Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

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

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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 #46, November 2024)

Final decision in relation to *Atropa belladonna*

Proposal

The Delegate of the Secretary of the Department of Health and Aged Care had proposed deletion of the Pharmacy medicine (Schedule 2) entry for *Atropa belladonna* (belladonna) from the Poisons Standard, making all preparations Prescription Only medicines (Schedule 4). *Atropa belladonna* is included in Schedule 2, Schedule 4 and Appendix G in the current Poisons Standard.

Final decision

Pursuant to regulation 42ZCZR of the Regulations, the delegate has decided to confirm the interim decision and amend the current Poisons Standard in relation to *Atropa belladonna* as follows:[2]

Schedule 4

ATROPA BELLADONNA (belladonna) **except** when included in Schedule 2.

Schedule 2 – Amend Entry

ATROPA BELLADONNA (belladonna):

(a) for external use in preparations containing 0.03% or less of total solanaceous alkaloids; or

(b) for oral use in adults and children 6 years of age and over:

(i) in undivided preparations containing 0.03% or less of total solanaceous alkaloids when labelled with a dose of 0.3 mg or less of total solanaceous alkaloids and a recommended daily dose of 1.2 mg or less of total solanaceous alkaloids; or

(ii) in divided preparations containing 0.3 mg or less of total solanaceous alkaloids per dosage unit, when labelled with a recommended daily dose of 1.2 mg or less of total solanaceous alkaloids.

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ATROPA BELLADONNA

Cross reference: BELLADONNA

Schedule 4

Schedule 2

Appendix G, clause 1

[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.

Materials considered

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

- The proposal to amend the current Poisons Standard with respect to *Atropa belladonna* (the **Proposal**)
- The 6 public submissions, all with a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**)
- The advice received from the 46th 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 14 March 2025.
- The 4 public submissions, 3 of which included a written component, received in response to the public consultation on the interim decision under regulation 42ZCZP of the Regulations.
- 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 *Atropa belladonna*. 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 submissions received in response to the public consultation on the interim decision.

All the submissions were in favour of the interim decision with 3 supporting it (2 with written justifications) and one partially supporting (also with written justifications). No response was submitted in opposition to the interim decision.

My decision to amend the Schedule 2 entry for *Atropa belladonna* to restrict oral use to adults and children 6 years of age and older addresses the high incidence of adverse events in children. One submission noted that the age restriction amendment was in response to the recent, high incidence of adverse events in children in extemporaneously compounded preparations. Overall, the submissions agreed that restricting the use of *Atropa belladonna* to children 6 years of age and over will reduce the possibility of misuse and the high incidence of adverse events, including those from compounding preparations, in children.

I remain of the view that due to the very low concentration of solanaceous alkaloids present in listed medicines containing the *Atropa belladonna* they should remain exempt from scheduling per Appendix G.

Considering the recent increase in adverse event reports in children under 6 years of age, I have decided on an immediate implementation date of 1 June 2025. This implementation date will not

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

adversely impact the current supply of listed medicines or the sale of proprietary products containing *Atropa belladonna* and represents an appropriate balance between public safety and access.

Implementation date

1 June 2025

Final decision in relation to astodrimer sodium

Proposal

The Delegate received an application to classify astodrimer sodium vaginal gels for the treatment, relief and prevention of bacterial vaginosis (BV) as Pharmacy medicines (Schedule 2). These preparations are currently listed as Pharmacist Only medicine (Schedule 3). The application also proposed an amendment to the Appendix H entry that would permit advertising of all Schedule 3 preparations of astodrimer sodium. The current Appendix H entry only allows advertising of preparations for the treatment and relief of bacterial vaginosis (BV) and prevention of recurrent bacterial vaginosis (RBV).

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 astodrimer sodium.

Materials considered

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

- the application to amend the current Poisons Standard with respect to astodrimer sodium **(the Application)**
- the 12 public submissions, including 11 with a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**)
- the advice received from the 46th meeting of the Advisory Committee on Medicines Scheduling (the **Committee**)
- the interim decision relating to astodrimer sodium and the materials considered as part of the interim decision, as published on 14 March 2025
- the 5 public 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) 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 astodrimer sodium. 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 submissions received in response to the public consultation on the interim decision.

Out of the 5 submissions, 2 were supportive and 3 were not supportive of the interim decision to not amend the scheduling of astodrimer sodium. The supportive submissions did not provide a written comment. The 3 submissions that did not support the interim decision highlighted the safety of astodrimer sodium in treating BV as illustrated by the lack of reported adverse events in consumers over the past several years. They also noted the efficacy of the product in treating BV and the benefits of increasing access to a non-antibiotic treatment amidst concerns of developing antibiotic resistance in microbes. As outlined in the interim decision, I note that astodrimer sodium is not systemically absorbed and agree that it has a low risk and is well tolerated.

One submission supported the creation of a Schedule 2 entry for astodrimer sodium for all indications as this would increase access to treatment for issues that affect a large portion of the female population. The submissions also highlighted the need for greater discretion when purchasing women's care products of a sensitive nature and argued that the inclusion of astodrimer sodium in Schedule 2 would allow for more discretion when purchasing the medicine or seeking advice from pharmacy staff. One submission acknowledged that private rooms are often available to consult with a pharmacist when purchasing Schedule 3 medicines but felt that accessibility over the counter allows for more discretion when seeking pharmacy advice. One submission acknowledged the risk of incorrect self-diagnosis but considered this is to be the case for many of the Schedule 2 medicines. This submission argued that most people understand that these medicines are only for transient or uncomplicated health issues and that if symptoms persist, they know to seek advice from a doctor.

While astodrimer is considered a safe and effective treatment for BV and RBV, it also has a low potential for treatment-related vulvovaginal candidiasis.[4] Furthermore, the clinical presentation of BV often overlaps with other conditions, including vulvovaginal candidiasis (thrush), sexually transmitted infections (STI) and urinary tract infections (UTI). BV is associated with serious complications such as pelvic inflammatory disease (PID) and an increase in the acquisition of STIs such as chlamydia, gonorrhoea, human immunodeficiency virus and herpes simplex type-2.[5] I remain concerned of the possibility that some women using the substance for BV may not only be at an increased risk of serious sequelae, but they may be suffering from underdiagnosis or misdiagnosis of more serious conditions. I continue to hold the that view consumers are not able to self-diagnose BV without the involvement of a health professional. I also note that vaginal candidiasis has a similar disease risk profile to BV with less serious complications and all the currently marketed vaginal candidiasis treatments are at least Pharmacist only medicines (Schedule 3).

One submission suggested the creation of a Schedule 4 entry for astodrimer sodium for the treatment of RBV and COVID-19 to allow for listing of the medicine on the Pharmaceutical Benefits Scheme (PBS). While this approach may reduce the cost of accessing these products, cost of access is not a consideration for scheduling of substances under s 52(E) of the Act or the SPF. Furthermore, listing of astodrimer sodium as Schedule 4 substance would create additional barriers as consumers will require a prescription to access astodrimer sodium medications.

Opposing submissions also argued for allowing advertising of these products as this would promote consumer awareness of the medicine. I note, however, that references to BV and RBV in advertising about therapeutic goods are restricted representations, as these conditions are considered as serious

[4] Mendling W, Holzgreve W. Astodrimer sodium and bacterial vaginosis: a mini review. Arch Gynecol Obstet. 2022 Jul;306(1):101-108. doi: 10.1007/s00404-022-06429-z.

[5] Bacterial vaginosis. HealthDirect. The Australian Government Department of Health and Aged Care.

forms of a disease, condition, or ailment that require diagnosis, treatment or supervision by a suitably qualified health practitioner.

In summary, whilst I agree with the efficacy and low risk of astodrimer sodium and acknowledge the need for discretion when purchasing medicines for BV, I remain of the view that diagnosis of BV is substantially safer with pharmacist oversight to mitigate the risk of consumer misdiagnosis and provision of appropriate advice for the prevention of BV.

Final decisions on proposed amendments referred to the Advisory Committee on Medicines and Chemicals Scheduling in joint session (Joint ACMS-ACCS #38, November 2024)

Final decision in relation to *Symphytum officinalis* (comfrey)

Proposal

The Delegate received an application to amend the Schedule 5 entry for *Symphytum officinalis* (comfrey) to allow dermal preparations for therapeutic or cosmetic use to be unscheduled when containing 20% or less of comfrey.

Comfrey is captured in the current Poisons Standard as a Caution (Schedule 5) substance for dermal therapeutic or dermal cosmetic use, and Schedule 10 for all other preparations for human or animal use. Schedule 5 preparations containing comfrey are also required to carry safety directions regarding not using on broken skins or under occlusive dressing.

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 comfrey.

Materials considered

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

- the application to amend the current Poisons Standard with respect to comfrey (the **Application**)
- the 6 public submission, with no written component was received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**)
- the advice received from the 38th meeting of the Advisory Committee on Medicines and Chemicals Scheduling in joint session (the **Committee**)
- the interim decision relating to comfrey and the materials considered as part of the interim decision, as published on 14 March 2025
- the 7 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) 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 comfrey. 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 submissions received in response to the public consultation on the interim decision.

Of the 7 submissions received, 3 were supportive and 4 were not supportive of the interim decision to not amend the scheduling of comfrey. The 4 submissions that did not support the interim decision highlighted the historic use of comfrey in traditional medicines and its wide-spread availability across Europe, USA and New Zealand.

One submission proposed that comfrey preparations containing 1% or less of total pyrrolizidine alkaloids (PA) could be exempted from scheduling and additional restrictions on listed medicines containing comfrey could be imposed through the Permissible Ingredients Determination. Another proposed exempting preparations containing 20% or less comfrey from scheduling provided products are labelled as per the current requirements. However, no evidence demonstrating the safety or low risk from preparations containing 20% comfrey extract or 1% PA was presented. PA content in comfrey products can vary substantially, increasing the potential for unintended over exposure and systemic absorption.

One submission noted that two grandfathered registered comfrey preparations are currently listed on the ARTG and therefore, the current scheduling 5 which makes topical comfrey preparations ineligible for use as listed medicines creates a regulatory anomaly and an anti-competitive environment. Historically registered complimentary medicines are evaluated as required.

The current scheduling of comfrey does not allow its use in listed medicines except when present at a concentration of 0.001% or less. I acknowledge topical comfrey preparations are used in traditional medicine to treat a variety of ailments including bruises, skin inflammation and musculoskeletal issues such as osteoarthritis, back pain, ankle sprains, knee joint injuries, joint distortion, myalgia and rheumatism. However, I remain concerned that the intended uses increase the likelihood of incorrect usage on broken skin and can lead to the systemic absorption of PA when applied over large areas of the body or used over a prolonged time.

Finally, I note that the European Union herbal monograph on *Symphytum officinale* L., radix recommends application of a thin layer of 10% liquid extract twice a day on intact skin and limits the daily exposure to PAs via any given topical product to 1 microgram per day for adults. Furthermore, the monograph does not recommend use in children and adolescents under 18 years of age or use for more than 10 days. Overall, in view of the potential toxicity from incorrect use of topical comfrey preparations I have decided not to exempt preparations containing 20% or less of comfrey from the current scheduling.

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:

- Fuzapladib sodium
- Ilunocitinib
- 1,4-Dimethylnapthalene
- Folpet.

Final decision in relation to fuzapladib sodium

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 fuzapladib sodium as follows:[6]

Schedule 4 – New Entry

FUZAPLADIB SODIUM

Index – New Entry

FUZAPLADIB SODIUM

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 fuzapladib sodium (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
- The Handbook.

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

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

The Application is to amend the current Poisons Standard to create a Prescription only (Schedule 4) entry for fuzapladib sodium. Fuzapladib sodium is the active ingredient of a currently unregistered veterinary medicine and is not included in the current Poisons Standard.

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

Fuzapladib sodium is a novel anti-inflammatory substance that helps prevent systemic inflammatory response by inhibiting leukocyte function-associated antigen type-1 (LFA-1). Regarding s 52E(1)(a) of the Act, I note that the benefit of fuzapladib sodium is in its use to manage clinical signs associated with the acute onset of pancreatitis in dogs (Schedule 4, scheduling factor 1). The Australian Pesticides and Veterinary Medicines Authority (APVMA) conducted a Human Health Risk Assessment and concluded that that the risk to human health from accidental exposure to fuzapladib sodium would be negligible when used in a controlled environment such as a veterinary clinic by qualified or trained staff and risks from direct use are not relevant for the general public. Considering the toxicity data (below) and proposed usage by professionals only, I agree with the APVMA's findings.

Regarding s 52E(1)(b) of the Act, I note that fuzapladib sodium is proposed for use as an intravenous injectable solution containing 4 mg/mL fuzapladib sodium. While the product is registered in Japan and has been granted conditional approval in the USA and limited market eligibility in the EU, there is no experience of its usage in Australia (Schedule 4, Scheduling factor 8). It is estimated that approximately 0.18% of the Australian dog population would be treated by the product.

In relation to s 52E(1)(c) of the Act, I note that the acute oral toxicity levels for fuzapladib sodium in rats are low (522-1,414 mg/kg bw). Short-term acute toxicity studies established a no observed adverse effect level (NOAEL) of 5 mg/kg bw/day in dogs (28-day study; based on histopathological changes in the thyroid at 15 mg/kg bw/day) and a NOAEL of 12.5 mg/kg bw/day in rats (14-day study; based on clinical signs, decreased spleen weights and histopathological changes at higher doses). No data was submitted on acute dermal toxicity, inhalation toxicity, skin and eye irritation or skin sensitisation for fuzapladib sodium. Fuzapladib sodium is considered unlikely to have genotoxic potential and there are also no evidence of reproductive and developmental toxicity testing as conducted by the intravenous route in rats and rabbits. The NOAEL for reproduction and development ranged from 45 to 80 mg/kg bw in rats and 60 mg/kg bw in rabbits.

With regards to s 52E(1)(d) of the Act, I noted that the fuzapladib sodium is the active ingredient in a currently unregistered product. The product contains 14 mg fuzapladib sodium in sterilised lyophilised powder which will be dissolved in sterile water and administered as intravenous bolus injection at 0.4 mg/kg bw once daily for three days. The product is intended for use by veterinarians only (Schedule 4, scheduling factor 2). The APVMA, as the regulator of all veterinary products, will consider the dosage, formulation, labelling, packaging and presentation of fuzapladib sodium containing products during the product registration process.

As fuzapladib will not be used in food producing animals, no Acceptable Daily Intake (ADI), Acute Reference Dose (ARfD) or Maximum Residue Limit (MRL) have been established. Absence of these factors has no impact on the scheduling considerations for fuzapladib sodium.

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

Implementation date

1 June 2025

Final decision in relation to ilunocitinib

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 ilunocitinib as follows:[7]

Schedule 4 – New Entry

ILUNOCITINIB

Index – New Entry

ILUNOCITINIB

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 Ilunocitinib (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.

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

The Application is to amend the current Poisons Standard to create a new entry for Ilunocitinib as a Prescription only (Schedule 4) substance. Ilunocitinib is an active ingredient for a currently unregistered veterinary medicine and is not listed in the current Poisons Standard.

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

Ilunocitinib is an inhibitor of Janus Kinase (JAK) receptors. JAK receptors are cytoplasmic non-receptor type tyrosine kinases that regulate transcription of selected genes through the signal transduction and activator of transcription (STAT) proteins. Inhibition of the JAK-STAT signalling pathway inhibit the transcription of several genes involved in inflammatory, immune, and cancer conditions.

In relation to s 52E(1)(a) and (b) of the Act, I note that the ilunocitinib is an active ingredient of 4 medicines yet to be registered in Australia for the treatment of pruritis associated with allergic dermatitis and clinical manifestations of atopic dermatitis in dogs. Allergic dermatitis and atopic dermatitis require veterinary diagnosis and intervention, and the underlying causes and/or

[7] 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

complicating factors may need further investigation and adjunctive therapy (Schedule 4, scheduling factors 1 and 2).

Regarding s 52E(1)(b) of the Act, it is estimated that 6,500 packs (90 tablets each) of the product will be sold in the first year, representing about 5,000 g of ilunocitinib across all product strengths. This number may increase to 8,000 packs (about 6,000 g of ilunocitinib) in the second year.

Immunosuppression is an expected pharmacological effect of ilunocitinib (see below). There may be increased susceptibility to infections in dogs receiving treatment, which should be monitored. The margin of safety between the therapeutic and toxic dose in dogs is at least 5 times (tablet formulation). However, there is no specific antidote and in the case of any overdose, dogs should be treated symptomatically. Therefore, monitoring or intervention by a veterinary practitioner is required to minimise the risk of harm (Schedule 4, scheduling factors 5 and 6).

With regards to s 52E(1)(c) of the Act, I note that the Application provided toxicology information for both ilunocitinib (the active ingredient) and the finished product. The acute oral toxicity level for ilunocitinib in rats is low (LD_{50} >2,000 mg/kg bw). No studies were submitted on acute dermal and inhalation toxicity. However, ilunocitinib is not considered a skin or eye irritant or a skin sensitiser.

In repeat dose oral toxicity studies in rats and dogs, immunosuppressive effects were observed in the haematopoietic, lymphoid systems and skin. The lowest observed adverse effect level (LOAEL) was 0.8 mg/kg bw/day. The immunosuppressive effects of ilunocitinib are consistent with its pharmacological activity of JAK inhibition.

Major bone abnormalities were observed in a key developmental study in rats which is likely due to inhibition of the JAK/STAT pathway which is involved in bone development. Similar observations have been made for other JAK inhibitors. Both the developmental LOAEL and the no observed adverse effect level (NOAEL) for maternal toxicity of ilunocitinib were estimated to be 1 mg/kg bw/day in rats. In rabbits, the NOAELs for both developmental and maternal toxicity were 10 mg/kg bw/day indicating rats are more sensitive to ilunocitinib than rabbits. However, a comprehensive battery of genotoxicity tests with ilunocitinib phosphate salt indicated that ilunocitinib is non-genotoxic.

Regarding the formulated product, no studies were submitted for acute oral, dermal, and inhalation toxicity or skin sensitisation. However, it is estimated that the acute oral and dermal toxicity levels are LD_{50} >2,000 mg/kg, and the inhalation toxicity level is LC_{50} >5,000 mg/m³. The product is not expected to be a skin sensitiser and based on *in vitro* skin and eye irritation studies, it is not a skin or eye irritant.

Since the product will not be used in food-producing animals, no Acceptable Daily Intake (ADI), Acute Reference Dose (ARfD) or Maximum Residue Limit (MRL) have been established for ilunocitinib. The absence of these factors has no impact on the scheduling considerations for ilunocitinib.

With regards to s 52E(1)(d) of the Act, ilunocitinib is intended to be used as 15 mg, 8.5 mg, 6.4 mg and 4.8 mg oral tablets for dogs. The film-coated and scored tablets will be packaged in child-resistant blister packaging, with 10 tablets/blister card, packed within a cardboard carton in pack sizes of 10, 30 and 90 tablets. Tablets will be administered orally to dogs by owners under the direction of a veterinarian. Handling the tablets can expose owners, especially when breaking them in half.

The Australian Pesticides and Veterinary Medicines Authority (APVMA) conducted a Human Health Risk Assessment (HHRA) that indicated a margin of exposure considerably greater than 100 for adults administering the intended products to dogs without any personal protective equipment. In the case of accidental oral ingestion where a single maximum dosing (3 x 15 mg tablets for a 75 kg dog) is ingested by a 10 kg child, the exposure (4.5 mg/kg bw) is well below the acute oral LD_{50} for ilunocitinib (>2,000 mg/kg). Use of child resistant packaging will further minimise the risk from accidental ingestion by children. The risk of developmental effects in pregnant women administering ilunocitinib to dogs is also considered negligible due to the low exposure and high MOE. I have considered usage and benefits against the relatively low risk of substance toxicity and it potential to elicit adverse effects from acute or repeat exposure. I am of the view that the benefits posed by ilunocitinib outweigh the risks to

human health and the proposed labelling for the product, including the safety directions, are appropriate to manage the risks.

Regarding s 52E(1)(f), I note that only experimental clinical experience is available for ilunocitinib (Schedule 4, scheduling factor 8). However, another JAK inhibitor, oclacitinib is approved in Australia to treat atopic dermatitis in dogs as a Schedule 4 medicine. Similarity, several JAK inhibitors approved for use in human (baricitinib, deucravacitinib, ruxolitinib, tofacitinib and upadacitinib) are also listed as Schedule 4 medicines.

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

Implementation date

1 June 2025

Final decision in relation to 1,4-dimethylnapthalene

Final Decision

Pursuant to regulation 42ZCZU of the Regulations, a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to 1,4-dimethylnaphthalene as follows.

Schedule 5 – New Entry

1,4-dimethylnaphthalene for use as agricultural chemicals

Index – New Entry

1,4-dimethylnaphthalene

Schedule 5

Materials considered

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

- The application to amend the current Poisons Standard with respect to 1,4-dimethylnaphthalene (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)

The Application is to amend the current Poisons Standard to create an entry for 1,4-dimethylnaphthalene (1,4-DMN) as a Caution (Schedule 5) substance. 1,4-DMN is the active ingredient in a currently unregistered agricultural product and is not listed in the current Poisons Standard.

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

1,4-DMN belongs to the chemical family of alkylated naphthalenes and acts as a plant growth regulator preventing sprouting of potato tubers. It also occurs naturally in different plant species with background values up to 60 µg/kg in potato, 0.4 µg/kg in poppy and up to 12 µg/kg in poppy tops.

In relation to s 52E(1)(a) and (b) of the Act, 1,4-DMN is proposed to be used in an agricultural product for enhancing dormancy of potatoes in storage and preventing sprouting. 1,4-DMN has been registered in the USA since the mid-1990's, and is registered in Canada, Kenya, and Mexico and received approvals in over 20 European countries.

Regarding s 52E(1)(b) and (d) of the Act, 1,4-DMN is proposed to be used as liquid formulation containing 980 g/L of the substance. The product is intended for professional use and will be applied mechanically via specialist thermal fogging equipment in enclosed area. The product will be available in 20 L fluorinated high-density polyethylene (HDPE) containers. The application provided that around 700 to 1,400 litres 1,4-DMN will be used per annum during the first 2 years of its registration.

The Australian Pesticides and Veterinary Medicines Authority (APVMA) has undertaken a Human Health Risk Assessment (HHRA) and recommended health-based guidance values including Acceptable Daily Intake (ADI) and the Acute Reference Dose (ARfD), and appropriate first aid instructions and safety directions along with other safety precautions for the label. In consideration of the toxicity information presented in the HHRA (see below), the proposed usage pattern of 1,4-DMN and the recommended label statements, I am satisfied that the risk of 1,4-DMN associated adverse effects can be adequately mitigated and 1,4-DMN containing product can be used safely in agricultural applications by adherence to product label instructions.

In relation to s 52E(1)(c) of the Act, I note that the acute toxicity of 1,4-DMN in rats is low (oral LD50 >2,000 mg/kg bw; dermal LD_{50} >2,000 mg/kg bw and inhalation LC_{50} >4.16 mg/L). Studies indicated that 1,4-DMN is a moderate eye irritant and slight skin irritant in rabbits and not a skin sensitiser in guinea pigs (Buehler method). Based on the limited, but sufficient data, the acute and repeat dose toxicological profile are aligned with scheduling factor 1 for Scheduling 5 classification.

I have also considered the repeat dose (sub-chronic and long-term) toxicity studies in rats. The major target tissue was the kidney with effects including chronic progressive nephropathy (CPN), basophilic tubules, mononuclear cell infiltration, karyomegaly of the cortical tubules, proteinosis in the papilla tubules, and papillary necrosis. CPN is a kidney finding repeatedly observed in aging rats and not considered relevant to humans.[8]

1,4-DMN is unlikely to be genotoxic based on an adequate range of *in vivo* and *in vitro* studies. I noted that no effects on reproduction, neurotoxicity or immunotoxicity were observed, and no evidence of carcinogenicity was found in rats. These findings are consistent with a Schedule 5 classification (scheduling factor 2). I also note that the HHRA concluded that the acute toxicity profile of the 1,4-DMN and the proposed product are considered identical, given their formulation.

In relation to s 52E(1)(e) of the Act, I am satisfied the potential for misuse or abuse of 1,4-DMN 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.

[8] Gordon C. Hard, Marcy I. Banton, Robert S. Bretzlaff, Wolfgang Dekant, Jefferson R. Fowles, Anthony K. Mallett, Douglas B. McGregor, Kathleen M. Roberts, Robert L. Sielken, Ciriaco Valdez-Flores, Samuel M. Cohen, Consideration of Rat Chronic Progressive Nephropathy in Regulatory Evaluations for Carcinogenicity, *Toxicological Sciences*, Volume 132, Issue 2, April 2013, Pages 268–275. DOI: https://doi.org/10.1093/toxsci/kfs305

Based on the above considerations and the information provided in the Application, I have decided to amend the current Poisons Standard regarding 1,4-DMN in the manner laid out above. This amendment was not referred to an expert advisory committee for advice.

Implementation date

1 June 2025

Final decision in relation to folpet

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 folpet as follows.

~~**Schedule 7 – Amend Entry**~~

~~FOLPET~~

Schedule 6 – New Entry

FOLPET

Index – New Entry

FOLPET

Schedule 6

~~Appendix J, clause 1~~

Materials considered

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

- The application to amend the current Poisons Standard with respect to folpet (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)

This proposal is to reschedule the substance folpet from Dangerous poisons (Schedule 7) into Poisons (Schedule 6) of the Poisons Standard and to remove the Appendix J entry that limits availability of folpet only to an appropriately authorised or licensed person.

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

Folpet is a phthalimide fungicide, which is a multi-site inhibitor acting simultaneously on several target sites in fungi. An agricultural fungicide, it has been used to control mildew, leaf spot, and other diseases in crops since the 1950s. The product is approved for use in USA, Europe, South Africa and New Zealand.

Regarding s 52E(1)(a) and (b) of the Act, folpet is proposed to be used in Australia as fungicide to control anthracnose (*Colletotrichum spp.*), grey mould (*Botrytis cinerea*), downy mildew (*Plasmopara viticola*), black spot (*Elsinoe ampelina*) and dead arm in grapes. While currently there is no folpet product available in Australia, it appears that other folpet-containing products (eg. 'Phaltan') were available in Australia during the 1960s. The Australian Pesticides and Veterinary Medicines Authority (APVMA) has conducted a Human Health Risk Assessment (HHRA) for folpet and concluded that the risks can be adequately mitigated via appropriate labelling. After considering the toxicity information presented in the HHRA (see below), the proposed usage pattern of the folpet product and the recommended label statements, I agree with the APVMA's conclusions.

In relation to s 52E(1)(b) and (d) of the Act, the product, Folpet 800WG Fungicide, is a professional-use product with 800 g/L folpet in a water dispersible granular formulation. It will be applied to grapevine foliage using banded or broadcast spray applicators at a final rate of 125 g/100 L. The Product will be available in 1-20 kg pack sizes in plastic bags for use by professionals.

With regard to s 52E(1)(c) of the Act, based on the data presented in the HHRA, the acute oral, dermal and inhalational toxicity levels for folpet are low in animal studies (LD_{50} >2,000 mg/kg bw for oral in rats and dermal routes in rats for folpet, and rabbits for the product). These low acute toxicity values meet the scheduling factor 1 for Scheule 5. However, folpet dust has moderate inhalational toxicity (LC_{50} >1,080 mg/m^3 for micronized dust) in rats when administered by the nose-only route (Schedule 6, scheduling factors 1 and 2).

Based on the animal studies, folpet is not a skin irritant, while the product is a moderate skin irritant. Further, both folpet and the product are severe eye irritants and severe skin sensitisers, which aligns with Schedule 6, scheduling factor 1.

In reference to the repeat dose toxicity, local irritating effects were observed in rats in feeding studies (acanthosis and hyperkeratosis and/or ulceration/erosion of the stomach) and following repeat dermal administration (acanthosis, exudate and skin ulcers). Folpet was not a developmental or reproductive toxicant in multigeneration studies. In 1984, the Pesticides and Agricultural Chemicals Standing Committee recommended rescheduling of folpet from exempt to S7 based on the induction of neoplastic growth in the duodenum of several strains of mice and positive results in multiple *in vitro* mutagenicity assays. The genotoxic potential of folpet was investigated in a battery of genotoxicity tests. While folpet showed positive results in *in vitro* studies, there was no indication of DNA damage *in vivo* up to 2,000 mg/kg bw/day.[9] It is considered that the genotoxic potential of folpet is not expressed *in vivo*, possibly because of the high reactivity of folpet with thiol groups in proteins in the mucous membrane of gastrointestinal tracts resulting in rapid degradation and reduced systemic exposure to folpet. Folpet metabolites phthalimide, phthalamic acid, phthalic acid, phthalic anhydride and 2-cyanobenzoic acid are unlikely to be genotoxic based on the available genotoxicity data and *in silico* predictions.[10] Based on the weight of evidence, folpet is not considered to pose a genotoxic or carcinogenic risk to humans. In relation to s 52E(1)(e) of the Act, I am satisfied the potential for misuse or abuse of folpet 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.

[9] European Food Safety Authority, 2009. Conclusion regarding the peer review of the pesticide risk assessment of the active substance folpet. *EFSA Journal* 2009; 7(8):RN-297, 80 pp. doi:10.2903/j.efsa.2009.297r

[10] EFSA (European Food Safety Authority), Álvarez, F., Arena, M., Auteri, D., Leite, S. B., Binaglia, M., Castoldi, A. F., Chiusolo, A., Cioca, A.-A., Colagiorgi, A., Colas, M., Crivellente, F., De Lentdecker, C., De Magistris, I., Egsmose, M., Fait, G., Ferilli, F., Gouliarmou, V., Halling, K., … Villamar-Bouza, L. (2023). Peer review of the pesticide risk assessment of the active substance folpet. *EFSA Journal,* 21(8), 1–32. https://doi.org/10.2903/j.efsa.2023.8139

Regarding s 52E(1)(f) of the Act, a closely related fungicide captan, is listed in Schedule 6 of the Poisons Standard with no cut-off. Captan has a toxicity profile similar to folpet (low acute oral and dermal toxicity but severe eye irritation) and was classified as Schedule 7 based on its mutagenic properties *in vitro*. However, captan was later down scheduled to Schedule 6 considering genotoxicity data *in vivo* was predominantly negative and the overall weight-of-evidence also indicating folpet unlikely to be genotoxic.

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

Implementation date

1 June 2025

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 June 2025.

DATOPOTAMAB DERUXTECAN

Schedule 4 – New Entry

DATOPOTAMAB DERUXTECAN

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DATOPOTAMAB DERUXTECAN

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Schedule 4

TEPROTUMUMAB

Schedule 4 – New Entry

TEPROTUMUMAB

Appendix F, clause 4 - New Entry

Item	Column 1 Poison	Column 2 Warning statement item number
332	Teprotumumab	7, 62, 76, 110

Appendix L, clause 2 - New Entry

Item	Column 1 Poison	Column 2 Warning statement item number
36	Teprotumumab	7, 62, 76, 110

Index – New Entry

TEPROTUMUMAB

Schedule 4

Appendix F, clause 4

Appendix L, clause 2

TEZEPELUMAB

Schedule 4 – New Entry

TEZEPELUMAB

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TEZEPELUMAB

Schedule 4

VELMANASE ALFA

Schedule 4 – New Entry

VELMANASE ALFA

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VELMANASE ALFA

Schedule 4

Version history

Version	Date	Description of changes
1.0	19 May 2025	Original document
2.0	23 June 2025	On p. 20, the amendment of NCEs in relation to DATOPOTAMAB DERUXTECAN was incorrectly shown as VELMANASE ALFA and now has been corrected.

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