Australian Government
Department of Health, Disability and Ageing
Therapeutic Goods Administration

Notice of final decisions to amend (or not amend) the current Poisons Standard

1 October 2025

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Contents

Notice of final decisions to amend (or not amend) the current Poisons Standard

This web publication comprises:

- the decisions made by a delegate[1] of the Secretary of the Department of Health, Disability and Ageing (the **Delegate**) pursuant to regulation 42ZCZU
- the decisions made by a delegate of the Secretary of the Department of Health and Aged Care (the Delegate) under subsection 52D(2) of the Act
- the reasons for those final decisions, and
- the date of effect of those decisions.

Defined terms

- In this notice the following defined terms are used in addition to those above:
- the *Therapeutic Goods Act 1989* (Cth) (the **Act**)
- the *Therapeutic Goods Regulations 1990* (the **Regulations**)
- the Scheduling Policy Framework 2018 (the **SPF**)
- the Scheduling handbook, Guidance for amending the Poisons Standard (the **Handbook**)
- the Australian Register of Therapeutic Goods (the **Register**) and
- the Therapeutic Goods Administration (the **TGA**).

Note: additional terms are also defined for individual decisions.

[1] For the purposes of s 52D of the *Therapeutic Goods Act 1989* (Cth).

Final decisions on proposed amendments to the current Poisons Standard under regulation 42ZCZU

In my capacity as a delegate of the Secretary for the purpose of regulation 42ZCZU of the Regulations, I have made final decisions under regulation 42ZCZU with respect to the following substances:

- Verdinexor
- Tasipimidine Sulfate
- Chlorthal-dimethyl
- Atinvicitinib
- 1-amino cyclopropane-1-carboxylic acid
- (Z,E)-7,9,11-dodecatrienyl formate
- Fluticasone propionate

Final decision in relation to verdinexor

Final decision

Pursuant to regulation 42ZCZU of the Regulations, a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to verdinexor as follows.

Schedule 4 – New Entry

VERDINEXOR

Index – New Entry

VERDINEXOR

Schedule 4

Materials considered

In making this final decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to verdinexor (the **Application**)
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance.
- Pursuant to paragraph 52E(2)(a) of the Act, the SPF, and
- The Handbook.

Reasons for the final decision (including findings on material questions of fact)

The Application is to amend the current Poisons Standard to create a new entry for verdinexor as a Prescription animal remedy (Schedule 4). Verdinexor is the active constituent for 4 new veterinary medicines for the treatment of canine large B-cell lymphoma and is not listed in the current Poisons Standard.

In determining that this matter will be a delegate-only decision I have taken into account the information provided in the Application and the matters outlined under s 52E of the Act and the SPF. My reasons for making the final decision follow.

In relation to s 52E(1)(a) and (b) of the Act, I note that verdinexor medicines will be used to treat canine lymphoma. Verdinexor is a reversible, selective inhibitor of Chromosome Region Maintenance 1 (CRM1) protein that shuttles tumour suppressor proteins and growth regulatory factors between the nucleus and cytoplasm. CRM1 is overexpressed in tumour cells and verdinexor inhibition of CRM1 activity causes semi-selective cytotoxicity and killing of tumour cells. Verdinexor congener selinexor, a human therapeutic with an almost identical mode of action, is currently listed in Schedule 4.

Regarding s 52E(1)(d) of the Act, verdinexor will be is presented as bi-convex, oval tablets available in three doses, 2.5 mg, 10 mg and 22.5 mg. The medicine will be available in packs on 50 tablets in wide mouth, high-density polyethylene bottles equipped with child resistant, induction sealed caps. The maximum dose rate is 1.75 mg/kg body weight (bw), administered twice per week with 3 days between doses.

In relation to s 52E(1)(c) of the Act, the APVMA provided limited toxicology data. In a single-dose toxicity study of Selinexor, no deaths were observed in rats at the highest tested dose of 500 mg/kg bw. Sub-chronic toxicity studies in healthy dogs noted treatment-related adverse effects at all doses of verdinexor studied. Verdinexor was negative in a limited battery of tests for genotoxicity and did not show any neurotoxicity in rats (oral acute dose of 15 mg/kg bw). However, impairment of male and female fertility in dogs is suggested and adverse effects on embryofetal development, including malformations and embryo lethality, were observed in rats at exposure levels consistent with the doses recommended for treating dogs.

The limited toxicity data does not preclude further consideration of verdinexor as a veterinary medicine. Verdinexor tablets will be administered orally to dogs by their owners under veterinarian oversight. The APVMA has undertaken a Human Health Risk Assessment and concluded that the risks to human health and safety posed by this substance are acceptable. After considering the toxicological profile, likely pathways of human exposure to verdinexor and control measures (presentation, child-proof packaging, proposed directions for use), I agree with the APVMA's conclusion. One Phase I clinical trial study in humans did not identify any adverse effects in healthy adults from 40 mg verdinexor (tablets) ingested twice in a week with one rest day in between.

In relation to s 52E(1)(e) of the Act, I am satisfied the potential for misuse or abuse of verdinexor is limited. In forming this view, I have considered that there is no known dependency potential and the low abuse potential of verdinexor and other inhibitors of CRM1 such as selinexor (a prescription-only medicine for human therapeutic use).

Verdinexor will be used to treat lymphoma in dogs which requires veterinary diagnosis and intervention (Schedule 4, factor 1). Adverse effects such as haematological changes will require laboratory confirmation. It is possible that both the treatment frequency and the dose level may require adjustment after commencement of treatment (Schedule 4, factor 2). The margin of safety is at least 2.5 times the therapeutic dose and the maximum tolerated dose in dogs. But there is no antidote and in case of overdose; dogs need to be treated symptomatically and will require veterinary intervention to minimise the risk of using the substance (Schedule 4, factor 6). Verdinexor is not available in Australia and is currently undergoing Phase 1 trials in humans to evaluate the safety and tolerability. International experience of using verdinexor is also limited as it is only conditionally approved in the USA since 2021 and yet to be approved by other countries with comparable regulations (Schedule 4, factor 8).

Based on the above considerations and the information provided in the application, I have decided to amend the current Poisons Standard in the manner laid out above. The proposed amendment was not referred to an expert advisory committee.

Implementation date

1 October 2025.

Final decision in relation to tasipimidine sulfate

Final decision

Pursuant to regulation 42ZCZU of the Regulations, a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to tasipimidine sulfate as follows.

Schedule 4 – New Entry

TASIPIMIDINE SULFATE

Index – New Entry

TASIPIMIDINE SULFATE

Schedule 4

Materials considered

In making this final decision, the Delegate considered the following material:

The application to amend the current Poisons Standard with respect to tasipimidine sulfate (the **Application**)

- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance.
- Pursuant to paragraph 52E(2)(a) of the Act, the SPF, and
- The Handbook.

Reasons for the final decision (including findings on material questions of fact)

The Application is to amend the current Poisons Standard to create a Prescription animal remedy (Schedule 4) entry for tasipimidine sulfate. Tasipimidine sulfate is the active ingredient of a currently unregistered veterinary medicine and is not included in the current Poisons Standard.

In determining that this matter will be a delegate-only decision I have taken into account the information provided in the Application and the matters outlined under s 52E of the Act and the SPF. My reasons for making the final decision follow.

Tasipimidine sulfate is a potent selective alpha-2A adrenoceptor agonist that inhibits the release of noradrenaline from noradrenergic neurons. Noradrenaline plays an essential role in the regulation of arousal, attention, cognitive function, and stress reactions. In relation to s 52E(1)(a) and (b) of the Act, tasipimidine sulfate is used for alleviation of situational anxiety and fear in dogs triggered by noise or owner departure. In addition, tasipimidine can cause sedation, analgesia and lowering of heart rate, blood pressure and rectal temperature. Tasipimidine sulfate is used in the short term under veterinary clinic setting or home setting with veterinarian oversight.

Regarding (d) of the Act, I note that the tasipimidine medicine will be available as oral solution for dogs. A tasipimidine medicine, Tessie 0.3 mg/mL Oral Solution for Dogs is currently registered in the EU and UK. The product is orally administered using a syringe at a dose of 0.1 mL/kg bw (equivalent to 30 µg/kg bw) and is available in 15 mL clear glass bottles with a polypropylene child-resistant closure.

With regard to s 52E(1)(c) of the Act, limited pharmacological and toxicological data were provided by the applicant. The European Medicines Agency's (EMA) has also assessed the safety of a 0.3 mg/mL Oral Solution of the substance for dogs.[2] From a GLP non-compliant 7-day maximum tolerated dose study, a LOAEL of 5 mg/kg bw/day was established in rats. No tasipimidine-associated deaths were observed in dogs (modest oral bioavailability species) following single doses of up to 2 mg/kg bw. However, in a maximum tolerated dose study in dogs, deaths occurred in both test animals dosed at 1 mg/kg bw/day for 3 days. From repeated dose 28-day oral toxicity studies a LOAEL of 1.5 mg/kg bw/day was established for rats while the LOAEL was 0.03 mg/kg bw/day in dogs. Oral bioavailability is considered to be very poor in rats when compared with dogs. No other repeated dose toxicity studies (short, sub-chronic or long term) were provided, including neurotoxicity, immunotoxicity, reproductive or carcinogenicity studies.

Tasipimidine is unlikely to be genotoxic as demonstrated by adequate *in vitro* assays. Tasipimidine caused an increase in post-implantation loss and had an adverse effect on foetal body weights in a developmental study in rats (low oral bioavailability species), at doses that resulted in maternal pharmacologically mediated sedation.

I also note that the product poses a slight risk of eye irritation, may cause hypersensitivity (allergy) but is unlikely to be a skin irritant or sensitiser. Currently, tasipimidine is being trialled for its safety and the treatment of insomnia in humans.[3]

As exposure to tasipimidine may cause adverse effects such as sedation, respiratory depression, bradycardia and hypotension, care must be taken to avoid oral ingestion and skin contact including hand-to-mouth contact. Children also should be prevented from accessing the product. The APVMA has undertaken a Human Health Risk Assessment for the substance, tasipimidine sulfate, and the proposed product, and concluded that human health risks are acceptable when used in accordance with the directions for use and adhering to the recommended safety directions. The EMA's Committee for Medicinal Products for Veterinary Use also concluded that the benefit-risk balance is positive and approved the market authorisation of tasipimidine sulfate.

Use of tasipimidine requires a correct veterinary diagnosis of separation/situational anxiety in dogs (Schedule 4, factor 1). It is a respiratory depressant and therefore should be used only after a veterinary evaluation and with clinical judgement, particularly in dogs with pre-existing cardiovascular respiratory conditions. In clinical trials with dogs, lethargy and emesis were very common adverse reactions (more than 1 in 10 treated animals). Other common adverse reactions (more than 1 but less than 10 animals in 100 animals treated) included sedation, behavioural disorders (barking, avoidance, disorientation, increased reactivity), ataxia, diarrhoea, urinary incontinence, nausea and gastroenteritis. Tasipimidine also induced mild to moderate cardiovascular depression in healthy dogs. Therefore, veterinary intervention may be required in treating such adverse effects or potential overdoses requiring antidote treatment (Schedule 4, factor 2). Further, there is limited experience in the use of tasipimidine for separation/situational anxiety disorders in dogs (Schedule 4, factor 8).

In relation to s 52E(1)(e) of the Act, given that tasipimidine is an alpha-2A agonist sedative/amnestic, I acknowledge that the potential for misdirection for drug abuse. This moderate propensity for misuse, or abuse (Schedule 4, factor 3) can be minimised by limiting its availability through Schedule 4 classification for veterinary use only. Overall, these findings consistently meet the Schedule 4 criteria based on their toxicity profile, proposed use, pharmacological effects and potential for misuse.

Based on the above considerations and the information provided in the application, I have decided to amend the current Poisons Standard in the manner laid out above. The proposed amendment was not referred to an expert advisory committee.

[2] CVMP assessment report for Tessie (EMEA/V/C/005427/0000)

[3] Study Details | NCT06956495 | Efficacy and Tolerability of Tasipimidine in Sleepless Patients | ClinicalTrials.gov

Implementation date

1 October 2025

Final decision in relation to chlorthal-dimethyl

Final decision

Pursuant to regulation 42ZCZU of the Regulations, a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to chlorthal-dimethyl as follows.

Schedule 5 – Delete Entry

~~CHLORTHAL-DIMETHYL~~

Schedule 7 – New Entry

CHLORTHAL-DIMETHYL

Index – Amend Entry

CHLORTHAL-DIMETHYL

Schedule ~~5~~7

Materials considered

In making this final decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to chlorthal-dimethyl (the **Application**)
- Subsection 52E(1) of the Therapeutic Goods Act 1989, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; and (d) the dosage, formulation, labelling, packaging and presentation of a substance
- Pursuant to paragraph 52E(2)(a) of the Act, the SPF, and
- The Handbook.

Reasons for the final decision (including findings on material questions of fact)

This proposal is to amend the current Poisons Standard to reschedule chlorthal-dimethyl from a Caution (Schedule 5) substance to a Dangerous poison (Schedule 7). This is because of the risks of serious injury or illness to unborn children, including potential thyroid hormone disruption leading to irreversible developmental and neurological impairments from chlorthal-dimethyl.

In determining that this matter will be a delegate-only decision I have taken into account the information provided in the Application and the matters outlined under s 52E of the Act and the SPF. My reasons for making the final decision follow.

Chlorthal-dimethyl, also known as dimethyl tetrachloroterephthalate (DCPA), dacthal, or chlorthal-methyl, is a pre-emergent herbicide classified under the phthalic acid group. Chlorthal-dimethyl is used to inhibit the growth of germinating seeds. However, the exact mode of herbicidal mechanism is unclear.

In relation to s 52E(1)(a) of the Act, I note that the United States Environmental Protection Agency (US EPA) issued an emergency order on 7 August 2024 to ban all use or sale of products containing

chlorthal-dimethyl.[4] The US EPA found a risk of thyroid hormone changes particularly in the unborn children of pregnant women who apply chlorthal-dimethyl or are bystanders or enter treated fields after the substance has been applied. The New Zealand EPA also issued red alert on 22 August 2024 following this matter. On 10 October 2024, the APVMA cancelled the registration of 12 agricultural products containing chlorthal-dimethyl with immediate effect.

Regarding s 52E(1)(b) and (d) of the Act, the cancelled products contained 750-900 g/kg of chlorthal-dimethyl in water-dispersible granule formulation. These products were intended to control a range of weeds in certain vegetable crops, strawberry, cotton, lucerne, perennial grass crops, lawns and ornamentals. The recommended application rate was 5-12.5 kg/ha, diluted in at least 450 L of water and applied as a spray.

In relation to s 52E(1)(c) of the Act, the APVMA provided a consolidated toxicology summary for chlorthal-dimethyl. Chlorthal-dimethyl has low acute oral, dermal and inhalational toxicity (LD_{50} >5,000 mg/kg bw in rats, LD_{50} >2,000 mg/kg bw in rabbits and 4 h LC_{50} >45,000 mg/m^3, respectively). Based on animal studies, it is a slight eye irritant and moderate skin irritant in rabbits, but not a skin sensitiser in guinea pigs. Chlorthal-dimethyl is unlikely to be genotoxic and teratogenic as demonstrated by an adequate range of assays, both in *vitro* and *in vivo*.

Although chlorthal-dimethyl exhibits low acute toxicity consistent with Schedule 5 factors, recent evidence from a comparative thyroid assay indicates developmental toxicity. By day 20 of gestation of rat foetuses, doses ≥1.0 mg/kg bw/day caused a 35-52% reduction in triiodothyronine (T3) and a 29-66% reduction in thyroxine (T4). These adverse effects are relevant to humans, as rats are established models for assessing thyroid-related developmental impacts. Disruption of thyroid hormones during gestation can lead to low birth weight and irreversible, life-long impacts to unborn children, including impaired brain development and motor function. I also note the revised Acceptable Daily Intake (ADI) of 0.001 mg/kg bw/day, derived from a NOAEL of 0.1 mg/kg bw/day.[5] Considering the significant risks of irreversible toxicity in children and the potential serious harm at low exposure levels, chlorthal-dimethyl meets the Schedule 7, Scheduling factors 2 and 4.

The APVMA has reassessed the risks from chlorthal-dimethyl and considers that dermal, ocular, and inhalation exposure to chlorthal-dimethyl can occur at multiple stages for workers handling chlorthal-dimethyl products, workers re-entering treated areas, and children playing on treated turf. Chlorthal-dimethyl dust may form during transport and pouring creating a risk of inhalation and accidental eye contact, particularly in the event of spills or during spray mix preparation. When the product is applied as a spray, exposure to the diluted solution, containing up to approximately 28% product, may occur through dermal, ocular, and inhalation routes. Remodelling of worker exposure scenarios demonstrated that the resulting margins of exposure (MOE) levels were unacceptable (<100) in all registered mixing, loading and application situations as well as during post-application activities following use on turf. The APVMA further concluded that compliance with current label directions cannot prevent unacceptable exposure, and additional mitigation measures would not reduce the risk to an acceptable level i.e. risk of injury in handling, storage and use cannot be mitigated through packaging and label warnings including strong label warnings, extensive safety directions and child-resistant packaging (Schedule 5, factor 4 and Schedule 6, factor 3).

Based on the above considerations and the information provided in the application, I have decided to amend the current Poisons Standard in the manner laid out above. The proposed amendment was not referred to an expert advisory committee. In view of the APVMA and other international regulators cancellation of all products containing chlorthal-dimethyl, this scheduling decision will be implemented immediately.

Implementation date

1 October 2025

[4] Pesticides; Emergency Order Suspending the Registrations of All Pesticide Products Containing Dimethyl Tetrachloroterephthalate (DCPA); accessed 30 August 2025.

[5] Agricultural and veterinary chemicals, APVMA Special Gazette, 10 October 2024; accessed 30 August 2025.

Final decision in relation to 1-aminocyclopropane-1-carboxylic acid

Final decision

Pursuant to regulation 42ZCZU of the Regulations, a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to 1-aminocyclopropane-1-carboxylic acid as follows:[6]

Schedule 5 – New Entry

1-AMINOCYCLOPROPANE-1-CARBOXYLIC ACID **except** in plant growth preparations containing 40% or less of 1-aminocyclopropane-1-carboxylic acid.

Index – New Entry

1-AMINOCYCLOPROPANE-1-CARBOXYLIC ACID
Schedule 5

Materials considered

In making this final decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to 1-aminocyclopropane-1-carboxylic acid (the **Application**)
- Subsection 52E(1) of the Act, in particular (a) risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters that the Secretary considers necessary to protect public health
- Pursuant to paragraph 52E(2)(a) of the Act, the SPF
- The Handbook.

Reasons for the final decision (including findings on material questions of fact)

The Application is to amend the current Poisons Standard to create an entry for 1-aminocyclopropane-1-carboxylic acid (ACC) as a Caution (Schedule 5) substance, exempting plant growth preparations containing 40% or less of ACC. ACC is the active ingredient in products used for agricultural purposes and is not listed in the current Poisons Standard.

In determining that this matter will be a delegate-only decision I have considered the information provided in the Application, and the matters outlined under s 52E of the Act and the SPF. My reasons for making the final decision follow.

ACC is the direct precursor of the plant hormone ethylene, which is essential for regulating a wide range of growth and developmental processes in plants, including seed germination, fruit ripening, leaf and flower senescence, and abscission.

In relation to s 52E(1)(a) and (b) of the Act, ACC is considered to pose low acute and sub-chronic hazards, with no significant effects on human health. The risk of adverse health outcomes associated with the intended product are also regarded as negligible. The formulated product is intended for professional use to induce crop thinning in apple, nectarine, peach, and plum orchards.

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

Although ingestion of ACC residues from treated fruit is possible, the associated human health risk is considered negligible due to its low toxicity, infrequent use, and rapid degradation (to ethylene) following application. Furthermore, ACC is a naturally occurring compound found in plant tissues and commonly present in the human diet. The proposed product will provide growers with an additional product option and help extend the application window for apples, nectarines, peaches and plums. It represents an alternative to existing chemical thinners. While its introduction may slightly reduce the use of current products, it is unlikely to fully replace any of them.

Regarding s 52E(1)(c) of the Act, the Australian Pesticides and Veterinary Medicines Authority (APVMA) has undertaken a Human Health Risk Assessment (HHRA) for both ACC (the active ingredient) and the formulated product. The findings of the toxicological studies evaluated indicate that the proposed product has low acute oral, dermal and inhalational toxicity and is neither an eye nor skin irritant or sensitiser. The repeat dose toxicity profile for ACC does not indicate any specific organ toxicity. ACC was not mutagenic or clastogenic in vitro and was not considered to be either a developmental of reproductive toxin. No neurological effects were seen in functional observation battery (FOB) studies undertaken in short-term and sub-chronic studies. Chronic and/or carcinogenicity studies were not carried out and not considered to be required by the US EPA or Health Canada, which is consistent with the APVMA policy for biological chemicals of low repeat dose sub-chronic toxicity or genotoxicity.

In accordance with paragraph 52E(1)(d) of the Act, I note that ACC is the active ingredient of a product yet to be registered. The proposed water-soluble granular formulation will be supplied in 500 g to 50 kg HDPE containers. The product is intended for professional application as a foliar spray, using either orchard airblast or ground boom equipment. I have considered that the APVMA has conducted a user risk assessment, resulting in the inclusion of appropriate safety directions on the product label. I am satisfied that human health exposure risks (of the intended product containing ACC) are acceptable when used in accordance with the directions for use and adherence to the recommended safety directions.

With regards to s 52E(1)(e) of the Act, ACC exhibited antidepressant and anxiolytic effects in animal model studies. It showed concentration-dependent agonist and antagonist activity at *N*-methyl-D-aspartate (NDMA) receptors within the mammalian central nervous system.[7] However, potential central nervous system effects were not addressed in the evaluations of ACC conducted by the US EPA and Health Canada. No data is available regarding its use as a human therapeutic agent or dietary supplement. ACC is also a naturally occurring chemicals found in plant-derived foods. Given its formulation in granular products, the likelihood of dependency, abuse, misuse, or diversion for illicit purposes is considered minimal, as extraction and purification would be required.

With regards to s 52E(1)(f) of the Act, the product is intended for professional use only. Therefore, risks from use are not relevant for the general public. Occupational risk management measures, including first aid instructions and safety directions, restraints/restrictions and re-entry statements have been established and will be required on the product label by the APVMA.

I am satisfied that that the proposed use pattern of ACC, along with the label safety directions recommended by APVMA, effectively mitigates potential adverse effects, resulting in a negligible risk from product exposure. I note that similar outcomes were observed by US EPA and Health Canada. I have considered the information provided on 1-aminocyclopropane-1-carboxylic acid by the APVMA to be sufficient for the purpose of scheduling.

Based on the above considerations and the information provided in the application, I have decided to amend the current Poisons Standard in the manner laid out above. I consider the toxicity profile of ACC to be consistent with a Schedule 5 classification, based on its slight irritant properties. Exemption is considered justified for preparations containing 40% or less of ACC, as potential adverse effects from exposure are negligible when adhering to the label safety directions recommended by APVMA. The proposed amendment was not referred to an expert advisory committee.

[7] Trullas R, Skolnick P. Functional antagonists at the NMDA receptor complex exhibit antidepressant actions. European journal of pharmacology. 1990 Aug 21;185(1):1-0. DOI: doi.org/10.1016/0014-2999(90)90204-J

Implementation date

1 October 2025

Final decision in relation to (Z,E)-7,9,11-dodecatrienyl formate

Final decision

Pursuant to regulation 42ZCZU of the Regulations, a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to (Z,E)-7,9,11-dodecatrienyl formate as follows:[8]

Schedule 6 – New Entry

(Z,E)-7,9,11-DODECATRIENYL FORMATE for agricultural use **except** when enclosed in an aerosol releasing device which in normal use prevents access to its contents.

Index – New Entry

(Z,E)-7,9,11-DODECATRIENYL FORMATE
Schedule 6

Appendix B, clause 3 – Delete Entry

~~LEPIDOPTEROUS SEX PHEROMONES~~

Materials considered

In making this final decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to (Z,E)-7,9,11-dodecatrienyl formate (the **Application**)
- Subsection 52E(1) of the Act, in particular (a) risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters that the Secretary considers necessary to protect public health
- Pursuant to paragraph 52E(2)(a) of the Act, the SPF
- The Handbook.

Reasons for the final decision (including findings on material questions of fact)

The Application is to amend the current Poisons Standard to create an entry for (Z,E)-7,9,11-dodecatrienyl formate as a Poisons (Schedule 6) substance due to its moderate eye irritation and skin sensitisation properties and to delete the Appendix B entry for lepidopterous sex pheromone.

Lepidopteran sex pheromones (aldehydes, ketones and acetates) are currently considered substances that do not require control by scheduling through an entry in Appendix B of the Poisons

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

Standard. In 1990, the Drugs and Poisons Scheduling Committee decided to include all straight chain (C10-C20) lepidopteran sex pheromones in Appendix B. However, this decision appears to have included pheromones that pose a hazard due to their slight to moderate eye irritation and moderate skin sensitisation potential.

In determining that this matter will be a delegate-only decision I have taken into account the information provided in the Application, and the matters outlined under s 52E of the Act and the SPF. My reasons for making the final decision follow.

In relation to s 52E(1)(a) of the Act, I note (Z,E)-7,9,11-dodecatrienyl formate is a synthetic insect pheromone that mimics sex pheromone produced by the female carob moth (*Ectomyelois ceratoniae*).[9] It is commercially used as an agricultural bio-pesticide in almond and other nut tree crops to interfere with mating behaviour. Due to its mode of action, (Z,E)-7,9,11-dodecatrienyl formate offers a favourable addition to current insect pest management (IPM) strategies, in combatting the development of insect resistance from repeated use of insecticides. Acute and sub-chronic hazards of arthropod pheromones are low and indicate these compounds have no significant human health effects. The risk of adverse health outcomes associated with the use of (Z,E)-7,9,11-dodecatrienyl formate as a biopesticide in the proposed aerosol emitting device is also negligible. Treatment is unlikely to result in any residues in food products, due to the fact that product is not applied directly to tree foliage or nuts.

Regarding paragraphs 52E(1)(b) and (d) of the Act, the formulated product will be available in a ready to use aerosol dispenser, for use in mating disruption of the carob moth in tree nuts orchards. The intended product is designed for professional use only and will be deployed via remotely operated aerosol canisters, each with a weight of 400 grams. A single application per crop season is sufficient to disrupt the pest's life cycle and each season. Treatment should commence prior to the onset of moth mating activity and continue through to post-harvest to ensure effective control.

With regards to paragraph 52E(1)(c) of the Act, I note that the application provided toxicology information for (Z,E)-7,9,11-dodecatrienyl formate (the active ingredient). (Z,E)-7,9,11-dodecatrienyl formate has low acute oral, dermal and inhalational toxicity. It is a moderate eye irritant and skin sensitiser. No genotoxicity studies have been submitted for (Z,E)-7,9,11-dodecatrienyl formate, but other similar straight chain C10-C20 pheromone acetates have been shown to be non-genotoxic.

No repeat-dose study data were available for the active ingredient, however, data available for other insect pheromones indicate that the hazards from repeated exposure are expected to be low. Exposure to the proposed product during use is unlikely due to its method of application. Also, residues in nuts from treated trees are unlikely. The APVMA considered the toxicity profile of (Z,E)-7,9,11-dodecatrienyl formate is consistent with a Schedule 6 classification, based on its acute hazards. However, as the product is enclosed in a device (aerosol canister), which, in normal use, prevents access to its contents, risk from use is negligible, an exception from scheduling is considered justified for the intended product.

In consideration of the toxicity information presented in the HHRA, the proposed usage pattern of (Z,E)-7,9,11-dodecatrienyl formate and the recommended label statements, I am satisfied that the risk of (Z,E)-7,9,11-dodecatrienyl formate associated adverse effects can be adequately mitigated and (Z,E)-7,9,11-dodecatrienyl formate containing products can be used safely in agricultural applications by adherence to product label instructions. I note that products containing (Z,E)-7,9,11-dodecatrienyl formate applied using the specified devices effectively reduce human exposure and therefore may be exempted from the labelling requirements outlined in Schedule 6.

Due to the physicochemical properties of the substance, specifically its low molecular weight and high volatility, and considering the intended use pattern of the product, potential dermal and inhalation exposure is expected to be negligible. These characteristics significantly limit the likelihood of systemic absorption under its professional use pattern.

[9] Todd, J.L., Millar, J.G., Vetter, R.S & Baker, T.C. Behavioral and electrophysiological activity of (Z, E)-7,9,11-dodecatrienyl formate, a mimic of the major sex pheromone component of carob moth,Ectomyelois ceratoniae (1992). Journal of Chemical Ecology 18, 2331–2352. link.springer.com/article/10.1007/BF00984953#citeas

I have considered the US EPA registered (Z,E)-7,9,11-dodecatrienyl formate as a pesticide under the Federal Insecticide, Fungicide, and Rodenticide Act. For the approval of (Z,E)-7,9,11-dodecatrienyl formate in USA, the US EPA waived the requirements for toxicokinetic and metabolism data, as well as repeat dose toxicity studies for reproductive, developmental, and carcinogenicity endpoints for lepidopterous sex hormones. This decision was based on the substance's low mammalian toxicity and a well-documented history of safe use for structurally and functionally similar pheromones. The US EPA consider Straight Chain Lepidopteran Pheromones (SCLP) act through a non-toxic mechanism and exhibit low human health hazard.

In relation to paragraph 52E(1)(e) of the Act, I am satisfied that the potential for misuse or abuse of (Z,E)-7,9,11-dodecatrienyl formate is minimal. It is specifically targeted to its intended pest and demonstrates low mammalian toxicity. There is no evidence or concern regarding dependency, abuse, misuse, or diversion for illicit purposes.

Regarding paragraph 52E(1)(f) of the Act, the intended product is for professional use only and will be deployed via remotely operated aerosol canisters. Given the minimal likelihood of farm worker exposure due to the proposed product's application method, the APVMA recommended appropriate first aid instructions and safety directions along with other safety precautions for the label. Additionally, a label signal header may be recommended upon its registration.

(Z,E)-7,9,11-dodecatrienyl formate is the second insect sex pheromone which has been considered for scheduling after a final decision was made for the arthropod sex pheromone, rescalure, in January 2022. The inclusion of multiple sex pheromone substances in Schedules of the Poisons Standard means that it is no longer appropriate to retain the current Appendix B entry excluding lepidopterous sex pheromones. Lepidoptera is an Order within the Class Insecta and Phylum Arthropoda. Lepidoptera is the second-largest insect order and includes butterflies and moths. Therefore, I have decided to delete the Appendix B entry for lepidopterous sex pheromones. This will not change the scheduling of other lepidopterous sex pheromones that may be in use – they will continue to be unscheduled. However, it will ensure there is no ambiguity regarding the scheduling of (Z,E)-7,9,11-dodecatrienyl formate and rescalure.

Based on the above considerations and the information provided in the application, I have decided to amend the current Poisons Standard regarding (Z,E)-7,9,11-dodecatrienyl formate in the manner laid out above. This amendment was not referred to an expert advisory committee for advice.

Implementation date

1 October 2025

Final decision in relation to Atinvicitinib

Final decision

Pursuant to regulation 42ZCZU of the Regulations, a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to atinvicitinib as follows:[10]

Schedule 4 – New Entry

ATINVICITINIB

Index – New Entry

ATINVICITINIB
Schedule 4

Materials considered

In making this final decision, the Delegate considered the following material:

1. The application to amend the current Poisons Standard with respect to atinvicitinib (the **Application**)
2. Subsection 52E(1) of the Act, in particular (a) risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters that the Secretary considers necessary to protect public health
3. Pursuant to paragraph 52E(2)(a) of the Act, the SPF and
4. The Handbook.

Reasons for the final decision (including findings on material questions of fact)

The Application is to amend the current Poisons Standard to create a new entry for atinvicitinib as a Prescription animal remedy (Schedule 4). Atinvicitinib is an active ingredient for a not yet registered veterinary medicine and is not listed in the current Poisons Standard.

In determining that this matter will be a delegate-only decision I have considered the information provided in the Application, and the matters outlined under s 52E of the Act and the SPF. My reasons for making the final decision follow.

Atinvicitinib belongs to a group of chemicals called Janus Kinase (JAK) inhibitors. These enzymes, JAK1, JAK2, JAK3, and TYK2, play important roles in cell growth and immune system function. Atinvicitinib is a highly selective JAK1 inhibitor that disrupts key signalling pathways associated with pruritus, inflammation, and allergic reactions. Lab tests studies indicate that it predominantly targets JAK1, exhibiting greater inhibitory activity on interleukin 6 (IL-6) signalling compared to JAK2-mediated pathways.

In accordance with paragraphs 52E(1)(a) and (b) of the Act, I note that atinvicitinib is the active ingredient in several veterinary medicines not yet registered in Australia. It is intended for the treatment of pruritus associated with allergic and atopic dermatitis in dogs. The safe use of the product during pregnancy, lactation, or for dogs intended for breeding has not been evaluated. Veterinarians

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

must diagnose these conditions and identify any underlying causes or complications, which may require further investigation and additional treatment (Schedule 4, scheduling factors 1 and 2).

In making my decision I have considered the European Committee for Veterinary Medicinal Products (CVMP) guidelines. The CVMP supports marketing authorisation of atinvicitinib containing products citing a positive benefit-risk balance that there were no serious adverse events reported during field studies. The common adverse events were emesis, diarrhoea, lethargy, and decreased appetite. These adverse events were mild and self-resolving. The concurrent use of atinvicitinib with glucocorticoids, cyclosporine, or other systemic immunosuppressants commonly used to treat allergic or atopic dermatitis requires monitoring by a veterinary practitioner (Schedule 4, scheduling factor 6). Atinvicitinib induces immunosuppression as part of its pharmacological action, potentially increasing susceptibility to infections. Therefore, atinvicitinib should not be used in dogs with serious infections (Schedule 4, scheduling factor 4).

With regard to s 52E(1)(c) of the Act, I note that the Application provided toxicology information comprising of acute toxicity studies, pharmacokinetic/pharmacodynamic studies, subacute, sub-chronic repeat dose oral and dermal toxicity studies, genotoxicity studies, developmental studies, and other supporting information. No long-term repeat dose toxicity studies, carcinogenicity studies or reproductive toxicity, neurotoxicity and immunotoxicity studies were provided.

The findings of the toxicology studies for atinvicitinib indicate that the substance has low acute oral toxicity. Other studies indicate that it is not neurotoxic or genotoxic and unlikely to be a carcinogen. In repeated-dose oral or dermal toxicity studies with atinvicitinib in rats, the key effect was observed in the haematological/clinical chemistry parameters, reduced sperm count or motility and reductions in spleen, thymus, and testes weights. These effects correlated with a decreased cellularity in thymus, spleen, bone marrow and peripheral (mesenteric and axillary) lymph nodes on microscopic examination and lower white blood cell counts in haematology investigations. The testicular weight reductions and effects on sperm counts were not associated with any gross and histopathology observations.

No acute inhalation toxicity studies were submitted for atinvicitinib. However, this was deemed acceptable based on its formulation type and intended use. Atinvicitinib did not cause skin or eye irritation and was not found to be a skin sensitiser in mouse studies. The estimated acute toxicity data indicate that the formulated product for dogs has low acute toxicity via oral, dermal, and inhalation routes. It does not cause eye or skin irritation and is unlikely to act as a skin sensitiser. No specific studies on reproductive toxicity were submitted. Standard screening *in vitro* and *in vivo* genotoxicity assays showed no evidence of genotoxic potential for atinvicitinib. Additionally, atinvicitinib is considered unlikely to be carcinogenic or neurotoxic.

Regarding the formulated product, I have considered that exposure to the product is primarily through medium to long-term skin contact during the tablet handling such as removing from packaging, placing in a feed bowl, or splitting scored tablets. Splitting tablets presents the highest exposure risk that can be minimised by washing hands after handling. Post-administration exposure is considered negligible. Child-resistant packaging significantly reduces the risk of accidental ingestion. Due to its short plasma half-life, repeat dosing of atinvicitinib did not result in significant bioaccumulation. Consequently, the risk of adverse effects in children from accidental ingestion of tablets intended for dogs is very low.

I have considered that the safety directions provided are aligned with the hazards outlined regarding atinvicitinib. The risk assessment demonstrates a wide margin of safety for human exposure, even without the use of personal protective equipment (PPE). While atinvicitinib is not recommended for use in pregnant, lactating, or breeding dogs due to limited data, standard hygiene measures—such as thorough hand washing after administration—are considered adequate to minimise potential human exposure risks. The formulated product has a safety margin of at least five times between the therapeutic and toxic dose in dogs. Since no specific antidote exists, veterinarians should manage overdoses with symptomatic treatment. Therefore, monitoring or intervention by a veterinary practitioner is required to minimise the risk of harm (Schedule 4, scheduling factor 5).

In relation to s 52E (1) (d) of the Act, atinvicitinib is formulated as an oral tablet and is available in 4 strengths, each designed for use in a specific dog weight category. The tablets will present as scored and marked with S, M, L, XL on each half of the tablet. The formulated product will be available

in packs of 30 or 90 tablets. Tablets are to be packaged either in HDPE bottles with child-resistant, tamper-evident screw caps, or in aluminium/PVC/Aclar blister strips. The product will be administered orally to dogs by their owners under the direction of a veterinarian once daily with food. Treatment is expected to be medium to long term.

In consideration of paragraph 52E(1)(e), there is no known dependency potential and the potential for abuse is low for atinvicitinib and other JAK inhibitors.

Regarding paragraph 52E(1)(f), I note that only experimental clinical experience is available for atinvicitinib (Schedule 4, scheduling factor 8). However, other JAK inhibitors, oclacitinib and ilunocitinib, are registered (or undergoing registration) in Australia for the treatment of atopic dermatitis in dogs under Schedule 4. In Australia, JAK inhibitors are approved for human therapeutic use in several chronic inflammatory conditions, including rheumatoid arthritis and atopic dermatitis.[11]

Based on the above considerations and the information provided in the application, I have decided to amend the current Poisons Standard regarding atinvicitinib in the manner laid out above. This amendment was not referred to an expert advisory committee for advice.

Implementation date

1 October 2025

Final decision in relation to fluticasone propionate

Final decision

Pursuant to regulation 42ZCZU of the Regulations, a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to fluticasone propionate as follows:[12]

Schedule 2 – Amend Entry

FLUTICASONE PROPIONATE (excluding derivatives) in aqueous nasal sprays delivering 50 micrograms or less of fluticasone per actuation when the maximum recommended daily dose is no greater than 400 micrograms, for the prophylaxis of allergic rhinitis or treatment of allergic rhinitis and rhino-conjunctivitis for up to 6 months in adults and children 12 years of age and over.

Index

FLUTICASONE PROPIONATE
Cross reference: FLUTICASONE
Schedule 2
Schedule 4

Materials considered

In making this final decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to fluticasone propionate (the **Application**)
- Subsection 52E(1) of the Act, in particular (a) risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (f) any other matters that the Secretary considers necessary to protect public health

[11] https://www.tga.gov.au/news/safety-updates/important-safety-information-janus-kinase-jak-inhibitors

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

- Pursuant to paragraph 52E(2)(a) of the Act, the SPF,
- The Handbook.
- The Therapeutic Guidelines

Reasons for the final decision (including findings on material questions of fact)

I have made a final decision to amend the Pharmacy medicine (Schedule 2) entry in relation to fluticasone propionate to include rhino-conjunctivitis as a permitted indication in the manner detailed above.

The applicant proposed to amend the Schedule 2 entry of fluticasone propionate to include the indication “treatment of rhino-conjunctivitis”. This indication is supported by clinical data generated on the TGA approved fixed dose combination azelastine and fluticasone nasal spray [Dymista AUST R 203131].

Pursuant to s 52E(1)(a) and (b) of the Act, I have considered the relative risks of fluticasone propionate when used for rhino-conjunctivitis. The risk profile for fluticasone propionate is low and well defined. I note other corticosteroid monotherapy and antihistamine/corticosteroid combination products are already listed on the Australian Register of Therapeutic Goods (ARTG) for the treatment of allergic rhinitis or allergic conjunctivitis – the two major aspects of rhino-conjunctivitis.

Turning to s 52E(b) of the Act, fluticasone propionate monotherapy and fluticasone propionate and azelastine as a combination nasal preparation are used for common conditions such as allergic rhinitis and rhino-conjunctivitis. The longstanding availability of over-the counter products for allergic rhinitis indicates that patients can successfully identify their symptoms, which are unlikely to be confused with other more serious conditions. In addition, while I am confident many patients can recognise the symptoms of allergic rhinitis and use it appropriately, a pharmacy medicine classification will provide the opportunity for certain patients to be screened, assessed and counselled before using a fluticasone propionate nasal formulation to ensure it is suitable and used safely. Pharmacy medicines training is mandatory for pharmacy assistants to identify when the patient should consult with a pharmacist, who can then appropriately refer the patient to a medical practitioner if required.

The availability of pharmacy only medicines for rhino-conjunctivitis aligns with the SPF and supports the inclusion of this indication in the Schedule 2 entry for fluticasone propionate. I consider that fluticasone propionate as a monotherapy, or in combination with antihistamines, both align with the scheduling factors for Schedule 2. Quality use of the medicine can be achieved through appropriate labelling, and access to advice from a pharmacist would maximise the safe use of the medicine.

In relation to s 52E(1)(a) and (d) of the Act, fluticasone propionate in nasal preparations has a favourable safety profile. Having reviewed the Database of Adverse Event Notifications (DAEN), I note post-marketing reports of adverse events for fluticasone propionate as a monotherapy, and in combination with azelastine as a nasal preparation are minimal to date. There is precedence for an antihistamine when combined with an intranasal corticosteroid in aqueous nasal spray being classified in Schedule 2 from the olopatadine decision made in June 2023.

While I recognise drowsiness as a possible adverse effect associated with fluticasone propionate, this can be managed by appropriate warnings on the label. Pursuant to s 52E(1)(c) of the Act, fluticasone propionate presents a similar safety profile to other over-the-counter substances used to treat the same conditions and offers low systemic absorption as a nasal formulation.

I have considered the Therapeutic Guidelines for the treatment of allergic rhinitis. Intranasal antihistamine use in combination with an intranasal corticosteroid is an appropriate first-line treatment of allergic rhinitis if a patient presents with moderate to severe symptoms. As combination therapy is considered a second-line treatment for mild symptoms, I acknowledge the concern regarding consumers resorting to combination therapy as their primary treatment option. Consistent with the Therapeutic Guidelines, I support the proposed requirement that use of fluticasone propionate is restricted to persons ‘12 years and over’.

Allergic rhinitis and rhino-conjunctivitis (a predominant symptom associated with allergic rhinitis) affect a large proportion of adult Australians both seasonally and perennially, with an annual incidence of 20% in adults.[13] In accordance with paragraphs 52E(1)(a) and (f) of the Act, increased access to efficacious topical treatment for a condition as common as allergic rhinitis and its associated symptoms is beneficial to public health.

In making my final decision to include rhino-conjunctivitis in the Schedule 2 entry for fluticasone propionate, I have considered the favourable risk profile, patient screening in a pharmacy setting, and the general ability for customers to identify and manage risks associated with the use of fluticasone propionate nasal preparations without direct pharmacist oversight.

Implementation date

1 October 2025

Final decisions to amend the current Poisons Standard under section 52D(2) of the Act

In my capacity as a delegate of the Secretary for the purpose of subsection 52D(2) of the Act, I have made final decisions with respect to the following substance:

- Fenbendazole
- Etomidate

Final decision in relation to fenbendazole

Proposal

The Department of Health and Aged Care has proposed creating a new Prescription only medicine (Schedule 4) entry in the current Poisons Standard for fenbendazole.

Decision

Pursuant to subsection 52D(2) of the Act, a Delegate of the Secretary has made a decision to amend the current Poisons Standard in relation to fenbendazole as follows:[14]

Schedule 4 – New Entry

FENDBENDAZOLE **except** when included in Schedule 5.

Schedule 5

FENDBENDAZOLE for the treatment of animals.

Index – New Entry

FENBENDAZOLE
Schedule 4

Schedule 5

[13] Australian Institute of Health and Welfare, Australian Government, *Allergic rhinitis*, www.aihw.gov.au/reports/chronic-respiratory-conditions/allergic-rhinitis-hay-fever/contents/allergic-rhinitis

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

Materials considered

In making this final decision, the Delegate considered the following material:

- Subsection 52E(1) of the Act, in particular (a) risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters that the Secretary considers necessary to protect public health
- Pursuant to paragraph 52E(2)(a) of the Act, the SPF, and
- The Handbook.

Reasons for the final decision (including findings on material questions of fact)

In exercising my power under section 52D(2) of the Act, I have taken into account the information provided in the materials listed above. I have made a decision to amend the current Poisons Standard to create a new entry for fenbendazole under Prescription only medicines (Schedule 4) with an exception for when listed in Schedule 5. This amendment was not referred to an expert advisory committee for its advice.

Fenbendazole (CAS No. 43210-67-9) is a broad-spectrum benzimidazole anthelmintic used against gastrointestinal parasites including roundworms, hookworms, whipworms, the tapeworm genus *Taenia* (but not effective against *Dipylidium caninum*, a common dog tapeworm). Fenbendazole can be administered to a variety of animals including sheep, cattle, horses, dogs, cats, and rabbits.

Fenbendazole works by binding to tubulin, a protein that is part of the microtubules in the cells of parasites. This leads to parasites being unable to absorb nutrients, resulting in their eventual death. Due to its poor absorption by oral administration, fenbendazole is particularly effective for targeting intestinal parasites.

In relation to paragraph 52E(1)(a) of the Act, fenbendazole has not been evaluated for safety, quality and efficacy by the TGA. Its pharmacokinetics and safety in humans have yet to be established in clinical trials or medical literature. Fenbendazole is not approved for human use in Australia or by overseas regulatory bodies including the US Food and Drug Administration and the European Medicines Agency. Despite this, it is increasingly being used for purported cancer treatment and parasite cleanses, with dosages ranging from 222-444 mg daily.

Turning to paragraphs 52E(1)(b) and (c) of the Act, I note that fenbendazole is currently only approved for veterinary uses in Australia and has no industrial uses in Australia.[15] However, there is an increasing trend in online content promoting its use for the treatment of cancer. Toxicological data for human use is limited, and the absence of safety data raises significant concerns about unsupervised use.

In the absence of completed clinical trials testing fenbendazole in humans, insights are drawn from in vitro and in vivo animal studies.[16] Known risks associated with fenbendazole use in humans are limited, however actual toxicities such as acute hepatitis, following self-administration of fenbendazole have been reported including a severe liver injury case in the United States.[17,18]

In terms of reproductive toxicity and teratogenicity, there is no comprehensive data available regarding fenbendazole in humans.[19] In rodents, lifetime studies indicated no maternal or reproductive toxicity and no carcinogenesis. However, morphologic changes in hepato-cellular hypertrophy and

[15] webarchive.nla.gov.au/awa/20200921012653/https://www.industrialchemicals.gov.au/news-and-notices/chemicals-non-industrial-uses-removed-australian-inventory-chemical-substances-old-inventory
[16] ar.iiarjournals.org/content/44/9/3725
[17] pmc.ncbi.nlm.nih.gov/articles/PMC11068125/
[18] pmc.ncbi.nlm.nih.gov/articles/PMC7025903/
[19] pmc.ncbi.nlm.nih.gov/articles/PMC8212976/

hyperplasia were observed.[20] Nevertheless, it is prudent to avoid exposure to benzimidazole compounds during pregnancy unless the benefits clearly outweigh the risks, as evaluated by a medical practitioner.[21]

The limited experience of human usage of fenbendazole also presents the possibility of adverse events, contraindications and drug interactions that have not been identified. Further clinical studies using fenbendazole are needed to accurately assess its safety, toxicity, and therapeutic dose in humans. Fenbendazole products intercepted at the Australian border are increasingly labelled for human use, with some explicitly marketed for cancer treatment. While not a substance of dependence, the unapproved use of fenbendazole for serious conditions like cancer without medical supervision presents a significant public health risk.

Regarding paragraph 52E(1)(d) of the Act, there are currently no therapeutic goods registered in Australia that contain fenbendazole as an active ingredient. There have been no applications for products containing fenbendazole to be considered for inclusion on the Australian Register of Therapeutic Goods (ARTG).

In accordance with paragraphs 52E(1)(e) and (f) of the Act, I am of the view that the increasing misuse and promotion of fenbendazole as a therapeutic or supplement is a risk to public health. Advertising of the human use of fenbendazole is widely available, mainly on digital platforms, and overseas. In December 2023, an enforceable undertaking was entered by Aussie Mega Supplements.[22] Conduct of concern related to advertising and supplying unregistered supplements, including fenbendazole (500 mg) bottles that were supplied. The label of the product read “Suggested use: Adults for wellbeing 1 veggie capsules once a day, half an hour before food, oral” and “For cancer treatment: 1 capsule 2 times a day, half an hour before food, oral”.

Since that enforceable undertaking, there has been a substantial increase in the number of fenbendazole-containing products referred to the TGA. The TGA has undertaken regulatory compliance and investigation of the importation of fenbendazole, including:

Recent Activity (10 September 2024 – 10 September 2025)

- 185 referrals were received from the Australian Border Force during this period.
- These referrals involved over 44,300 units of fenbendazole.
- Approximately 34,500 units were seized.
- None of the referred products were released under the Personal Importation Scheme.

Previous activity comparison (Late 2020 – 9 September 2024)

- 11 referrals were received during this period.
- These involved a total of just over 3,000 units.

The products assessed were all unregistered, manufactured offshore and labelled for human therapeutic use, with dosage strengths of 150 mg, 222 mg, 444 mg, 500 mg, and up to 1,000 mg. Many of the products intercepted are advertised or labelled with parasite-cleansing claims alongside detoxification, wellbeing and anti-ageing. Others are purported for treating various types of cancer.

Listing non-animal use of fenbendazole as a Schedule 4 substance will allow for increased efficacy of enforcement activities and protection of public health. Readily being able to identify human use of fenbendazole as a Schedule 4 substance will enable border and custom authorities to intercept unauthorised shipments, preventing uncontrolled entry of fenbendazole into Australia.

Fenbendazole is an anti-parasitic that is only approved in Australia for the treatment of animals. To deter misuse and to assist in regulatory compliance action, I have decided to immediately list fenbendazole as a Prescription-only medicine (Schedule 4) in the Poisons Standard.

[20] pubmed.ncbi.nlm.nih.gov/17994667/

[21] pubmed.ncbi.nlm.nih.gov/11280072/

[22] www.tga.gov.au/news/compliance-undertakings/enforceable-undertaking-yossef-wahib-trading-aussie-mega-supplements

Implementation date

1 October 2025

Final decision in relation to etomidate

Proposal

The Department of Health and Aged Care has proposed creating a new Prescription only medicine (Schedule 4) entry in the current Poisons Standard for etomidate.

Decision

Pursuant to subsection 52D(2) of the Act, a Delegate of the Secretary has made a decision to amend the current Poisons Standard in relation to etomidate as follows:[23]

Schedule 4 – New Entry

ETOMIDATE

Index – New Entry

ETOMIDATE
Schedule 4

Materials considered

In making this final decision, the Delegate considered the following material:

- Subsection 52E(1) of the Act, in particular (a) risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse of a substance; and (f) any other matters that the Secretary considers necessary to protect public health
- Pursuant to paragraph 52E(2)(a) of the Act, the SPF, and
- The Handbook.

Reasons for the final decision (including findings on material questions of fact)

In exercising my power under section 52D(2) of the Act, I have taken into account the information provided in the materials listed above. I have made a decision to amend the current the Poisons Standard to create a new entry for etomidate under Prescription only medicines (Schedule 4). This amendment was not referred to an expert advisory committee for its advice.

Etomidate (CAS No. 33125-97-2) is a non-barbiturate sedative and hypnotic agent without analgesic properties. It elicits its effect by enhancing gamma-amino butyric acid type A (GABA-A) receptor performance in the central nervous system (CNS)[24]. In relation to paragraph 52E(1)(a) of the Act, etomidate is a relatively fast-acting and potent anaesthetic and hypnotic agent. It does not produce

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

[24] "Etomidate: Uses, Interactions, Mechanism of Action", DrugBank, Published August 2025, go.drugbank.com/drugs/DB00292.

respiratory depression (unlike other anaesthetic agents).[25] Risks involve adrenocortical suppression following prolonged use of the substance, which make it a poor choice for maintaining sedation under anaesthesia, particularly in immunocompromised patients. Its use as a single-dose induction agent in surgery remains clinically compelling when benefits outweigh risks.

Turning to paragraphs 52E(1)(b) and (c) of the Act, I note that while etomidate has therapeutic potential by inducing anaesthesia for clinical and operative purposes, it generally cannot be used long-term – noting the above risks of adrenocortical suppression, the effect of which can long outlast its sedative and hypnotic effects. Adrenal suppression has also been reported following administration of etomidate via a vaping device. It is worth noting an application for general marketing approval for etomidate was evaluated by the Department of Health in 1983, which was unsuccessful due to concerns related to adrenal suppression in prolonged use.

Etomidate generally has a higher safety profile than other anaesthetic agents, with a safety margin (LD_{50}/ED_{50}) of 26 in rats when administered through IV injection (in comparison to barbiturate anaesthetic agents such as thiopental (4.6) and methohexital (9.5)). These elements align with factor 5 of Schedule 4. There has been one reported case of death following oral ingestion of liquid containing etomidate, which caused acute intoxication.[26] Etomidate is registered for intravenous (IV) use in several comparable overseas jurisdictions, including (but not limited to) the EU, USA, Canada and UK in 2 mg/mL vials[27], almost exclusively for hospital use and administered by physicians specialised in anaesthesia (factor 2 of Schedule 4).

Regarding paragraph 52E(1)(d) of the Act, there are currently no therapeutic goods registered in Australia that contain etomidate as an active ingredient. There have also been no applications for products containing etomidate to be considered for inclusion on the Australian Register of Therapeutic Goods (ARTG).

In accordance with paragraphs 52E(1)(e) and (f) of the Act, I acknowledge that etomidate has become a public safety concern in other jurisdictions, namely Hong Kong, Taiwan and Singapore. The Department has been made aware that etomidate is also being used for recreational purposes in vaping devices. Listing etomidate as a Schedule 4 substance will allow for greater enforcement benefits and protection of public health. Readily being able to identify etomidate as a Schedule 4 substance will enable border and custom authorities to intercept unauthorised shipments, preventing uncontrolled entry of etomidate into Australia. Etomidate has been increasingly detected in illicit drug markets and vaping goods across Asia, Oceania, and beyond, often in uncontrolled and dangerous forms. There are significant risks to consumer safety if products containing etomidate are introduced into the Australian supply chain, particularly given the limited understanding of their misuse potential and associated health impacts.

Etomidate is a sedative and hypnotic drug, that while not currently approved for use in Australia, is used as an anaesthetic internationally. To deter misuse and to assist in regulatory compliance action, I have decided to immediately list etomidate as a Prescription only medicine (Schedule 4) in the Poisons Standard.

Implementation date

1 October 2025

[25] Yang Ding et al., “Pharmacokinetic and pharmacodynamic evaluation study of etomidate: a randomized, open-label, 2-period crossover study in healthy Chinese subjects”, *Scientific Reports* 14, issue number 7071 (Mar 2024). www.nature.com/articles/s41598-024-57581-2

[26] Yinyu Chen et al., “A case of fatal poisoning caused by etomidate: evidence from pathological and toxicological analyses”, *Forensic Science, Medicine, and Pathology* 20, 1453-1457 (April 2024). doi.org/10.1007/s12024-024-00813-8.

[27] C. Morris and C. McAllister, “Etomidate for emergency anaesthesia; mad, bad and dangerous to know?” *Anaesthesia* 60, issue number 8, 737-840 (August 2005). associationofanaesthetists-publications.onlinelibrary.wiley.com/doi/10.1111/j.1365-2044.2005.04325.x

Amendments to the Poison Standard in relation to New Chemical Entities (NCEs)

The NCEs listed below will be included in the new Poisons Standard that will come into effect on 1 October 2025.

SELADELPAR

Schedule 4 – New Entry

SELADELPAR

Index – New Entry

SELADELPAR

Schedule 4

SEBETRALSTAT

Schedule 4 – New Entry

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