Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

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

27 September 2024

Contents

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

This web publication constitutes a notice for the purposes of regulation 42ZCZS and regulation 42ZCZX of the *Therapeutic Goods Regulations 1990* (the **Regulations**). In accordance with regulations 42ZCZS and 42CZX, this notice publishes:

- the decisions made by a delegate[1] of the Secretary of the Department of Health and Aged Care (the **Delegate**) pursuant to regulations 42CZR, 42ZCZU AND 42ZCZW
- 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 Scheduling Policy Framework 2018 (the **SPF**)
- the Scheduling handbook, Guidance for amending the Poisons Standard (the **Handbook**) 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 referred to the Advisory Committee on Medicines Scheduling (ACMS #44, March 2024)

Final decision in relation to cytisine

Proposal

The Delegate received an application to create new Pharmacy medicine (Schedule 2) and Prescription only medicine (Schedule 4) entries for cytisine. The proposed amendment would include cytisine in divided preparations for oral use containing 1.5 mg or less of cytisine per dosage unit in Schedule 2, and all other preparations containing cytisine in Schedule 4. Cytisine is currently unscheduled and an unapproved ingredient in preparations for therapeutic use.

Final decision

Pursuant to regulation 42ZCZQ of the Regulations the Delegate has reconsidered the interim decision and has made a final decision, pursuant to regulation 42ZCZR of the Regulations, to vary the interim decision and amend the current Poisons Standard in relation to cytisine as follows:[2]

Schedule 4 – New entry

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

Schedule 3 – New entry

CYTISINE in divided oral and oromucosal preparations with a recommended daily dose of 9 mg or less of cytisine as an aid in withdrawal from tobacco smoking in adults.

Appendix H – New entry

CYTISINE

Index – New entry

CYTISINE

Schedule 4
Schedule 3

Appendix H

Materials considered

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

- The application to amend the current Poisons Standard with respect to cytisine (the **Application**)
- The 41 public submissions including eight written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the Submissions)

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

- The advice received from the 44th meeting of the Advisory Committee on Medicines Scheduling (the **Committee**)[3]
- The interim decision and the materials considered as part of the interim decision, as published on 26 July 2024
- The three submissions received in response to the public consultation on the interim decision under regulation 42ZCZP of the Regulations
- Subsection 52E(1) of the Act, 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; and (f) any other matters considered 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)

I have made a final decision to vary my interim decision to amend the current Poisons Standard with respect to cytisine. In making my final decision, I have taken into account the material in the interim decision and the 3 submissions received through public consultation on the interim decision.

The submissions were in favour of the interim decision (3 in support, 2 in partial support and no opposition). One supportive submission and 1 partially supportive submission argued that advertising should be permitted through an Appendix H entry for the Schedule 3 cytisine preparations. This would allow the public to be aware of the new smoking cessation treatment available from pharmacies. However, the other partially supportive submission recommended Schedule 4 classification for all cytisine preparations because of possible contraindications and drug-drug interactions that may not be adequately managed in pharmacy settings.

While I recognise the contraindications, drug-drug interactions, and limited experience of cytisine in Australia, the common adverse effects of cytisine use are rare and non-serious. Interactions and contraindications are known, identifiable and manageable by a pharmacist. I remain satisfied that pharmacist oversight can sufficiently mitigate the potential risks from cytisine. Further, cytisine has been used in many European countries for years as an over-the-counter medicine. Also, cytisine is approved as a natural health product in Canada and does not require a prescription. I note that advertising can only occur for a TGA approved product. Access to cytisine products from a pharmacy will increase the options available to assist smokers to cease smoking. Overall, I am of the view that the creation of Prescription only medicine (Schedule 4), Pharmacist only medicine (Schedule 3), and Appendix H entry for cytisine provides benefit to the public through increased access for short term use as an aid in withdrawal from tobacco smoking under the supervision of a pharmacist.

Implementation date

1 October 2024

[3] Established under sections 52B and 52C of the *Therapeutic Goods Act 1989* (Cth).

Final decision in relation to dextromethorphan

Proposal

The Delegate of the Secretary of the Department of Health and Aged Care proposed to move the current Pharmacy medicine (Schedule 2) entry for dextromethorphan to Pharmacist only medicine (Schedule 3). Under the proposal, preparations containing 600 mg or less of dextromethorphan with a recommended daily dose of 120 mg or less, will be available only after consultation with a pharmacist (Schedule 3). All other preparations of dextromethorphan will remain in Schedule 4 (prescription-only).

Final decision

Pursuant to regulation 42ZCZR of the Regulations, the Delegate has made a final decision to confirm the interim decision and not amend the current Poisons Standard in relation to dextromethorphan.

Materials considered

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

- The proposal to amend the current Poisons Standard with respect to dextromethorphan (the **Proposal**)
- The 14 public submissions received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations
- the advice received from the 44th meeting of the Advisory Committee on Medicines Scheduling (the **Committee**)[4]
- the interim decision relating to dextromethorphan and the materials considered as part of the interim decision, as published on 24 July 2024
- the 4 submissions received in response to the public consultation on the interim decision under regulation 42ZCZP of the Regulations
- publications and references cited in the reasons below
- subsection 52E(1) of the Act, 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 (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)

I have made a final decision to confirm my interim decision to not amend the current Poisons Standard with respect to dextromethorphan. My reasons for making the final decision are those set out in the interim decision. In making my final decision, I have taken into account the material in the interim decision and the 4 public submissions which were received in response to the consultation on the interim decision.

[4] Established under sections 52B and 52C of the *Therapeutic Goods Act 1989* (Cth).

Out of the 4 submissions, 3 were supportive and 1 was partially supportive of the interim decision to not amend the scheduling of dextromethorphan. The supportive submissions raised that data or evidence showing the misuse and abuse of dextromethorphan is lacking in Australia. As detailed in the interim decision, dextromethorphan poses a risk of misuse or abuse and also serotonin syndrome when combined with other serotonergic agents. There is a strong indication for abuse of dextromethorphan from the data supplied by NSW Poisons Information Centre, one research paper[5] and anecdotal reports. The Australian Drug Foundation recently published a factsheet about dextromethorphan. Similar harm reduction information is also available from several reputable Australian[6,7] and international organisations.[8,9] However, there is a lack of formal research about the scale of misuse of dextromethorphan in Australia. The submission in partial support of the interim decision commented that with the up-scheduling of dihydrocodeine, people may turn to using more dextromethorphan and sales data should be recorded to proactively address potential abuse of dextromethorphan in future. The Committee also commented on the underreporting of substance misuse or abuse in general and the limited evidence currently available on the scale of misuse or abuse of dextromethorphan in Australia.

Overall, I am of the view that currently there is not enough evidence to support moving the Schedule 2 entry for dextromethorphan to Schedule 3. I am therefore making the final decision not to amend the scheduling of dextromethorphan. However, I remain concerned about the potential for the misuse or abuse of dextromethorphan which needs to be monitored for future consideration of the appropriateness of the scheduling of dextromethorphan.

Final decision in relation to ethylmorphine

Proposal

The Delegate of the Secretary of the Department of Health and Aged Care has proposed deletion of the Pharmacy medicine (Schedule 2) entry for ethylmorphine. This will effectively classify all preparations containing ethylmorphine as prescription-only medicines.

Final decision

Pursuant to regulation 42ZCZR of the Regulations, the Delegate has made a final decision to confirm the interim decision and amend the current Poisons Standard in relation to ethylmorphine as follows:[10]

Schedule 8 – Amend Entry

ETHYLMORPHINE **except** when included in Schedule ~~2 or~~ 4.

Schedule 4 – Amend Entry

ETHYLMORPHINE when compounded with one or more other therapeutically active substances:

(a) in divided preparations containing not more than 100 mg of ethylmorphine per dosage unit; or

[5] Revol B, Lapeyre-Mestre M, Fouilhé Sam-Laï N, Jouanjus E. Association between NMDAR antagonists, drug abuse and dependence: A disproportionality analysis from the WHO pharmacovigilance database. Br J Clin Pharmacol. 2022; 88(11): 4937-4940. doi:10.1111/bcp.15430

[6] https://www.cahma.org.au/article/safer-using-dxm/

[7] https://hi-ground.org/substances/dxm/

[8] https://www.dea.gov/factsheets/dxm/

[9] https://www.poison.org/articles/dextromethorphan

[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.

(b) in undivided preparations with a concentration of not more than 2.5% of ethylmorphine~~;~~.

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

Schedule 2 – Delete Entry

~~ETHYLMORPHINE when:~~

(a) compounded with one or more other therapeutically active substances:

~~(i) in divided preparations containing 10 mg or less of ethylmorphine per dosage unit; or~~

~~(ii) in undivided preparations containing 0.25% or less of ethylmorphine; and~~

(a) labelled with a recommended dose not exceeding 15 mg of ethylmorphine.

Index – Amend Entry

ETHYLMORPHINE

Schedule 8
Schedule 4
~~Schedule 2~~

Materials considered

- the application to amend the current Poisons Standard with respect to ethylmorphine (the **Application**)
- the 10 public submissions received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations
- the advice received from the 44th meeting of the Advisory Committee on Medicines Scheduling (the **Committee**)[11]
- the interim decision relating to ethylmorphine and the materials considered as part of the interim decision, as published on 24 July 2024
- the one submission received in response to the public consultation on the interim decision under regulation 42ZCZP of the Regulations
- subsection 52E(1) of the Act, 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; and (f) any other matters considered necessary to protect public health
- publications and references cited in the reasons below
- pursuant to paragraph 52E(2)(a) of the Act, the SPF, and
- the Handbook.

[11] Established under sections 52B and 52C of the *Therapeutic Goods Act 1989* (Cth).

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

I have made a final decision to confirm my interim decision to amend the current Poisons Standard with respect to ethylmorphine. My reasons for making the final decision are those set out in the interim decision. In making my final decision, I have considered the material in the interim decision and the public submission from the Pharmacy Guild of Australia (PGA), which was received in response to the interim decision.

I have considered the suggestion from the PGA to create a new Appendix M entry for ethylmorphine to require record keeping of ethylmorphine supply using Real Time Prescription Monitoring (RTPM). I acknowledge that such a measure would better assist pharmacists to supply ethylmorphine appropriately and set barriers to accessing large quantities of ethylmorphine from multiple pharmacies. It will also enable greater pharmacovigilance activity and enable data collection to better understand ethylmorphine use and misuse. However, the implementation of the Poisons Standard is given effect through relevant state and territory legislations and implementation of such measure requires agreement from state and territory governments, especially as the RTPM system is only implemented for medicines requiring a prescription (Schedules 4 and 8). Currently no ethylmorphine product is listed on the Australian Register of Therapeutic Goods. Therefore, creation of an Appendix M entry for ethylmorphine has no practical implication at this stage.

Implementation date

1 October 2024

Final decisions on proposed amendments referred to the Advisory Committee on Chemicals Scheduling (ACCS #38, March 2024)

Final decision in relation to niclosamide

Proposal

The Delegate received an application to create a Caution (Schedule 5) entry for niclosamide when in tablet or paste preparations for companion animals, and a Poisons (Schedule 6) entry for niclosamide except when included in Pharmacy medicine (Schedule 2) or Schedule 5.

Final decision

Pursuant to regulation 42ZCZR of the Regulations, the Delegate has made a final decision to confirm the interim decision and amend the current Poisons Standard in relation to niclosamide as follows:[12]

Schedule 6 – New entry

NICLOSAMIDE **except** when included in Schedule 2 or 5.

Schedule 5 – New entry

NICLOSAMIDE in tablet or paste preparations for use in companion animals.

Schedule 2

NICLOSAMIDE for human therapeutic use.

Index – Amend entry

NICLOSAMIDE

Schedule 6
Schedule 5
Schedule 2

Materials considered

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

- the application to amend the current Poisons Standard with respect to niclosamide (the **Application**)
- the 6 public submissions received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations
- the advice received from the 38th meeting of the Advisory Committee on Chemicals Scheduling (the **Committee**)
- the interim decision relating to niclosamide and the materials considered as part of the interim decision, as published on 26 July 2024

[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.

- 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; and (f) any other matters considered 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)

I have made a final decision to confirm my interim decision to amend the current Poisons Standard with respect to niclosamide. No public submission was received in response to the interim decision in response to the consultation on interim decision. My reasons for making the final decision are those set out in the interim decision.

Implementation date

1 June 2025

Final decisions on proposed amendments referred to the Advisory Committee on Medicines and Chemicals Scheduling in joint session (Joint ACMS-ACCS #36, March 2024)

Final decision in relation to oxytetracycline

Proposal

The applicant proposed to amend the Caution (Schedule 5) entry for oxytetracycline to include topical preparations for animals to treat superficial skin infections. These preparations are currently included in the Prescription only medicine (Schedule 4) entry for the substance.

Final decision

Pursuant to regulation 42ZCZR of the Regulations, the Delegate has made a final decision to confirm the interim decision and not amend the current Poisons Standard in relation to oxytetracycline.

Materials considered

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

- the application to amend the current Poisons Standard with respect to oxytetracycline (the **Application**)
- the 23 public submissions received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations
- the advice received from the 36th meeting of the Advisory Committee on Medicines and Chemicals Scheduling in joint session (the **Committee**)
- the interim decision relating to oxytetracycline and the materials considered as part of the interim decision, as published on 26 July 2024
- the one public submission received in response to the public consultation on the interim decision under regulation 42ZCZP of the Regulations
- 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)

I have made a final decision to confirm my interim decision to not amend the current Poisons Standard with respect to oxytetracycline. My reasons for making the final decision are those set out in the interim decision. In making my final decision, I have considered the material in the interim decision and 1 submission received in response to the public consultation on the interim decision.

The submission did not support the interim decision and raised the following concerns:

- Farmers can adequately identify and treat superficial skin infections where topical oxytetracycline may be used, such as foot rot in sheep and digital dermatitis in cattle.
- The availability of topical oxytetracycline is important for animal welfare.
- Oxytetracycline as a highly important antimicrobial should be reconsidered as alternatives and newer tetracyclines with greater activity are available.
- The use of topical oxytetracycline by farmers carries a similar or lower potential for antibiotic resistance development compared to large scale use as feed additives.

In considering the issue of farmers being able to diagnose and treat foot rot and digital dermatitis, I note the resources on foot rot referenced in the submission. The resource available from the New South Wales (NSW) Department of Primary Industries[13] describes the symptoms, diagnosis and scoring for disease severity. The resources describe benign and virulent forms of the disease, the distinction of which may require laboratory tests. Further, these resources specify that suspect cases of foot rot should be notified to a district veterinarian and outbreaks must be reported to an inspector of livestock. In NSW for example, virulent foot rot in sheep and goats can only be diagnosed by a registered veterinarian. I am of the opinion that these resources are targeted specifically towards veterinary specialists and not farmers in general to consistently recognise and manage these conditions while abiding by the appropriate use of antibiotics. Further, topical oxytetracycline products are to be used against susceptible microorganisms and the submission is unclear about how farmers can make this distinction.

I recognise the costs involved in consulting a veterinarian and testing for oxytetracycline susceptible microorganisms. However, in accordance with s 52E of the Act, I have given greater weight to the benefits and risks to public health. There are other regulatory mechanisms for upholding appropriate animal production and welfare standards, including the Australian Animal Welfare Standards and Guidelines.

I note that alternatives to tetracyclines are available to treat *Brucella* spp., *Chlamydia* spp. and *Rickettsia* spp. and newer tetracyclines have been developed for treatment of pathogens resistant to naturally occurring oxytetracyclines. Previously, tetracyclines were categorised as 'critically important' for human medicine by the World Health Organization, partly because of their use in treatment of zoonotic *Brucella spp*. infections.[14] I acknowledge these infections have become less important with eradication of the animal reservoir in many countries. While brucellosis is a rare occurrence in Australia, chlamydia remains a significant public health issue[15] and human rickettsial diseases such as Queensland tick typhus is an emerging public health threat.[16] As such, tetracyclines are still considered antimicrobials of high importance. While the members of the tetracycline class can have different activities and mechanisms for developing antimicrobial resistance, resistance that develops against one member can still apply to others. For example, antimicrobial resistance to tetracycline through mutations in the ribosomal subunit protein S10 also confers resistance to tigecycline – a

[13] https://www.dpi.nsw.gov.au/about-us/services/laboratory-services/veterinary/footrot-in-sheep

[14] https://iris.who.int/bitstream/handle/10665/255027/9789241512220-eng.pdf

[15] Munari, S.C., Goller, J.L., Hellard, M.E. and Hocking, J.S. (2022), Chlamydia prevention and management in Australia: reducing the burden of disease. Med J Aust, 217: 499-501. https://doi.org/10.5694/mja2.51749

[16] Dehhaghi, M., Panahi, H. K. S., Holmes, E. C., Hudson, B. J., Schloeffel, R., & Guillemin, G. J. (2019). Human tick-borne diseases in Australia. Frontiers in Cellular and Infection Microbiology, 9, 1–17. https://doi.org/10.3389/fcimb.2019.00003

semisynthetic tetracycline introduced in 2005.[17] The submission did not provide evidence that the differences in activity and/or resistance mechanism would have an insignificant impact on antibiotic resistance development and disease control.

I acknowledge the important issue of oxytetracycline in feed additives and development of antimicrobial resistance through possible overuse. Oxytetracycline products as feed additive are classified as Prescription Only (Schedule 4) medicines and are available to treat oxytetracycline sensitive microorganisms in animals. The prescribing behaviour of veterinarians is regulated by veterinary statutory boards in each state and territory and is not a matter for scheduling. There are also several prescribing guidelines available from the Australian Veterinary Association, Animal Medicines Australia, Meat and Livestock Australia and the National Centre for Antimicrobial Stewardship on use of antimicrobials in animals including feedlot cattle.

Overall, the submission did not provide sufficient evidence to alleviate my concerns regarding risks of communal harm from the development of resistant strains of microorganisms from inappropriate or overuse of tetracycline under a less restrictive schedule. This is in addition to the challenges posed by the proper diagnosis and treatment of superficial skin infections in animals, particularly foot rot. I therefore remain of the opinion that oxytetracycline for topical application to animals to treat superficial skin infections should remain a Prescription Only (Schedule 4) medicine.

Final decision in relation to tranexamic acid

Proposal

The Delegate received an application proposing an exemption for topical cosmetic preparations containing up to 3% tranexamic acid from the Prescription only medicine (Schedule 4) entry for the substance. At present, the scheduling exemption is limited to the derivative cetyl tranexamate.

Final decision

Pursuant to regulation 42ZCZR of the Regulations, the Delegate has made a final decision to confirm the interim decision and amend the current Poisons Standard in relation to tranexamic acid as follows:[18]

Schedule 4 –Amend Entry

TRANEXAMIC ACID **except** in preparations containing 3% or less of ~~cetyl tranexamate hydrochloride~~ tranexamic acid for dermal cosmetic use.

Index – Amend entry

TRANEXAMIC ACID
~~cross reference: CETYL TRANEXAMATE~~

Schedule 4

[17] Grossman TH. Tetracycline Antibiotics and Resistance. Cold Spring Harb Perspect Med. 2016 Apr 1;6(4):a025387. doi: 10.1101/cshperspect.a025387.

[18] 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:

- The application to amend the current Poisons Standard with respect to tranexamic acid (the **Application**)
- The 9 public submissions received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations
- the advice received from the 36th meeting of the Advisory Committee on Medicines and Chemicals Scheduling in joint session (the **Committee**)
- the interim decision relating to tranexamic acid and the materials considered as part of the interim decision, as published on 26 July 2024
- 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)

I have made a final decision to confirm my interim decision to amend the current Poisons Standard with respect to tranexamic acid. No public submission was received in response to the interim decision in response to the consultation on interim decision. My reasons for making the final decision are those set out in the interim decision.

Implementation date

1 October 2024

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:

- Dimethylacetamide
- Epyrifenacil
- Metarylpicoxamid
- Moxidectin
- Modlidustat
- Vatinoxan
- Homobrassinolide

Final decision in relation to dimethylacetamide

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 dimethylacetamide as follows: [19]

Schedule 6

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

Schedule 5 – Amend entry

DIMETHYLACETAMIDE in preparations containing 40%~~20%~~ or less of dimethylacetamide in single dose flow-limited tubes of 5 mL or less for dermal application to companion animals.

Index

DIMETHYLACETAMIDE

Schedule 6
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 dimethylacetamide (the **Application**)
- Subsection 52E(1) of *the Therapeutic Goods Act 1989*, in particular (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a

[19] 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.

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)

In determining that this matter will be a delegate-only decision I have taken into account the information provided by the Australian Pesticides and Veterinary Medicine Authority (APVMA), and the matters outlined under s 52E of the Act and the SPF. My reasons for making the final decision follow.

Dimethylacetamide is currently captured as 'Poison' (Schedule 6) in the Poisons Standard except when in preparations containing 20% or less of dimethylacetamide which are captured as Caution (Schedule 5) substances. The Application proposes the cut-off for the 'Caution' (Schedule 5) entry be increased to 40% for small volume (5 mL or less) spot-on products for dogs and cats such that the products will be captured as Caution (Schedule 5) instead of the Poisons (Schedule 6) entry.

Regarding 52E(1)(b), dimethylacetamide is used as a non-aqueous solvent (34%) in spot-on products for the control of specified fleas, ticks and mites, and associated conditions, as well as heartworm, and specified intestinal worms in dogs and cats by animal healthcare specialists and pet owners. The active ingredients in the spot-on products are fluralaner and moxidectin. There is only one agricultural insecticide product containing 60% dimethylacetamide in its formulation that is classified under the 'Poison' (Schedule 6) entry. All other registered agricultural or veterinary chemicals containing dimethylacetamide are Prescription only (Schedule 4) injectable products.

Regarding s 52E(1)(d) of the Act, I note that the products intended for spot-on use in dogs and cats contain up to 33.9% dimethylacetamide in flow-limited pipettes up to 5 mL in volume. The largest available pack size contains 1,695 mg of dimethylacetamide per pipette. Each pack contains up to 6 pipettes, representing a single dose, and each pipette is enclosed in a child-resistant sachet with a non-removable twist-and-use cap. The products are also labelled with an APVMA approved label containing first-aid instructions, safety directions and additional user safety statements.

With respect to s 52E(1)(c) of the Act, I note that based on animal studies, dimethylacetamide is a slight skin irritant, a moderate eye irritant and not a skin sensitiser. Recent findings show that 34% dimethylacetamide solution has low acute oral and dermal toxicity and is a slight eye irritant with an estimated low acute inhalation toxicity. These are consistent with the scheduling factor 1 for Schedule 5 substances. Liver inflammation, necrosis, and hypertrophy have been observed in rats and mice at high doses in the short and long term. Further, liver damage has been reported in workers exposed to dimethylacetamide via the lungs and skin for periods of up to 10 years, though the levels of exposure were not known. Foetal malformations can occur in mice, rats and rabbits after high inhalational or oral exposures which is of concern.[20] Based on oral developmental toxicity studies, a No-Observed Adverse Effect Level (NOAEL) of 65 mg/kg bw/d is considered the most appropriate toxicological end-point. Using the NOAEL of 65 mg/kg bw/d, the risks of developmental effects for domestic and professional users from dermal or oral exposures to the spot-on products containing 34% dimethylacetamide were estimated to be very low to low. Based on the data provided by the applicant, I am of the opinion that 34% dimethylacetamide has low toxicity and is a low health hazard (scheduling factors 1 and 2 for Schedule 5). I am also of the opinion that the toxicity of preparations containing 40% dimethylacetamide are unlikely to be substantially higher than 34% formulations and increasing the cut-off limit to 40% is suitability justified based upon Margins of Exposure (MOE) in excess of 100 for users of the product.

[20] SM Munley, 'DMAC: Development toxicity study in Sprague-Dawley rats', 1997 - unpublished

Regarding 52E (1)(d), the spot-on products containing dimethylacetamide are available in 5 mL flow limited pipettes. The dosage is in small volumes (5 mL maximum) for application every 3 to 6 months. The entire content of these products is applied directly to the dog or cat's skin. Noting the finding from the developmental risk studies are based on 5 mL dosage and 100% oral or dermal absorption, I agree with the applicant that 34% dimethylacetamide is capable of causing only minor adverse effects to humans in normal use (scheduling factor 3). The likelihood of injury can be further minimised through appropriate packaging and simple label warnings that are already in place (factors 4 and 5 for Schedule 5).

Based on the above considerations and the information provided in the application, I have decided to amend the Caution (Schedule 5) entry for dimethylacetamide in the current Poisons Standard in the manner set out above. The proposed amendment was not referred to an expert advisory committee.

Implementation date

1 October 2024

Final decision in relation to epyrifenacil

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 epyrifenacil as follows: [21]

Schedule 5 – New entry

EPYRIFENACIL.

Index – New entry

EPYRIFENACIL

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 epyrifenacil (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; and (f) any other matters considered necessary to protect public health
- Pursuant to paragraph 52E(2)(a) of the Act, the SPF, and
- The Handbook.

[21] 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.

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

In determining that this matter will be a delegate-only decision I have taken into account the information provided by the Australian Pesticides and Veterinary Medicine Authority (APVMA), and the matters outlined under s 52E of the Act and the SPF. My reasons for making the final decision are as follows.

The Application proposed to amend the current Poisons Standard to create an entry for epyrifenacil as a Caution (Schedule 5) substance. Epyrifenacil is a phenyl-uracil herbicide which interferes with chlorophyll synthesis in plants by inhibiting protoporphyrinogen oxidase.

In relation to s 52E(1)(a) of the Act, the proposal to create a Caution (Scheduled 5) entry is based upon its benefits as herbicide. Epyrifenacil is likely to provide an additional option to other approved agricultural herbicides.

Regarding s 52E(1)(b) of the Act, the intended use of the substance is the control of broadleaf weeds in a range of broadacre crops and non-crop situations. However, no estimates of the quantities of epyrifenacil to be used in Australia were included in the application.

In relation to s 52E(1)(c) of the Act, the APVMA provided a Human Health Risk Assessment (HHRA) for both the active ingredient and the intended product formulation containing epyrifenacil at 55 g/L. The HHRA concluded that the risks to human health and safety posed by epyrifenacil were acceptable according to the criteria stipulated in Section 5A of the *Agricultural and Veterinary Chemicals Code Act*, 1994.

The HHRA provides that the acute oral, dermal and inhalational toxicity levels for epyrifenacil in rats (LD_{50} >2,000 mg/kg bw for oral and dermal routes, LD_{50} >2,000 mg/m^3 for inhalation) are low. Epyrifenacil, as an active ingredient is only a slight eye and skin irritant in rabbits and not a skin sensitiser in Guinea pigs. These findings are consistent with a Caution (Schedule 5) classification for epyrifenacil. However, the product formulation is also a severe skin and eye irritant in rabbits and a skin sensitiser in Guinea pigs which align with Poisons (Schedule 6) scheduling factors. Overall, I have decided that epyrifenacil aligns better with the Schedule 5 factors, and consistent with the HHRA, the toxicity of the product formulation precludes any lower concentration cut-off to exempt scheduling of epyrifenacil.

Epyrifenacil is not considered to be a reproductive toxicant based on the no observed adverse effect level (NOAEL) of 100 ppm (6.6 mg/kg bw/d) established for maternal and offspring (pup) effects in rats. However, delayed vaginal patency was observed at high doses (300 ppm) at which maternal mortality and moribundity were also observed.

Epyrifenacil is not considered to be a developmental toxicant in either rats or rabbits and has maternal NOAELs of 20 mg/kg bw/d and 250 mg/kg bw/d, respectively. An increased incidence of supernumerary cervical ribs was observed in rat foetuses only at doses sufficiently high (60 mg/kg bw/d) to cause adverse haematology and hepatic effects in dams. No foetal effects were seen in rabbits with doses up to 750 mg/kg bw/d.

Epyrifenacil is unlikely to be genotoxic as demonstrated by *in vitro* and *in vivo* testing.

There was no evidence of carcinogenicity in a 2-year rat study. However, epyrifenacil induced liver tumours in carcinogenicity testing on male mice at 40 ppm – a dose higher than the NOAEL (15 ppm). Several high-quality mode-of-action studies showed that humans are substantially less susceptible to the hepatocarcinogenic effects of epyrifenacil. Therefore, I am satisfied that the human relevance of the nonclinical carcinogenic effects of epyrifenacil are consistent with a Caution (Schedule 5) classification.

I have also considered the results of *in vitro* studies on the effects of epyrifenacil on the endocrine system. Epyrifenacil did not have any effect on androgen or estrogen receptors as studied by

Androgen Receptor Transcriptional Activation Assays and Estrogen Receptor Transcriptional Activation Assays.

The intended product formulation will contain 55 g/L of epyrifenacil as the active constituent in an emulsifiable concentrate (EC). I consider the risk of adverse health effects in humans through accidental exposure to epyrifenacil can be adequately mitigated through appropriate packaging and labelling. I am satisfied that, for the purposes of s 52E(1)(d) of the Act, the APVMA, as the regulator of all veterinary products, will consider the dosage, formulation, labelling, packaging and presentation of epyrifenacil-containing products during the product registration process.

In relation to s 52E(1)(e) of the Act, I am satisfied the potential for misuse or abuse of epyrifenacil is limited. In forming this view, I have considered the substance has no established therapeutic value in humans that would indicate that there is a risk of dependency, abuse, misuse, or diversion into illicit use.

I note under paragraph 52E(1)(f) of the Act, that porphyria is a potential hazard for both humans and animals from excessive exposure to this class of chemicals. However, I agree with the applicant that this is a reversible effect, and the associated risk can be adequately mitigated through the appropriate use of personal protective equipment.

Other chemicals in this class include butafenacil and saflufenacil, which have different toxicological profiles to epyrifenacil and are already included in the Poisons Standard in Appendix B and Dangerous Poisons (Schedule 7), respectively.

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

Implementation date

1 October 2024

Final decision in relation to metarylpicoxamid

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 metarylpicoxamid as follows: [22]

Schedule 5 – New entry

METARYLPICOXAMID.

Index – New entry

METARYLPICOXAMID

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 metarylpicoxamid (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
- 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 determining that this matter will be a delegate-only decision I have taken into account the information provided by the Australian Pesticides and Veterinary Medicine Authority (APVMA), and the matters outlined under s 52E of the Act and the SPF. My reasons for making the final decision follow.

The Application proposes that a new entry for metarylpicoxamid be created in the Poisons Standard under Caution (Schedule 5). Metarylpicoxamid is a fungicide to control Asian soybean rust and is not currently listed in the Poisons Standard.

Regarding s 52E(1)(a) of the Act, I note the benefit of metarylpicoxamid is its use to control Asian soybean rust. I have considered this against the relatively low risk of substance toxicity and it potential to elicit adverse effects from acute or repeat exposure (see below). I am of the view that the benefits posed by metarylpicoxamid outweigh the risks to human health.

Regarding s 52E(1)(c) of the Act, the Application provided data showing metarylpicoxamid has low acute oral and dermal toxicity and low to moderate inhalation toxicity. The substance is not a skin irritant but is a slight eye irritant and a skin sensitiser. The key adverse events noted in repeat dose toxicity were reductions in bodyweight, bodyweight gain, food intake and/or food efficiency. However, there was no evidence of developmental toxicity, neurotoxicity or immunotoxicity or effects on reproduction. Similarly, the substance poses no risk of developmental toxicity or genotoxicity and is

[22] 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.

not a carcinogen. I agree with the applicant that metarylpicoxamid has a low toxicity profile and poses a low health hazard (Schedule 5, scheduling factors 1 and 2). The risks from metarylpicoxamid use can be adequately mitigated by the safety directions on the label (Schedule 5, scheduling factor 3).

In consideration of s 52E(1)(b) and (d) of the Act, metarylpicoxamid is intended to be used as an active constituent in products formulated for spray-on application on soybean plants. The formulated product is an emulsifiable concentrate containing 150 g/L metarylpicoxamid, other scheduled substances. The formulated product is regarded as a severe skin irritant, eye irritant and skin sensitiser and the exposure and risk assessment indicated that the potential risks from exposure to the product are moderate. APVMA has followed a health-protective approach in relation to the label directions for the formulated product requiring it to be labelled as 'POISON' and have first aid instructions, safety directions, re-entry statement and restraints and restrictions on the label. These restrictions are also considered adequate to manage risks from metarylpicoxamide present in the formulated product. Further, users of the product containing metarylpicoxamid are unlikely to be exposed to metarylpicoxamid given closed mixing/loading requirements and PPE, and appropriate label instructions.

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

Implementation date

1 October 2024

Final decision in relation to moxidectin

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 moxidectin as follows: [23]

Schedule 7

MOXIDECTIN except when included in Schedule 4, 5 or 6.

Schedule 6

MOXIDECTIN:

(a) in preparations for external use containing 2.5% or less of moxidectin when packed in single dose tubes for the treatment of cats and dogs; or

(b) in preparations for external use containing 2% or less of moxidectin for the treatment of animals; or

(c) in preparations for internal use containing 10% or less of moxidectin for the treatment of sheep or cattle;

except when included in Schedule 5.

[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.

Schedule 5 – Amend entry

MOXIDECTIN:

(a) in preparations for external use for the treatment of animals other than cats and dogs, containing 0.5% or less of moxidectin; or

(b) in preparations for external use for the treatment of cats and dogs, containing ~~2.5%~~25 mg or less of moxidectin packed in single dose tubes ~~with a volume of 1 mL or less~~; or

(c) for internal use for the treatment of animals:

(i) in divided preparations for dogs, containing 250 micrograms or less of moxidectin per dosage unit in a pack containing six or less dosage units; or

(ii) in other preparations containing 2% or less of moxidectin.

Schedule 4

MOXIDECTIN in preparations for injection containing 10% or less of moxidectin except when included in Schedule 5 or 6.

Index

MOXIDECTIN

Schedule 7
Schedule 6
Schedule 5
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 moxidectin (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)

In determining that this matter will be a delegate-only decision I have taken into account the information provided by the Australian Pesticides and Veterinary Medicine Authority (APVMA), and the matters outlined under s 52E of the Act and the SPF. My reasons for making the final decision follow.

Moxidectin is used for the control of internal and external parasites in animals. The current Caution (Schedule 5) entry for moxidectin captures preparations for external use for the treatment of cats and dogs, containing 2.5% or less of moxidectin packed in single dose tubes with a volume of 1 mL or less.

The proposal is to amend the current Caution (Schedule 5) entry to include preparations for external use for the treatment of cats and dogs, containing 25 mg or less of moxidectin in single dose tubes. The proposal will allow higher volumes of lower concentration moxidectin preparations available in the market to be classified as Caution (Schedule 5) without changing the total amount of moxidectin permissible under the current Schedule 5 entry.

In relation to s 52E(1)(a) and (c) of the Act, the proposed amendment achieves the same maximum exposure to moxidectin as the existing entry, but at lower concentrations. Therefore, the toxicity and any risk to public health is equivalent or lower when compared to the current scheduling.

Regarding s 52E(1)(b) and (e) of the Act, the intended use and potential of misuse or abuse of moxidectin have previously been considered by ACCS in 2018 (ACCS #22). The proposed uses and potential for misuse or abuse of moxidectin remain unchanged from previous considerations.

With respect to s 52E(1)(c) and (d) of the Act, the moxidectin preparation that will be affected by the proposed changes contain 1.4% moxidectin in a ready-to-use liquid spot-on formulation. It is registered in pack sizes containing up to 6 x 1.79 mL single use, flow-limited pipettes. The pipettes are enclosed in a child-resistant foil sachet, which is contained within a box that contains an APVMA approved label. The toxicity and safety of the affected moxidectin products remain unchanged from previous considerations by ACCS in 2018 (ACCS #22).

On the basis of the above considerations and the information provided by the application, I have decided to amend the current Poisons Standard in the manner set out above. The proposed amendment was not referred to an expert advisory committee.

Implementation date

1 October 2024

Final decision in relation to vatinoxan hydrochloride

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 vatinoxan hydrochloride as follows: [24]

Schedule 4 – New Entry

VATINOXAN HYDROCHLORIDE

Index – New Entry

VATINOXAN HYDROCHLORIDE
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 vatinoxan (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,

[24] 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.

- The Handbook.

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

In determining that this matter will be a delegate-only decision I have taken into account the information provided by the Australian Pesticides and Veterinary Medicine Authority (APVMA), and the matters outlined under s 52E of the Act and the SPF. My reasons for making the final decision are as follows.

The Application proposed to amend the current Poisons Standard to create a Prescription only (Schedule 4) entry for vatinoxan hydrochloride. Vatinoxan is currently not included in the Poisons Standard.

Regarding s 52E(1)(a) and (b) of the Act, vatinoxan is intended to be used in injectable preparations also containing medetomidine hydrochloride. The co-formulated product is intended as a sedative and analgesic in dogs during veterinary medical procedures. Vatinoxan is not proposed for use for its inherent pharmacological effects but is instead added to the formulation to reduce the adverse peripheral effects of medetomidine. Medetomidine is captured under Prescription only (Schedule 4) entries in the current Poisons Standard.

With regards to s 52E(1)(c) of the Act, the Application highlighted the limited availability of toxicity data for vatinoxan. It has low acute oral toxicity (LD_{50}: >2000 mg/kg bw, rat). No information was available to indicate the substance's acute dermal and inhalational toxicity, skin and eye irritation, or its potential to be a skin sensitiser. In a 28 day repeat dose dietary study in rats the key adverse effect observed was soft stools in male rats. A NOAEL of 20 mg/kg bw/d was derived from this study.

No genotoxicity was detected but no information is available on the neurotoxicity, immunotoxicity, developmental or reproductive toxicity or carcinogenicity of vatinoxan. However, the substance is well tolerated, and no mortality was observed at 5 times the recommended dose. Further, it is unlikely to cause drug-drug interactions and has no known abuse potential (s 52E(1)(e) of the Act).

With regard to s 52E(1)(d) of the Act, the Application notes that the APVMA received an application for registration of a new product containing 10 mg/mL vatinoxan hydrochloride and 0.5 mg/mL medetomidine hydrochloride for intramuscular injection in dogs. The product will be available in 10 mL vials intended for professional use by veterinarians at a dose of 1 mg medetomidine hydrochloride and 20 mg vatinoxan hydrochloride per square metre of body surface area.

The proposed use of vatinoxan is in the veterinary clinical setting. The co-formulated product containing vatinoxan and medetomidine hydrochloride will be administered via intramuscular injection for sedation and analgesia of short medical and surgical procedures. I am of the view that the administration of the substance requires veterinary intervention. Veterinary supervision of animals is also required to monitor pharmacological or adverse effects during sedation and performance of procedures. The requirement of veterinarian supervision aligns with scheduling factors 1, 2 and 4 for Schedule 4 substances.

Further, there is minimal human experience with vatinoxan alone. Experimental IV infusion in humans resulted in nausea, vomiting, GIT discomfort/cramps, perspiration, tingling/paraesthesia of forearms and legs, palpitations, light-headedness, urinary urgency and increased noradrenaline levels. There is no human experience with the co-formulated product. Such lack of experience of the use of the substance under normal clinical conditions is consistent with Schedule 4, scheduling factor 8.

On the basis of the above considerations and the information provided by the application, I have decided to amend the current Poisons Standard in the manner set out above. The proposed amendment was not referred to an expert advisory committee.

Implementation date

1 October 2024

Final decision in relation to homobrassinolide

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 homobrassinolide as follows.[25]

Schedule 5 – New Entry

HOMOBRASSINOLIDE

Index – New Entry

HOMOBRASSINOLIDE
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 homobrassinolide (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
- The Human Health Risk Assessment (HHRA) technical report on homobrassinolide (93642)
- 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 determining that this matter will be a delegate-only decision I have taken into account the information provided by the Australian Pesticides and Veterinary Medicine Authority (APVMA), and the matters outlined under s 52E of the Act and the SPF. My reasons for making the final decision follow.

The Application proposed to amend the current Poisons Standard to create a Caution (Schedule 5) entry for homobrassinolide. Homobrassinolide is a naturally-occurring plant steroidal hormone, prevalent in foods such as Chinese cabbage. Homobrassinolide is currently not included in the Poisons Standard. The APVMA provided a Human Health Risk Assessment (HHRA) for the substance, homobrassinolide.

In relation to s 52E(1)(a) and (b) of the Act, the proposed amendment to the Poisons Standard is to include an entry for homobrassinolide in Schedule 5 based upon its benefits to enhance plant growth and development. Homobrassinolide has been shown to protect against a variety of abiotic stresses

[25] 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.

and it has demonstrated significant improvement in plant growth, water uptake, photosynthesis, and yield. Preparations containing homobrassinolide have been approved in the UK, USA, and India as foliar spray for agricultural and horticultural crops. However, there are no specific data regarding the use pattern for homobrassinolide.

In relation to s 52E(1)(c) of the Act, the HHRA indicated that homobrassinolide has a low acute oral (LD_{50}: > 2000 mg/kg bw, no deaths), dermal (LD_{50}: > 2000 mg/kg bw, no deaths), and inhalational toxicity (LC_{50}: > 5.02 mg/L, no deaths) in rats. Homobrassinolide was a slight eye and skin irritant but was not a skin sensitiser.

Rats treated daily for 90 days with oral doses of up to 1000 mg/kg bw homobrassinolide (the highest dose tested), did not reveal any significant clinical signs or changes in organ weights and clinical chemistry.

There was no evidence for genotoxic potential of homobrassinolide based upon an *in vivo* genotoxicity study (chromosome aberrations) in mice treated up to a single oral dose of 2000 mg/kg bw. No data were available regarding homobrassinolide's carcinogenic potential.

Based on the limited but adequate toxicology data available, the HHRA concluded that the risks to human health and safety posed by this substance are acceptable. These findings align with scheduling factors 2 and 3 for Schedule 5 substances. An acceptable daily intake (ADI) and an acute reference dose (ARfD) were not considered necessary. This was consistent with previous evaluations by the US EPA (2010)[26] and EFSA (2020)[27].

No products containing homobrassinolide are currently available in Australia, and no applications for product registration have yet been received. Regarding s 52E(1)(d) of the Act, the APVMA, as the regulator of all veterinary products, will consider the dosage, formulation, labelling, packaging and presentation of homobrassinolide-containing products at the time of registration.

In relation to s 52E(1)(e) of the Act, I am satisfied that the potential for misuse or abuse of homobrassinolide is limited. In forming this view, I have considered the substance has no established therapeutic value in humans that would indicate that there is no risk of dependency, abuse, misuse, or diversion into illicit use.

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 2024

[26] US EPA (2010). 40 CFR Part 180 [EPA–HQ–OPP–2007–1187; FRL–8831–2] Homobrassinolide; Exemption from the Requirement of a Tolerance https://www.govinfo.gov/content/pkg/FR-2010-07-09/pdf/2010-16771.pdf.

[27] EFSA (2020). Peer review of the pesticide risk assessment of the active substance 24-epibrassinolide. EFSA journal. European Food Safety Authority, 18(6), e06132. https://doi.org/10.2903/j.efsa.2020.6132

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

Final decision in relation to Prescription only (Schedule 4) substances contained within research-only kits in very small amounts

Final Decision

Pursuant to r 42ZCZW of the Regulations, the Delegate has made a final decision not to amend the current Poisons Standard in relation to Schedule 4 substances contained within research-only kits in very small amounts.

Materials considered

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

- the Application
- the interim decision notified in writing to the applicant on 4 September 2024
- subsection 52E(1) of the *Therapeutic Goods Act 1989* (Cth) (the **Act**), 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 (f) any other matters considered necessary to protect public health
- the Scheduling Policy Framework 2018 (the **SPF**), and
- the Scheduling handbook: Guidance for amending the Poisons Standard (the **Handbook**).

The applicant did not make a submission on the interim decision.

Proposal

The applicant proposed to exempt from scheduling substances listed in Schedule 4 of the Poisons Standard, such as insulin-like growth factors, interleukins, and interferons, when presented in very small quantities within kits used for research purposes only (the Proposal). The proposal aims to enable consumers who are using small quantities of Prescription only (Schedule 4) substances for research purposes to access these substances without requiring a permit or approval from the relevant state and territory authorities.

Interim decision

The proposal was not referred to an advisory committee for advice. Pursuant to r 42ZCZV of the Regulations, I made an interim decision to not amend the current Poisons Standard in relation to substances included in the Poisons Standard as Prescription only (Schedule 4) substances that are contained within research-only kits in very small amounts. The detailed reasons for my decision follow.

In relation to s 52E (1)(a) of the Act, I noted the application aims to facilitate greater access to Prescription only (Schedule 4) substances for research purposes by exempting these substances from scheduling when contained within kits used in research. Typically, substances within these kits are present only in very small amounts, and it is the applicant's position that there is a very low risk of diversion of these substances under these circumstances. However, there are no mechanisms available under the scheduling framework to restrict supply of these kits to qualified researchers with appropriate authority, or to prevent open supply outside of a research environment. Further, I noted that there are many Prescription only (Schedule 4) substances in research kits which are potent enough in even the quantities present in such kits to pose risks to health from inappropriate use. I formed the view that the supply of Prescription only (Schedule 4) substances to any individuals, regardless of the quantities involved, without any control over access is inappropriate and presents unacceptable public health risks.

Turning to s 52E (1)(b) and (d) of the Act, I acknowledge that Schedule 4 substances are commonly used for research purposes and play significant roles in medical and scientific research. I noted the application stated that the substances are presented in lyophilised form in small quantities in the kits, and as such there are low risks to health associated with these substances. However, I noted that many of these substances can be reconstituted and extracted from the kits, and the amendment does not prevent individuals from accessing significant quantities of these substances by obtaining multiple units of the product. I was not convinced that these measures set sufficient barriers to prevent individuals from accessing and misusing them.

As outlined in the SPF, and with reference to sections 52E(1)(c) and (e) of the Act, substances listed in Schedule 4 of the Poisons Standard are medicines that pose a level of risk such that their use requires medical, veterinary or dental intervention. Many of these substances can cause significant adverse events when used without medical supervision or appropriate training, and some of these substances may also produce dependency or present with potential for abuse. I formed the view that the proposal which enables the direct supply of Prescription only (Schedule 4) substances to any individuals, including unqualified individuals who did not receive appropriate training, may potentially result in misuse and therefore result in toxicity from exposure to these substances.

In considering s 52E (1)(f) of the Act, I note that the Poisons Standard is given legal effect through the drugs and poisons legislation of each state and territory. There are already mechanisms in place in each jurisdiction to enable qualified researchers (with appropriate authority) to access these substances for research purposes. While there is some administrative burden associated with this framework, as indicated by the applicant, I considered the additional burden to be justified given the potential health risks that these substances can present. I therefore concluded that the proposed amendment to the Poisons Standard is not appropriate or necessary.

Based on the above reasons, I decided that the proposal does not align with the SPF. Access to scheduled substances for research purposes is currently managed by the legislation of the states and territories, which provides approvals and permits for qualified researchers with appropriate authority. In my view the risks associated with the proposal outweigh any potential benefits to public health, and therefore I decided not to amend the Poisons Standard in relation to the proposal.

In accordance with r 42ZCZV of the Regulations, the interim decision was communicated to the applicant on 21 June 2024 and written submissions on the interim decision was invited.

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

Pursuant to regulation 42ZCZW of the Regulations I have made a final decision to confirm my interim decision not to amend the current Poisons Standard with respect to Prescription only (Schedule 4) substances contained within research-only kits in very small amounts. My reasons for making the final decision are those set out in the interim decision sent to the applicant. No submission on the interim decision was received from the applicant.

I retain the concerns raised in the interim decision. In particular, I am of the view that the supply of Schedule 4 substances to any individuals, regardless of the quantities involved, without any control over access is inappropriate and presents unacceptable public health risks. Access to Prescription only medicines (Schedule 4) research purposes is effectively managed under state and territory legislation.

Final decision in relation to Azelaic acid

Final Decision

Pursuant to regulation 42ZCZW of the Regulations, I have made a final decision to confirm my interim decision to not amend the Poisons Standard as proposed by the applicant and to amend the Poisons Standard as per the final Decision to amend the Poisons Standard in relation to azelaic acid published on 4 September 2023 (the 2023 Final Decision). The amendments from the 2023 Final Decision are as follows:[28]

Schedule 5 – New Entry

AZELAIC ACID **except** when included in Schedules 2 or 4.

Schedule 4 – Amend Entry

AZELAIC ACID for therapeutic use **except**~~:~~

~~a)~~ when included in Schedule 2.~~; or~~

~~b) in preparations containing 1% or less of azelaic acid for non-human use~~

Schedule 2 – Amend Entry

AZELAIC ACID in dermal preparations for human therapeutic use.

Appendix E – New Entry

Item	Poison	Statement code	First aid instructions
31a	Azelaic acid	A, E1	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

[28] 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

Appendix F – New entry

Item	Poison	Statement code for safety directions	Safety Direction
32a	Azelaic acid	1, 4	1 - Avoid contact with eyes 4 - Avoid contact with skin

Index – Amend Entry

AZELAIC ACID
cross reference: NONANEDIOIC ACID

Schedule 5
Schedule 4
Schedule 2
Appendix E, clause 3
Appendix F, clause 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 azelaic acid (the Application)
- the interim decision notified in writing to the applicant on 4 September 2024
- the 2023 Final Decision
- the interim decision that preceded the 2023 Final Decision (the 2023 Interim Decision)
- the interim decision to not amend the Poisons Standard in relation to azelaic acid published on 3 February 2021 (the 2021 Interim Decision)
- subsection 52E(1) of the Therapeutic Goods Act 1989 (Cth) (the Act), 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 (f) any other matters considered necessary to protect public health
- the Scheduling Policy Framework 2018 (the SPF)
- the Scheduling handbook: Guidance for amending the Poisons Standard (the Handbook), and
- the pregnancy database.

The applicant did not make a submission on the interim decision provided on 4 September 2024.

Proposal

The applicant proposed to amend the current Poisons Standard with regards to azelaic acid through two sequential amendments.

Azelaic acid entry in the current Poison Standard

Schedule 4

AZELAIC ACID **except**:

a) when included in Schedule 2; or

b) in preparations containing 1% or less of azelaic acid for non-human use.

Schedule 2

AZELAIC ACID in dermal preparations.

2023 Final Decision

In the 2023 Final Decision, the Delegate decided to amend the current Poisons Standard in relation to azelaic acid as below:[29]

Schedule 5 – New Entry

AZELAIC ACID **except** when included in Schedules 2 or 4.

Schedule 4 – Amend Entry

AZELAIC ACID for therapeutic use **except**~~:~~

~~a)~~ when included in Schedule 2.~~; or~~

~~b) in preparations containing 1% or less of azelaic acid for non-human use~~

Schedule 2 – Amend Entry

AZELAIC ACID in dermal preparations for human therapeutic use.

Additional First Aid Instructions and Safety Directions under Appendices E and F, respectively, were also included.

These amendments, to be effective on 1 October 2024, will allow industrial uses of azelaic acid under Schedule 5 and retain all therapeutic uses in Schedule 4, with the sole exception for human dermal therapeutic uses in Schedule 2. Under these amendments, all azelaic acid preparations for cosmetic use will be classified as Schedule 5 substances and will require First Aid Instructions and Safety Directions.

[29] 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.

Proposed amendments to the current azelaic acid entry

In November 2023, the applicant proposed to amend the current entry for azelaic acid in 2 tranches. In tranche 1, the current entry will be amended as below with immediate effect.[30]

Schedule 5 – New Entry

> AZELAIC ACID **except** when included in Schedules 2 or 4 or in preparations containing 1% or less of azelaic acid for non-human use.

Schedule 4 – Amend Entry

> AZELAIC ACID for therapeutic use **except**~~:~~
>
> ~~a)~~ when included in Schedule 2.~~; or~~
>
> ~~b) in preparations containing 1% or less of azelaic acid for non-human use.~~

Schedule 2 – Amend Entry

> AZELAIC ACID in dermal preparations for human use except in preparations for cosmetic use when containing no more than 10% azelaic acid.

First Aid Instructions and Safety Directions under Appendices E and F, respectively, as in the 2023 Final Decision will also be included.

In tranche 2, only the Schedule 5 entry will be amended to remove the exemptions for preparations containing 1% or less of azelaic acid for non-human use. The Schedule 5 entry after the second tranche of amendment will read as:[31]

> AZELAIC ACID except when included in Schedules 2 or 4.

There will be no changes to the Schedule 2 and Schedule 4 entries, and First Aid Instructions and Safety Directions from the amendments proposed under tranche 1. Amendments under tranche 2 will come into effect on 1 October 2024.

The immediate implementation of tranche 1 of the proposed amendments will allow early entry into markets of certain non-therapeutic products. These include industrial preparations and cosmetic preparations containing no more than 10% azelaic acid.

The effect of tranche 1 and tranche 2 of the amendments proposed by the applicant, i.e. exempting products containing 1% or less azelaic acid for non-human use products until tranche 2 of the amendments are implemented, is intended to provide industry the lead time required comply with labelling requirements for such products.

The applicant stated that the proposed amendments will result in early availability of a safer product for use during pregnancy and breastfeeding. Limited supporting data or information was provided.

The applicant stated that there is no intention to change the 2023 Final Decision. However, the proposed amendments would cause dermal cosmetic preparations containing more than 10% azelaic acid to be retained in Schedule 2. Such preparations are classified as Schedule 5 substances under the 2023 Final Decision.

I decided under regulation 42ZCZT not to seek advice from the Advisory Committees on Medicines and Chemicals Scheduling for this application.

[30] 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.

[31] 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.

Interim Decision

Pursuant to regulation 42ZCZV of the Regulations, I made an interim decision to not amend the Poisons Standard as proposed by the applicant and to amend the Poisons Standard as per the 2023 Final Decision. The interim decision was provided in writing to the applicant on 4 September 2024.

The amendments to azelaic acid in the 2023 Final Decision have been described above and are to be implemented on 1 October 2024.These amendments will create a new Schedule 5 entry covering the range of industrial uses of azelaic acid while continuing to capture the therapeutic use of azelaic acid under Schedules 2 and 4. This will also provide that any cosmetic preparations containing azelaic acid will be subject to the labelling requirements of Schedule 5 without any exemption as there is not enough evidence to support an exemption from scheduling based on a concentration cut-off.

The applicant submitted that azelaic acid, even in oral medicine form, is safe to use whilst pregnant or breastfeeding and, therefore, azelaic acid in cosmetics provides a safer alternative to retinol and retinol derivatives. In relation to 52E(1)(a) of the Act, topical azelaic acid is listed under category B1 in the TGA's pregnancy database. I noted category B1 substances, such as azelaic acid, have been used by only a limited number of pregnant women and women of childbearing age. I placed less weight on the potential use of azelaic in those pregnant or breastfeeding since my primary concerns are in relation to the potential for skin and eye irritation.

In the 2023 Interim Decision, I set out several risks associated with azelaic acid when used in dermal preparations, including its potential to cause eye and skin irritation. There are various international limitations or restrictions placed upon azelaic acid-containing cosmetics. Under the Association of Southeast Asian Nations (ASEAN) Cosmetics Directive, azelaic acid is a substance that must not form part of the composition of cosmetic products (Annex II Part 1). In New Zealand, dermal use of preparations containing azelaic acid are pharmacy medicines. I have taken into account the Australasian College of Dermatologists submission on the 2023 Interim Decision which expressed a view that the risk of skin irritation from cosmetic preparations containing less than 10% of azelaic acid would be less common. However, they also supported that cosmetic preparations containing azelaic acid should be in Schedule 5.

I noted there are several azelaic acid containing products available in Australia marketed as cosmetics that are used to treat acne and rosacea and claim to reduce inflammation. There is potential for these products to be considered as therapeutic goods due to the nature of such claims.[32]

New compelling evidence has not been presented that support a lower potential for skin and eye irritation at concentrations less than 10%. I also noted that in the 2023 Interim Decision the reasons stated that "any future applications to exempt topical azelaic acid at low concentrations, should include evidence to support the cut-off concentrations". I remained concerned that for products that could be supplied outside a pharmacy environment, with the known potential for azelaic acid to cause skin and eye irritation, that a requirement for First Aid Instructions and Safety Directions remain appropriate.

Therefore, I decided to not amend the Poisons Standard as proposed by the applicant and to amend the Poisons Standard as per the 2023 Final Decision. The decision to not amend the Poisons Standard as proposed in relation to azelaic acid does not preclude reconsideration of scheduling of azelaic acid, should new information on safety and usage become available.

[32] www.tga.gov.au/about-tga/what-we-do/what-are-therapeutic-goods

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 substances:

- Thiafentanil
- Phenidine
- Carbendazim

Decision in relation to thiafentanil

Decision

Pursuant to section 52D(2) of the Act, a Delegate of the Secretary has made a decision to amend the current Poisons Standard in relation to thiafentanil as follows:[33]

Schedule 8 – New Entry

THIAFENTANIL

Index – New Entry

THIAFENTANIL
Schedule 8

Materials considered

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

- 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; and (f) any other matters considered necessary to protect public health
- Pursuant to paragraph 52E(2)(a) of the Act, the SPF, and
- The Handbook.

Reasons for the 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 thiafentanil under Controlled drugs (Schedule 8). This amendment was not referred to an expert advisory committee for its advice.

Thiafentanil (CAS No. 101345-60-2; not be confused with thiofentanyl) is an ultra-potent opioid used internationally. It is available as an intramuscular injection to immobilise certain minor species of hoof stock, excluding minor species that are food producing or may become eligible for consumption by

[33] 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.

humans.[34] There have been reports in Australia of veterinarians importing thiafentanil for this purpose with uncertainty in relation to its scheduling status in Australia. I note there has been uncertainty in relation to its scheduling status in Australia as thiafentanyil is not explicitly listed in the Poisons Standard.

In relation to s 52E(a) of the Act, there is literature to support the use of thiafentanil for immobilising certain hoof stock.[35,36,37,38,39,40] The use of thiafentanyil for this purpose provides specific benefits, including a shorter duration of action and fewer cardiopulmonary depressant effects compared to carfentanyl, which is used for the same purpose and is listed as a Controlled drug (Schedule 8) substance in the Poisons Standard.

Thiafentanil and carfentanyl share a similar chemical structure.[41,42] While their effects can be reversed using an opioid antagonist such as naloxone, both substances are several thousand times more potent than morphine and there is a very high risk of overdose and potential for misuse, abuse, or illicit use. A review by the Department of Health and Human Services in the United States indicated thiafentanil presents a significant risk to public health and should only be used in certain animals for very limited purposed and with extreme caution. The United States Drug Enforcement Administration has classified thiafentanil as a Schedule II substance (dangerous substances considered to have high potential for abuse with the potential to cause dependence).[43]

In accordance with s 52E(a) of the Act, I acknowledge the very high risks associated with thiafentanil exposure in humans. It should only be applied by trained zoologic, wildlife, or exotic animal veterinarians or field biologists supervised by veterinarians. While thiafentanil has a wide margin of safety for the target species when dosed and applied appropriately,[44] introduction of the drug into the human or animal food chain should be avoided.

Safety precautions include use of personal protective equipment and working in pairs with a second person also knowledgeable about the hazards of working with ultra potent opioids. Used needles and syringes contaminated with thiafentanil should also be secured and disposed of in a safe manner.

Based on the available information thiafentanil is expected to used by highly specialised and experienced veterinarians in specific settings. Veterinarians operating in zoo environments are knowledgeable, highly competent and experienced professionals who are aware of the serious health consequences of thiafentanil exposure. I am not aware of any incidents in Australia where a specialised user of thiafentanil has been harmed. I am satisfied these veterinarians will abide by the required processes when handling thiafentanil. Introduction in human or animal food chain is not an issue with zoological animals.

Since thiafentanil has therapeutic value and its risks can be appropriately managed in the circumstances in which it is expected to be used, I have decided to explicitly list thiafentanil as a Controlled drug (Schedule 8) of the Poisons Standard.

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[34] https://www.fda.gov/media/101539/download#:~:text=THIANIL%20contains%20thiafentanil%2C%20a%20high,caution%20to%20avoid%20accidental%20exposure

[35] Lapid R, King R, Bdolah-Abram T, Shilo-Benjamini Y. A retrospective comparison of chemical immobilization with thiafentanil, thiafentanil-azaperone, or etorphine-acepromazine in captive Persian fallow deer (*Dama dama mesopotamica*). J. Zoo Wildl. Med. 2017 Sep;48(3):627-635. doi: 10.1638/2016-0280.

[36] Wolfe LL, Lance WR, Miller MW. Immobilization of mule deer with thiafentanil (A-3080) or thiafentanil plus xylazine. J Wildl Dis. 2004 Apr;40(2):282-7. doi: 10.7589/0090-3558-40.2.282.

[37] Kilgallon CP, Lamberski N, Larsen RS. Comparison of thiafenantil-xylazine and carfentanil-xylazine for immobilization of gemsbok (Oryx gazella). J Zoo Wildl Med. 2010 Sep;41(3):567-71. doi: 10.1638/2010-0021.1.

[38] Cooper DV, Grobler D, Bush M, Jessup D, Lance W. Anaesthesia of nyala (Tragelaphus angasi) with a combination of thiafentanil (A3080), medetomidine and ketamine. J S Afr Vet Assoc. 2005 Mar;76(1):18-21. doi: 10.4102/jsava.v76i1.388.

[39] Citino SB, Bush M, Grobler D, Lance W. Anaesthesia of roan antelope (Hippotragus equinus) with a combination of A3080, medetomidine and ketamine. J S Afr Vet Assoc. 2001 Mar;72(1):29-32. doi: 10.4102/jsava.v72i1.605. PMID: 11563714.

[40] Citino SB, Bush M, Grobler D, Lance W. Anesthesia of boma-captured Lichtenstein's hartebeest (Sigmoceros lichtensteinii) with a combination of thiafentanil, medetomidine, and ketamine. J Wildl Dis. 2002 Apr;38(2):457-62. doi: 10.7589/0090-3558-38.2.457. PMID: 12038149.

[41] https://pubchem.ncbi.nlm.nih.gov/

[42] https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/carfentanil

[43] https://www.dea.gov/drug-information/drug-scheduling

[44] https://veteriankey.com/thiafentanil-oxalate-a3080-in-nondomestic-ungulate-species/

Implementation date

1 October 2024

Decision in relation to phenidines

Decision

Pursuant to section 52D(2) of the Act, a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to phenidines as follows: [45]

Schedule 9 – New entries

DIPHENIDINE

EPHENIDINE

METHOXPHENIDINE

PROPYLPHENIDINE

ISOPHENIDINE

Index – New entries

DIPHENIDINE
cross reference: CAS No. 28383-15-5

Schedule 9

EPHENIDINE
cross reference: CAS No. 60951-19-1, EPHENIDINE HYDROCHLORIDE (CAS No. 6272-97-5)

Schedule 9

METHOXPHENIDINE
cross reference: CAS No. 127529-46-8, METHOXPHENIDINE HYDROCHLORIDE (CAS No. 2055777-48-3), MXP

Schedule 9

PROPYLPHENIDINE
cross reference: CAS No. 6266-42-8

Schedule 9

ISOPHENIDINE
cross reference: CAS No. 774118-46-6, NPDPA, ISOPHENIDINE HYDROCHLORIDE (CAS No. 6267-56-7), ISOPROPYLPHENIDINE

Schedule 9

[45] 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 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; and (f) any other matters considered necessary to protect public health
- The review by the United Kingdom's Advisory Council on the Misuse of Drugs (ACMD) of the evidence on the use and harms of diphenidine
- The World Health Organization's Critical Review Reports on diphenidine and methoxphenidine
- 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 paragraph 52D(2)(a) of the Act, I have taken into account the information provided in the materials listed above. I have decided to create new Prohibited substances (Schedule 9) entries for diphenidine, ephenidine, methoxphenidine, propylphenidine and isophenidine. This amendment was not referred to an expert advisory committee for their advice.

The five substances that are the subject of this decision are dissociative anaesthetics of the phenidine (1,2-diarylethylamine) class (hereafter referred to as phenidines). In Australia, propylphenidine was identified in laboratory testing by the ACT's CanTEST Health and Drug Checking Service in January 2024.[46] Phenidines are currently not included in the Poisons Standard.

Regarding s 52E(1)(a) and (b) of the Act, I note that phenidines are used for recreational purposes mainly in Europe, Japan and the United States of America and use has resulted in several cases of severe intoxication and death. Based on the information before me, substances in this class appear to have no recognised legitimate use, whether therapeutic or otherwise, outside of a research setting and any public exposure appears to be entirely recreational. The dissociative properties of these substances and the lack of reliable toxicity data (see below) means that their abuse and illicit use poses a significant risk to public health.

In relation to s 52E(1)(c) of the Act, phenidines, like ketamines, are antagonists of *N*-methyl-D-aspartate (NMDA) receptors and are noted for their dissociative properties. Depending on the specific substance, the effects of phenidines can include behavioural, emotional, motivational, cognitive and somatosensory and motoric changes, as well as cardiovascular effects including hypertension and tachycardia. While the relatively recent rise in the recreational use of these substances means that information on their toxicity is limited, I note that there have been several recorded cases of intoxication and death resulting from ingestion of phenidines.[47,48]

With regards to s 52E(1)(d) of the Act, in considering material from the Advisory Council on the Misuse of Drugs and the WHO, I note that the detection of phenidines is almost entirely from seizures of drugs that were suspected to be for recreational use.

[46] https://pubmed.ncbi.nlm.nih.gov/38205685/

[47] Critical Review Report: Diphenidine, WHO Expert Committee on Drug Dependence, October 2020
[48] A review of the evidence on the use and harms of Diphenidine and other related substances, Advisory Council on the Misuse of Drugs, United Kingdom, May 2023.

In consideration of s 52E(1)(e) of the Act, phenidines present a high potential for abuse. This is expected for substances with dissociative anaesthetic activity. Notable drugs with similar activity include ketamine and phencyclidine. This aligns with the factor for an entry in Prohibited substances (Schedule 9) of the Poisons Standard that 'the substance has no currently established therapeutic value and is likely to present a high risk of dependency, abuse, misuse or illicit use'. Moreover, I am satisfied that the risks are of such significance as to warrant limiting access to these substances to strictly controlled medical and scientific research.

Finally, regarding s 52E(1)(f) of the Act, the novel nature of these substances means that in many international jurisdictions phenidines are not regulated as a class of substances and many individual substances within the class do not have controls on their manufacture, supply or use. Ephenidine, diphenidine and methoxphenidine have been included as Class B substances in the *Misuse of Drugs Act 1971* in the United Kingdom. The Class B classification recognises the potential harm to public health associated with a substance and includes substances such as amphetamines, barbiturates and cannabis. Diphenidine is also included in Schedule II of the *United Nations' Convention on Psychotropic Substances 1971*. Several phenidines are listed as controlled substances in international jurisdictions including China, Canada, Japan, and many countries in Europe. Import of diphenidine into Australia is controlled under the *Customs (Prohibited Imports) Regulations 1956*.

On the basis of the above considerations, I have decided to amend the Poisons Standard in the manner set out above. The 5 substances to be included in the Poisons Standard are selected due to their inclusion in international regulation and the means available for detection. Further substances in this class may be added in future should the need arise. Due to the clear and immediate public health risks associated with these substances, and there being no current legitimate use of the substances that would be restricted by their inclusion in Prohibited substances (Schedule 9), this amendment was not referred to an expert advisory committee for their advice.

Implementation date

1 October 2024

Decision in relation to carbendazim

Decision

Pursuant to section 52D(2) of the Act, a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to carbendazim as follows: [49]

Schedule 7 – Amend entry

CARBENDAZIM e**xcept** in paints, jointing compounds and sealants containing ~~0.1%~~ 0.35% or less of carbendazim

Index

CARBENDAZIM
Schedule 7

Materials considered

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

- 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
- Australian Industrial Chemicals Introduction Scheme (AICIS) evaluation statement on carbendazim published on 22 December 2022 (AICIS evaluation statement)
- Pursuant to paragraph 52E(2)(a) of the Act, the SPF, and
- The Handbook.

Reasons for the 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 Dangerous poisons (Schedule 7) entry for carbendazim to increase the concertation limit for exemption from 0.1% to 0.35%. This amendment was not referred to an expert advisory committee for their advice.

In considering s 52E(1)(a) and (b) of the Act, carbendazim is a systemic fungicide used to control a broad range of diseases on pulses and macadamias. It is also as a timber treatment to improve the durability and quality of paints, jointing compounds, and sealants.[50] Carbendazim protects the timber, paints, jointing compounds, and sealants against fungal growth, which can affect the aesthetic, integrity and safety of the products over time. Fungal growth can also lead to respiratory issues and allergic reactions. This makes carbendazim particularly useful in moist environments which can promote fungal growth. Currently carbendazim is captured in the Poisons Standard as a Dangerous poison (Schedule 7) substance except in paints, jointing compounds and sealants containing 0.1% or less of carbendazim.

In relation to s 52E(1)(c) of the Act, carbendazim has significant safety concerns but the harm is substantially mitigated at a concentration of 0.35% in paints, jointing compounds, and sealants. I have reviewed the toxicity of carbendazim at 0.35% concentration including the new findings from the AICIS

[49] 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.

[50] https://echa.europa.eu/documents/10162/4230c62d-7422-4c3d-a1e2-38a7f2dd2067

evaluation statement and I am satisfied that that the risks can be managed at the higher concentration limit. I recognise that the critical health effects for carbendazim include systemic long-term effects such as mutagenicity and reproductive toxicity. However, dermal absorption of carbendazim is minimal, with studies demonstrating less than 2% absorption in both human and rat skin when exposed to paint formulations containing carbendazim. Additionally, inhalation risks during typical use of these products are low. The dermal and inhalation margin of exposure's (MOEs) for both methods of paint application (brush and airless spray) were greater than 100 when assuming a maximum concentration of 0.35% carbendazim in paints. This presents an acceptable risk to people applying paint and other surface coverings containing carbendazim at 0.35% or less.

Overall, I find the evidence presented in the AICIS evaluation statement supports an increase in the concentration limit for exempting carbendazim in paints, jointing compounds, and sealants from Dangerous Poisons (Schedule 7) classification from 0.1% to 0.35%. This amendment provides scope to enhance the effectiveness of carbendazim containing products while ensuring that the risks remain controlled and within acceptable limits.

Implementation date

1 October 2024.

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 2024.

Vutrisiran

Schedule 4 – New Entry

VUTRISIRAN

Index – New Entry

VUTRISIRAN

Schedule 4

Ritlecitinib

Schedule 4 – New Entry

RITLECITINIB

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RITLECITINIB

Schedule 4

Odevixibat

Schedule 4 – New Entry

ODEVIXIBAT

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ODEVIXIBAT

Schedule 4

Pinaverium bromide

Schedule 4 – New Entry

PINAVERIUM BROMIDE

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PINAVERIUM BROMIDE

Schedule 4

Lumasiran

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Schedule 4

Version history

Version	Description of change	Author	Effective date
1.0	Original publication	Scheduling and Chemicals Policy Section	September 2024
2.0	Correction of implementation date for homobrassinolide from 1 February 2025 to 1 October 2024 (p. 29)	Scheduling and Chemicals Policy Section	November 2024

Therapeutic Goods Administration

PO Box 100 Woden ACT 2606 Australia
Email: info@tga.gov.au Phone: 1800 020 653 Fax: 02 6203 1605
https://www.tga.gov.au