole as an active ingredient.
- Triticonazole is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)⁹⁵ No.2 of 2020.
- There are no warning statements pertaining to Triticonazole in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)⁹⁶.

⁹² EU Pesticides MRL <https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=pesticide.residue.CurrentMRL&language=EN&pestResidueId=224>

⁹³ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

⁹⁴ ARTG database <https://www.tga.gov.au/artg>

⁹⁵ Therapeutic Goods (Permissible Ingredients) Determination [https://www.legislation.gov.au/Search/Therapeutic%20Goods%20\\$LB\\$Permissible%20Ingredients\\$RB\\$%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LBPermissible%20IngredientsRB%20Determination)

⁹⁶ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

- As of 6 August 2020, there were no reports of adverse events for products containing Triconazole as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#)⁹⁷, with no reports where triconazole was the single suspected medicine.
- As of 6 August 2020, there were 6 products containing Triconazole listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#)⁹⁸.

International regulations

- Triconazole was first approved by the [US EPA in September 2002](#)⁹⁹ for use as pesticide.
- Triconazole was approved for use as a pesticide in the [European Union in January 2007](#)¹⁰⁰. The [European Chemicals Agency \(ECHA\)](#)¹⁰¹ hazard classification and labelling for triconazole identifies it as “*this substance is toxic to aquatic life with long lasting effects.*”
- Triconazole is not included in the New Zealand (NZ) Environmental Protection Authority’s (EPA) [Inventory of chemicals \(NZIoC\)](#)¹⁰².
- As of August 2020, there are 11 insecticide products associated with Triconazole registered with [Health Canada](#)¹⁰³.

3 Proposed amendments referred for scheduling advice to the Joint ACMS-ACCS #26

3.1 Azelaic acid

CAS Number:

123-99-9

Alternative names

Nonanedioic acid

Applicant

Private applicant

⁹⁷ Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

⁹⁸ Public Chemical Registration Information System Search (PubCRIS) https://portal.apvma.gov.au/pubcris?p_auth=E74TsCid&p_id=pubcrisportlet_WAR_pubcrisportlet&p_p_lifecycle=1&p_p_state=normal&p_p_mode=view&p_p_col_id=column-1&p_p_col_pos=2&p_p_col_count=4&pubcrisportlet_WAR_pubcrisportlet_javax.portlet.action=search

⁹⁹ United States Environmental Protection Agency’s (US EPA) Office of Pesticides Programs https://iaspub.epa.gov/apex/pesticides/f?p=CHEMICALSEARCH:3:::NO:1.3.31.7.12.25:P3_XCHEMICAL_ID:4176

¹⁰⁰ EU Pesticides database <https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=2001>

¹⁰¹ ECHA information card for Triconazole <https://echa.europa.eu/substance-information/-/substanceinfo/100.126.137>

¹⁰² NZ EPA, NZ Inventory of Chemicals <https://www.epa.govt.nz/database-search/new-zealand-inventory-of-chemicals-nzioc/DatabaseSearchForm/?SiteDatabaseSearchFilters=36&Keyword=triconazole&DatabaseType=NZIOC>

¹⁰³ Health Canada, product listing for Azoxystrobin <https://pesticide-registry.canada.ca/en/active-ingredient-details.html?q=TRT>

Current scheduling

Azelaic acid is currently in Schedules 2 and 4 of the Poisons Standard as follows:

Schedule 4

AZELAIC ACID **except**:

- a) When included in Schedule 2; or
- b) In preparations containing 1 per cent or less of azelaic acid for non-human use.

Schedule 2

AZELAIC ACID in dermal preparations.

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AZELAIC ACID

Schedule 4
Schedule 2

Proposed scheduling

A request has been made to amend the Poisons Standard as follows:

Schedule 5 – New Entry

AZELAIC ACID for human therapeutic or cosmetic use, **except in preparations for topical use containing 10 per cent or less of azelaic acid.**

Schedule 4 – Amend Entry

AZELAIC ACID **except**:

- a) when included in **Schedule 5** ~~or Schedule 2~~; or
- b) in preparations containing 1 per cent or less of azelaic acid for non-human use.

Schedule 2 – Delete Entry

~~AZELAIC ACID in dermal preparations.~~

Index

AZELAIC ACID

Schedule 5
Schedule 4
~~Schedule 2~~

Key uses / expected use

Medicines, cosmetic, industrial use etc.

Reasons for proposal put forward by the applicant

- Azelaic acid is a naturally occurring dicarboxylic acid produced by *Malassezia furfur* and found in whole grain cereals, rye, barley and animal products. Azelaic acid possesses antibacterial, keratolytic, comedolytic, and antioxidant activity. Azelaic acid is bactericidal

against *Propionibacterium acnes* and *Staphylococcus epidermidis* due to its inhibitory effect on the synthesis of microbial cellular proteins. Azelaic acid also possesses a direct anti-inflammatory effect due to its scavenger activity of free oxygen radical.

- It is used topically to reduce inflammation associated with acne and rosacea.
- A change in scheduling would allow Australian producers to benefit from sales of a more superior ingredient in their product(s), since it is widely used in the UK, US and EU in cosmetic and cosmeceuticals as a functional buffer and masking ingredient, but also has additional performance benefits for the consumer.
- Azelaic acid is found in products sold over the counter in Australia and online by US, UK and EU brands. These brands are able to formulate products using azelaic acid in their cosmetic creams however, Australian producers are not allowed to use azelaic acid in cosmetics and cosmeceuticals.
- Cosmetic chemists can make products using other acids such as lactic acid, salicylic acid, glycolic acid, mandelic acid, tartaric acid, citric acid, ascorbic acid. Azelaic acid use in cosmetics and cosmeceutical products should also be permitted as it is beneficial rather than harmful having excellent anti-inflammatory properties, making it a superior acid choice for use in skincare products.

Australian regulations

- According to the [TGA Ingredient Database](#)¹⁰⁴, azelaic acid is:
 - available as active ingredients in: biologicals, export only, over the counter and 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 31 July 2020, there were 4 medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)¹⁰⁵ that contain azelaic acid as an active ingredient. These include 2 non-prescription medicines.
- Azelaic acid is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)¹⁰⁶ No.2 of 2020.
- The [TGA prescribing medicines in pregnancy database](#)¹⁰⁷ classifies azelaic acid as:

Drug name	Category	Classification Level 1	Classification Level 2	Classification Level 3
Azelaic acid	B1	Drugs used in dermatology	Topical	
<p>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.</p> <p>Studies in animals have not shown evidence of an increased occurrence of foetal damage.</p>				

¹⁰⁴ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

¹⁰⁵ ARTG database <https://www.tga.gov.au/artg>

¹⁰⁶ Therapeutic Goods (Permissible Ingredients) Determination

[https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB\\$%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20IngredientsRB%20Determination)

¹⁰⁷ TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

- There are no warning statements pertaining to azelaic acid in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)¹⁰⁸.
- As of 31 July 2020, there were 3 reports of adverse events for products containing azelaic acid as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#)¹⁰⁹, with 3 reports where azelaic acid was the single suspected medicine.
- As of 31 July 2020, there were no products containing azelaic acid listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#)¹¹⁰.

International regulations

- The [European Chemicals Agency \(ECHA\)](#)¹¹¹ hazard classification for azelaic acid is, 'Warning! According to the classification provided by companies to ECHA in REACH registrations this substance causes serious eye irritation and causes skin irritation.'
- According to the [European Commission database for information on cosmetic substances and ingredients database \(CosIng\)](#)¹¹²:
 - Azelaic acid is approved for use as a buffer and a fragrance.
- In the United States, azelaic acid is registered as an ingredient on the [United States Food and Drug Administration Approved Drug Products Database \(Drugs@FDA\)](#)¹¹³.
- In New Zealand, there are entries for azelaic acid on the [New Zealand Inventory of Chemicals \(NZIoC\)](#)¹¹⁴ (added Dec 2006) and on the [New Zealand Medicines and Medical Devices Safety Authority \(MedSafe\)](#)¹¹⁵ where it is approved for use as a prescription only medicine except for dermal use and a pharmacy only medicine for dermal use.

3.2 2-Hydroxyethyl methacrylate

CAS Number:

868-77-9

Alternative names

2-hydroxyethyl methacrylate, ethylene glycol mono methacrylate, HEMA

Applicant

Private applicant

¹⁰⁸ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

¹⁰⁹ Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

¹¹⁰ Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

¹¹¹ European Chemicals Agency <https://echa.europa.eu/>

¹¹² European Commission database for information on cosmetic substances and ingredients database <https://ec.europa.eu/growth/tools-databases/cosing/>

¹¹³ FDA Approved Drug Products Database <https://www.accessdata.fda.gov/scripts/cder/daf/>

¹¹⁴ New Zealand Inventory of Chemicals (NZIoC) <https://www.epa.govt.nz/database-search/new-zealand-inventory-of-chemicals-nzioc/DatabaseSearchForm/?SiteDatabaseSearchFilters=36&Keyword=acequinocyl&DatabaseType=NZIOC>

¹¹⁵ New Zealand Medicines and Medical Devices Safety Authority (MedSafe)

<https://www.medsafe.govt.nz/profs/class/classintro.asp>

Current scheduling

Hydroxyethyl methacrylate is currently in Schedule 5 of the Poisons Standard as follows:

Schedule 5

2-HYDROXYETHYL METHACRYLATE **except** when included in dental restorative preparations for therapeutic use or in nail preparations when labelled “Avoid contact with skin”.

Appendix E, Part 2

2-HYDROXYETHYL METHACRYLATE

Poison	Standard Statements
2-HYDROXYETHYL METHACRYLATE	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)). E1 (If in eyes wash out immediately with water.), S1 (If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water.)

Appendix F, Part 3

Poison	Warning Statements	Safety Direction
2-HYDROXYETHYL METHACRYLATE	28 ((Over) (Repeated) exposure may cause sensitisation	4 (Avoid contact with skin.)

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2-HYDROXYETHYL METHACRYLATE

Schedule 5

Appendix E, Part 2

Appendix F, Part 3

Proposed scheduling

A request has been made to amend the Schedule 5 entry in the Poisons Standard as follows:

Schedule 5 - Amended entry

2-HYDROXYETHYL METHACRYLATE **except**:

- a) when included in dental restorative preparations for therapeutic use or in nail preparations when labelled “Avoid contact with skin”; or
- b) in other preparations not for human therapeutic or cosmetic use containing 1 per cent or less of 2-hydroxyethyl methacrylate.

Key uses / expected use

Cosmetic, domestic, commercial, medical devices etc.

Reasons for proposal put forward by the applicant

- 2-hydroxyethyl methacrylate is not hazardous to human health at low concentrations in preparations that are not cosmetics or for therapeutic use. It is proposed that a lower limit be added consistent with the entries for methyl- and ethyl-methacrylate to support the supply of products containing the substance at low concentrations without warnings that imply a hazard that does not exist.
- Methyl- and ethyl-methacrylate are listed in Schedules 6 and 5 respectively for preparations containing more than 1 per cent of the substances. However, the lack of a lower limit in the listing for 2-hydroxyethyl methacrylate makes this listing more onerous than those for the related substances that have been acknowledged to be more toxic.
- The proposed change is not expected to have any impact to public health as concentration of 2-hydroxyethyl methacrylate of less than 1 per cent would not cause the preparation in which it is included to be considered hazardous. The change would allow the substance to be used in non-cosmetic and non-therapeutic preparations at low concentrations without precautionary warnings.
- There has been no change in opinion on the toxicity and safety of the substance since it was first considered for scheduling in 2014. The reason for this application is that the listing didn't consider the use of the substance at low concentrations in preparations that are not cosmetics or medicines.
- Noting the delegate's expressed concern with the '*potential use in other product at high concentrations*' in the 2015 decision, the NICNAS IMAP human health Tier II assessment and use of 2-Hydroxyethyl Methacrylate at very low concentrations in certain consumer products, it is appropriate to introduce a lower limit for the Schedule entry for 2-hydroxyethyl methacrylate in line with those for methyl- and ethyl-methacrylate.

Australian regulations

- According to the [TGA Ingredient Database](#)¹¹⁶ 2-hydroxyethyl methacrylate is:
 - not available as active ingredients in any application;
 - available for use as an excipient ingredient in: devices
 - not available as an equivalent ingredient in any application.
- As of 7 August 2020, there were 19 medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)¹¹⁷ that contain 2-hydroxyethyl methacrylate as an ingredient in a medical device.
- 2-hydroxyethyl methacrylate is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)¹¹⁸ No.2 of 2020.
- 2-hydroxyethyl methacrylate is not listed on the [TGA prescribing medicines in pregnancy database](#)¹¹⁹.
- There are no warning statements pertaining to 2-hydroxyethyl methacrylate in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)¹²⁰.

¹¹⁶ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

¹¹⁷ ARTG database <https://www.tga.gov.au/artg>

¹¹⁸ Therapeutic Goods (Permissible Ingredients) Determination

[https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB\\$%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20IngredientsRB%20Determination)

¹¹⁹ TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

¹²⁰ Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

- As of 7 August 2020, there were no reports of adverse events for products containing 2-hydroxyethyl methacrylate as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#)¹²¹.
- As of 7 August 2020, there were no products containing 2-hydroxyethyl methacrylate listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#)¹²².

International regulations

- The [European Chemicals Agency \(ECHA\)](#)¹²³ hazard classification for 2-hydroxyethyl methacrylate is, '*Warning!* According to the harmonised classification and labelling (CLP00) approved by the European Union, this substance causes serious eye irritation, causes skin irritation and may cause an allergic skin reaction.'
- A 2005 Cosmetic Ingredient Review (CIR) report concluded that methacrylate ester monomers are safe to use in nail enhancement products when skin contact is avoided. Products containing these ingredients should be accompanied with directions to avoid skin contact, because of the sensitising potential of methacrylates' (CIR, 2005).¹²⁴
- 2-hydroxyethyl methacrylate is not listed on the [European Commission database for information on cosmetic substances and ingredients database \(CosIng\)](#)¹²⁵.
- In New Zealand, there is an entry for 2-hydroxyethyl methacrylate on the [New Zealand Inventory of Chemicals \(NZIoC\)](#)¹²⁶ (added Dec 2006).

3.3 Magnesium hydroxide

CAS Number: 1309-42-8

Alternative names

Dihydroxy magnesium

Applicant

The Australian Pesticides and Veterinary Medicines Authority (APVMA)

Current scheduling

Magnesium hydroxide is not included in the Poisons Standard.

Proposed scheduling

A request has been made to formally exclude magnesium hydroxide from Scheduling via inclusion in Appendix B.

¹²¹ Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

¹²² Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

¹²³ ECHA Substance Infocard <https://echa.europa.eu/substance-information/-/substanceinfo/100.011.621>

¹²⁴ Final report of the safety assessment of methacrylate ester monomers used in nail enhancement products: <https://online.personalcarecouncil.org/ctfa-static/online/lists/cir-pdfs/pr339.pdf>

¹²⁵ European Commission database for information on cosmetic substances and ingredients database <https://ec.europa.eu/growth/tools-databases/cosing/>

¹²⁶ New Zealand Inventory of Chemicals (NZIoC) <https://www.epa.govt.nz/database-search/new-zealand-inventory-of-chemicals-nzioc/DatabaseSearchForm/?SiteDatabaseSearchFilters=36&Keyword=acequinocyl&DatabaseType=NZIOC>

Key uses / expected use

Pesticide formulation, medicines and medical devices.

Reasons for proposal put forward by the applicant

- APVMA has received an application for registration of an insecticide product containing 60% magnesium hydroxide (as active constituent) in a suspension concentrate formulation for use as an insecticide to control whiteflies, mites, thrips and aphids in vegetable crops.
- Magnesium hydroxide is an inorganic compound with the formulation $Mg(OH)_2$. It occurs naturally in the environment as the mineral 'brucite'. It has many uses including: flame retardants, antiperspirant/deodorant, wastewater treatment, food additive (E528) and in human medicines, orally as an antacid, laxative and tocolytic and dermally for the topical treatment for canker sores.
- Although magnesium hydroxide is an ingredient in a number of veterinary feed additives, it has not been approved by APVMA as an active constituent or listed in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP). The ubiquitous use of magnesium hydroxide under therapeutic conditions, with direct oral and skin exposure, indicate it to be a substance of low toxicological concern and sufficient toxicological data are available to recommend a scheduling decision.
- Magnesium hydroxide is of low oral, dermal and inhalation toxicity and is not an eye or skin irritant or sensitiser. Evidence indicates magnesium salts are neither genotoxic nor carcinogenic and have no effects on fertility, reproduction and development. Observed adverse effects from repeated exposure to high doses are due to an electrolyte imbalance manifested by increased Mg^{2+} / Ca^{2+} blood level ratios. Effects are reversible on cessation of exposure. Exposure to hazardous levels of magnesium hydroxide is unlikely to occur from its use as pesticide. Risks are manageable from appropriate product labelling and adherence to safety directions.
- For the purpose of its use as an active ingredient in agricultural pesticides and/or veterinary feed products, APVMA propose that, based on its toxicological profile, magnesium hydroxide be exempt from Scheduling.

Australian regulations

- According to the [TGA Ingredient Database](#)¹²⁷,
 - Magnesium hydroxide is available for use as an active and excipient ingredient in biologicals, export only, listed medicines, over the counter, prescription medicines and as an excipient in devices. It is not available as a homoeopathic ingredient in listed medicines nor as an equivalent ingredient in any application.
 - Aluminium magnesium hydroxide carbonate is available for use as an excipient ingredient in prescription medicines and is not available as an active or equivalent ingredient in any application.
- As of August 2020, there were 74 medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)¹²⁸ that contain magnesium hydroxide as an active ingredient. These include 13 non-prescription medicines, 59 listed medicines, one medical device and one export only medicine.

¹²⁷ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

¹²⁸ ARTG database <https://www.tga.gov.au/artg>

- According to the [European Commission Cosing database](#)¹³⁶, magnesium hydroxide is used as an absorbent and a buffering agent. As of August 2020, there are no cosmetic or other restrictions on its use.
- Magnesium hydroxide is included in the [New Zealand Inventory of Chemicals \(NZIoC\)](#)¹³⁷ without restriction.

3.4 Tetrahydrofurfuryl alcohol (THFA)

CAS Number:

97-99-4

Alternative names

Oxolan-2-ylmethanol, Tetrahydrofuran-2-yl methanol

Applicant

Australian Pesticides and Veterinary Medicines Authority (APVMA)

Current scheduling

THFA is not currently included in the Poisons Standard.

Proposed scheduling

A request has been made to include THFA in the Poisons Standard as follows:

Schedule 6 – New Entry

TETRAHYDROFURFURYL ALCOHOL, excluding its derivatives.

Key uses / expected use

Cosmetic, agriculture, industrial use, medicines

Reasons for proposal put forward by the applicant

- THFA is approved as an industrial chemical. It is used as a solvent in certain agricultural chemicals. As it is currently unclassified, it does not need to be declared on the product label. Based on the assessment of new agricultural chemicals, the presence of THFA in the formulation is identified during assessment, and suitable product-based safety directions are recommended. However, as the solvent is not declared on the label, there can be challenges for industry and end users in determining the justification for warning statements and personal protective equipment. The inclusion of THFA in a Schedule of the Poisons Standard, with the accompanying requirement to declare it on the label, would assist in this risk communication.
- Internationally, reported uses of THFA in cosmetics include uses as a fragrance ingredient, as a masking agent and as a solvent for nail cleaning products. Commercial uses which have been reported for THFA include use as an adhesive agent or sealant in general

¹³⁶ https://ec.europa.eu/growth/tools-databases/cosing/index.cfm?fuseaction=search.details_v2&id=35096

¹³⁷ NZIoC <https://www.epa.govt.nz/database-search/new-zealand-inventory-of-chemicals-nzioc/view/5520>

manufacturing, as a fuel additive and as a solvent. It forms an intermediate in the production of certain fungicides and pharmaceuticals. It is used as a solvent in a limited number of emulsifiable concentration formulations of agvet products. This last use is anticipated to represent the only likely use with major public exposure, however it is noted that all of the currently registered products are intended for commercial use, without home garden applications.

- THFA is classified as hazardous in the Hazardous Chemical Information System (HCIS) (Safe Work Australia), based on serious eye irritation and reproductive toxicity.

Australian regulations

According to the [TGA Ingredient Database](#)¹³⁸, THFA is:

- available as active ingredients in: biologicals, export only, over the counter and 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 31 July 2020, there were 2 medicines currently active on the [Australian Register of Therapeutic Goods \(ARTG\)](#)¹³⁹ that contain THFA as an ingredient. These include 2 non-prescription medicines.
- THFA is not permitted to be included in listed medicines as it is not included in the [Therapeutic Goods \(Permissible Ingredients\) Determination](#)¹⁴⁰ No.2 of 2020.
- THFA is not listed in the [TGA prescribing medicines in pregnancy database](#)¹⁴¹.
- There are no warning statements pertaining to THFA in the [Therapeutic Goods \(Medicines Advisory Statements\) Specification 2019](#)¹⁴².
- As of 31 July 2020, there were no reports of adverse events for products containing THFA as an active ingredient on the [Database of Adverse Event Notifications \(DAEN\)](#)¹⁴³.
- As of 31 July 2020, there were no products containing THFA listed on the [Public Chemical Registration Information System Search \(PubCRIS\)](#)¹⁴⁴.

International regulations

- The [European Chemicals Agency \(ECHA\)](#)¹⁴⁵ hazard classification for THFA is, 'Danger! According to the harmonised classification and labelling (ATP06) approved by the European Union, this substance may damage the unborn child and is suspected of damaging fertility and causes serious eye irritation. Additionally, the classification provided by companies to ECHA in REACH registrations identifies that this substance may damage fertility or the unborn child'.

¹³⁸ TGA Ingredient Database <https://www.ebs.tga.gov.au/>

¹³⁹ ARTG database <https://www.tga.gov.au/artg>

¹⁴⁰ Therapeutic Goods (Permissible Ingredients) Determination

[https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB\\$Permissible%20Ingredients\\$RB\\$%20Determination](https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LB$Permissible%20IngredientsRB%20Determination)

¹⁴¹ TGA prescribing medicines in pregnancy database <https://www.tga.gov.au/prescribing-medicines-pregnancy-database>

¹⁴² Therapeutic Goods (Medicines Advisory Statements) Specification 2019 <https://www.legislation.gov.au/Details/F2019L00213>

¹⁴³ Database of Adverse Event Notifications (DAEN) <https://apps.tga.gov.au/Prod/daen/daen-entry.aspx>

¹⁴⁴ Public Chemical Registration Information System Search (PubCRIS) <https://portal.apvma.gov.au/pubcris>

¹⁴⁵ ECHA <https://echa.europa.eu/>

- According to the [European Commission database for information on cosmetic substances and ingredients database \(CosIng\)](#)¹⁴⁶:
 - tetrahydrofurfuryl alcohol is approved for use as a solvent and fragrance.
- THFA is not listed on the [United States Food and Drug Administration \(US FDA\) Approved Drug Products Database \(Drugs@FDA\)](#)¹⁴⁷.
- THFA is not listed on [New Zealand Inventory of Chemicals \(NZIoC\)](#)¹⁴⁸.
- THFA is not listed by [Canada's Pest Management Regulation Agency](#)¹⁴⁹.

4 Enquiries

Any questions relating to submissions should be directed by email to medicines.scheduling@health.gov.au (for substances referred to the ACMS or Joint ACCS-ACMS) or chemicals.scheduling@health.gov.au (for substances referred to the ACCS).

¹⁴⁶ Cosing [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/>

¹⁴⁷ FDA approved drugs database <https://www.accessdata.fda.gov/scripts/cder/daf/>

¹⁴⁸ NZIoC <https://www.epa.govt.nz/database-search/new-zealand-inventory-of-chemicals-nzioc/>

¹⁴⁹ Health Canada Pesticide Product Information database <https://pesticide-registry.canada.ca/en/active-ingredient-search.html>