Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

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

13 December 2024

Confidentiality

All submissions received will be placed on the TGA's Internet site, unless marked confidential. Any confidential material contained within your submission should be provided under a separate cover and clearly marked "IN CONFIDENCE". Reasons for a claim to confidentiality must be included in the space provided on the TGA submission form. For submission made by individuals, all personal details, other than your name, will be removed from your submission before it is published on the TGA's Internet site. In addition, a list of parties making submissions will be published. If you do not wish to be identified with your submission you must specifically request this in the space provided on the submission form.

Contents

Notice of interim decisions made under Regulation 42ZCZV and 42ZCZN of the *Therapeutic Goods Regulations 1990*

This publication constitutes a notice for the purposes of regulation 42ZCZP of the *Therapeutic Goods Regulations 1990* (the **Regulations**). This notice sets out:

- the interim decision for nicotinic acid made by a delegate of the Secretary under regulation 42ZCZV in relation to proposed amendments to the current Poisons Standard which were not referred to an expert advisory committee[1] under subdivision 3D.3 of the Regulations.
- the interim decision for intravenous potassium salts made by a delegate of the Secretary under regulation 42ZCZN in relation to proposed amendments to the current Poisons Standard which were referred to an expert advisory committee under subdivision 3D.2 of the Regulations in June 2024;
- the proposed date of effect of the proposed amendments (in circumstances where the interim decision proposes an amendment to the current Poisons Standard).

Interested persons (including the applicant requesting the amendment) are invited to make submissions to the Secretary in relation to these interim decisions on or before 7 January 2024.

Submissions should be provided through our consultation hub. Submissions will be considered by the Delegate in making the final decision.

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 be defined for individual decisions.

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

Interim decision in relation to intravenous potassium salts

Proposal

The Delegate received an application to create a new Prescription Only medicine (Schedule 4) entry for preparations of potassium salts for injection or infusion. Potassium salts for intravenous (IV) administration are currently unscheduled.

Interim decision

Pursuant to regulation 42ZCZN of the Regulations, the Delegate has, in relation to the proposed amendment, made an interim decision create a new entry for potassium salts in Schedule 4 of the Poisons Standard as follows:[2]

Schedule 4 – New Entry

POTASSIUM SALTS, including chloride, phosphate or acetate salts of potassium alone or in any combination, in preparations for therapeutic use for injection or infusion **except**:

a) those with a concentration of less than 10 mmol/100 mL of potassium; AND
b) pre-mixed infusion bags with a total amount of 25 mmol or less of potassium per bag

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POTASSIUM SALTS
cross reference: POTASSIUM CHLORIDE, POTASSIUM PHOSPHATE, POTASSIUM DIHYDROGEN PHOSPHATE, POTASSIUM ACETATE
Schedule 4

Materials considered

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

- The application to amend the current Poisons Standard with respect to potassium salts (the **Application**)
- The 3 public submissions, with 2 including a written component, received in response to the pre-meeting consultation and a targeted consultation with hospital pharmacy representative peak body - Advanced Pharmacy Australia (AdPha) (the **Submissions**)
- The advice received from the 37th meeting of the Advisory Committee on Medicines and Chemicals Scheduling in Joint session (the **Committee**)
- 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
- The SPF
- The Handbook

[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.

Summary of Committee advice to the Delegate

The Committee agreed on the principles for the creation of a Schedule 4 entry for IV potassium salts. The wording and any concentration thresholds in the Poisons Standard to be created should be decided following further consultation and input – in particular, with hospital pharmacists.

It was agreed the intent of the Schedule 4 entry should:

- include intravenous and injectable potassium salt products used for potassium replacement, which have a high concentration of potassium and can be life threatening if administered incorrectly.
- consider including larger bags (500 mL and 1 L bags) with a total amount of potassium that might cause hyperkalaemia and severe adverse effects if administered incorrectly.
- consider including supply of extemporaneously manufactured products but could exclude premade products.
- consider excluding products used for total parenteral nutrition which are supplied through hospitals, noting that such products are already exempt through Appendix A of the Poisons Standard.

The Committee recommended that the scheduling of potassium salts for intravenous use in Schedule 4 is appropriate. The Committee recommended a potential implementation date of **1 October 2025** as further consultation on the potential impacts in the hospital setting should be sought.

The Committee recommended that the wording of the entry should be developed by the Delegate pending further advice on suitable cut-off values and impact on hospitals.

Members agreed that the relevant matters under subsection 52E(1) of the Act included: (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.

The reasons for the advice included:

a) the risks and benefits of the use of a substance

Risks:

– Risks of inadvertent hyperkalaemia which can potentially be life threatening.

– Rapid IV administration or overdose may cause cardiac arrest.

– Cardiac depression, arrythmia, death.

– Fluid overload

– Peripheral vein extravasation/thrombophlebitis.

Benefits:

– Prevention and treatment of moderate to severe potassium deficiency (hypokalaemia) when oral therapy is not possible or rapid replacement is necessary.

– Moderate to severe potassium deficiency can lead to life threatening complications including arrhythmias, paralysis and rhabdomyolysis.

b) the purposes for which a substance is to be used and the extent of use of a substance

- Intravenous potassium is used for the prevention and treatment of moderate to severe potassium deficiency (hypokalaemia) when oral therapy is not possible or rapid replacement is necessary.
- Potassium chloride at high concentration is also used for parenteral administration (for nutritional reasons).
- Potassium chloride and potassium acetate: treatment of hypokalaemia, digitalis intoxication.
- Potassium phosphate: treatment of hypophosphatemia

c) the toxicity of a substance

- Injection of undiluted solution or infusion without controlled rate of delivery, such as rapid administration, can cause cardiac arrest or death.

d) the dosage, formulation, labelling, packaging and presentation of a substance

- 80 products containing potassium chloride for injection and infusion on ARTG.
- The strength and dose of intravenous potassium salts is described in millimoles. Therefore, the labelling of products should display the strength in millimoles.
- Various pack sizes of concentrated solutions from 10 mL ampoule to 100 mL infusion

e) the potential for abuse of a substance

- High potential for inadvertent misuse.
- May be misused as a ‘wellness therapy’ or hangover treatment.
- Given its cardiotoxic properties, potassium chloride has been included, albeit rarely used, in assisted dying protocols.
- Although rare, lethal injection of concentrated intravenous potassium chloride has been used in suicide.

f) any other matters that the Secretary considers necessary to protect public health

- Consideration of regulation and controls in other jurisdictions e.g., in the UK and USA – intravenous potassium chloride is a prescription only medicine.
- Impacts on users and may change prescribing practice (possibility of need for dual prescribing – fluid chart and prescription).
- Delegate should consider cut off levels so that low strength products and total parenteral nutrition products are not captured.
- 10 mmol in 10 mL to capture the ampoules only and not any of the premixed bags

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

I agree with the Committee's findings on the relevant provisions of section 52E of the Act.

I have made an interim decision to amend the Poisons Standard with regard to potassium salts in preparations for therapeutic use for injection or infusion. In making this decision I have balanced the potential benefits of increased prescriber oversight against the unintended possibility of decreasing access to potassium salts used for the treatment of hypokalaemia, digitalis intoxication and treatment of hypophosphatemia.

I have considered the risk of potassium salts remaining unscheduled and the potential for administration in “wellness” settings or as a hangover treatment, in the absence of prescription controls. If left unscheduled, there is a risk that untrained or unregistered people might purchase it for injection, which could result in infection related deaths, as has been seen with high dose vitamin C injection use outside of hospitals.

I have considered the 2 written public submissions received during the pre-meeting consultation period. Both written responses received were fully supportive of the applicant’s proposal. One further response was received and indicated support for the proposal while not providing reasons for their support, noting that the submissions were all in favour of the scheduling proposal.

Within hospital settings, I note that all Australian jurisdictions have rigorous protocols for the management, storage, charting and administration of potassium and they have been managing potassium salts in preparations for injection or infusions for many years.

Feedback was received from the hospital pharmacy representative peak body, Advanced Pharmacy Australia (AdPha), for the proposed Schedule 4 entry for intravenous potassium salts. In its view, it is not envisaged that a Schedule 4 listing for intravenous potassium salts will impede patient access or the established workflows of care in the hospital and health service environment, if reasonable steps are taken to ensure Nurse Practitioners can continue to prescribe and chart them in hospital settings. AdPha supports increased safety measures to reduce inappropriate use of intravenous potassium salts, as misuse can be fatal.

The risks involved in the administration of these products are documented and a Schedule 4 entry is intended to reflect the dangers posed to human health and safety through the use of these products. It is not intended to further inconvenience hospital activities. It is my understanding that most hospital protocols ensure that dosage forms containing stronger concentrations of potassium salts, including ampoules, are not available on general wards. Ampoules are generally restricted to specific departments, such as emergency department and critical care units and/or locked in a medication safe.

I have considered that concentrated solutions of potassium salts, when administered intravenously, or through any other injection route, meet with the SPF factors for Schedule 4. This includes vials of diluted potassium salts and the mini bags containing 10 mmol in 100 mL. In considering exemptions from a Schedule 4 entry, I have considered that a higher concentration of potassium in a fluid poses a greater risk commensurate to a Schedule 4 entry. The total volume is a factor which can contribute to the risk of adverse events, if not carefully administered under instruction of a medical practitioner. Consequently, I have chosen to include a concentration cut off and a total volume to address the risks posed.

Premix bags are first line treatments and are safer to use in all settings, however, they are still not without risk. When additional potassium is added by a registered health practitioner, there is still a greater risk to the patient than premixed bags. Bags with additional potassium present an increased risk as the patient may receive a bolus of concentrated potassium which would cause an adverse incident. Both a premixed bag, and that with additional potassium added, have a risk of causing adverse incidents if infused at too fast a rate. I have considered whether pre-mixed bags could be exempt from the Schedule 4 entry. However, an overly rapid infusion rate or incorrect medicine selection could also have catastrophic consequences for the patient. To minimise this risk, I have not excluded the majority of premixed infusion bags from the Schedule 4 entry, except those manufactured in lower doses and at lower concentrations.

I have decided at this stage to exclude lower dose, premixed electrolyte combination bags with multiple ingredients. These pre-mixed formulations have a lower risk of a bolus dose being administered as potassium is not added manually at the point of dispensing, but rather added during the manufacturing process, resulting in the production of a standardised uniform (homogenous) mixture.

While in most jurisdictions, IV potassium is prescribed in hospitals using a fluid chart, there were concerns raised by the Committee that prescribers may also chart on the patient medication chart, resulting in duplicate prescribing and potential for an increase in medication errors. It is my intention that a change to the scheduling of potassium does not generate further unforeseen impacts, such as workflow issues, storage or accessibility issues in the hospital environment. Further, I acknowledge the importance of the accessibility of these products required during diabetes ketoacidosis and invite further submissions from affected non-prescribers on this interim decision.

I note that most international jurisdictions, including the UK and USA, regulate intravenous potassium as prescription only medicines.

I note also that medicine bags for total parenteral nutrition, prepared in hospital by pharmacists and dietitians, are exempt from Scheduling under Appendix A of the Poisons Standard.

I have decided to depart from the Committee's recommended implementation date of 1 October 2025 and allow for a greater transition time for industry and to accommodate for changes that may have to occur within health professional settings.

Implementation date

1 June 2026

Interim decision in relation to nicotinic acid

Proposal

The Delegate received an application to create a new Schedule 5 entry for the use of nicotinic acid as an agricultural chemical and to amend the Schedule 4 entry to include preparations for animal therapeutic use when packed and labelled for injection.

Interim decision

Pursuant to regulation 42ZCZV of the Regulations, a Delegate of the Secretary has made an interim decision to amend the current Poisons Standard in relation to nicotinic acid as follows:[3]

Schedule 5 – New Entry

NICOTINIC ACID when packed and labelled for use as an agricultural chemical.

Schedule 4 – Amend Entry

NICOTINIC ACID in preparations:

(a) for human therapeutic use **except:**

i. when separately specified in these Schedules; or

ii. in preparations containing 100 mg or less of nicotinic acid per dosage unit; or

iii. nicotinamide.

(b) for animal therapeutic use when packed and labelled for injection.

[3] 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.

Index – Amend entry

NICOTINIC ACID
cross reference: NICOTINAMIDE
Schedule 5
Schedule 4
Schedule 3

Materials considered

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

(c) The application to amend the current Poisons Standard with respect to nicotinic acid (the **Application**)

(d) 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.

(e) The SPF, and

(f) The Handbook.

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

I have made an interim decision to amend the entry in Schedule 4 and create a new entry in Schedule 5 in relation to nicotinic acid. Veterinary and agricultural use of nicotinic acid have not been previously considered for scheduling. I have found the use of nicotinic acid as an agricultural chemical to have a low potential for causing harm and is consistent with the factors for Schedule 5 with appropriate labelling. I have also decided to require veterinary oversight for injectable formulations containing nicotinic acid that are used for animal therapeutic use due to the risks, and complexity, of this dosage form.

Agricultural use of nicotinic acid

In relation to s 52E(1)(a) and (b) of the Act, the proposal is for the first-time use of nicotinic acid as an active ingredient in an herbicidal formulation. It has been proposed for professional use as a synergist, to enhance the effectiveness of the herbicide in the formulation. I note that nicotinic acid itself does not have herbicidal activity. This use of nicotinic acid is intended to enhance the performance of the herbicide against a range of grass weeds in various food crops, turf and lawns.

I have reviewed the toxicity of nicotinic acid and its risks from the proposed agricultural use in accordance with s 52E(1)(a) and (c) of the Act. Nicotinic acid is not a skin sensitiser or irritant but is a slight to moderate eye irritant. The toxicity profile of nicotinic acid meets the following scheduling factors for Schedule 5:

- Nicotinic acid has a low health hazard consistent with Scheduling Factor 2 for Schedule 5 of the SPF. It is not genotoxic and did not produce maternal or foetal toxicity at doses up to 200 mg/kg bw/d. The repeat dose toxicity data showed a no observed adverse effect level (NOAEL) of 50 mg/kg bw/day with effects at higher doses limited to slight changes in bodyweight and relative kidney size.
- The acute oral, dermal and inhalational toxicity values of nicotinic acid show it has low toxicity. In addition, it is non-corrosive, which is aligned with Scheduling Factor 1 for Schedule 5 of the SPF.

In relation to s 52E(1)(d) of the Act, the proposed product contains 10 mg/kg of nicotinic acid in a water dispersible granule formulation in a range of pack sizes from 250 g to 25 kg. The product will be

packed in High Density Polyethylene (HDPE) containers with tamper evident closures with a self-adhesive labels and leaflets or directly printed on to the bags. The product will be applied at sowing and pre- and post-emergence of weeds using handheld or backpack sprayers or ground booms.

The product is intended for professional use and is to include specific warnings and appropriate label instructions overseen by the regulator (Australian Pesticides and Veterinary Medicines Authority). I note that the proposed herbicide products that nicotinic acid is to be used with, have higher toxicities arising from other ingredients in their formulation. To minimise the risks to the user, safety measures such as wearing cotton overalls, goggles, and chemical resistant gloves will be required. Additionally, the APVMA will require buffer zones for ground boom applications to prevent bystander exposure. There will also be re-entry label statements that restrict access to treated areas until the product has dried. This precaution is particularly relevant to any turf and lawn applications in public areas, where the public may otherwise re-enter before the product has dried.

Due to the low toxicity of nicotinic acid and the proposed use pattern, I am of the view there is a low potential for causing harm, the extent of which can be reduced using appropriate packaging with simple warnings and safety directions on the label as proposed by the APVMA.

Veterinary use of nicotinic acid

In relation to s 52E(a) and (b) of the Act, nicotinic acid is an essential vitamin and is widely available. Nicotinic acid belongs to the vitamin B3 class and is required for the functioning of a wide range of enzymes that are vital for humans and other animals. A variety of foods naturally contain, or are fortified with, nicotinic acid. It is also used in dietary supplements and for the treatment of vitamin deficiencies and other medical conditions occurring in humans and animals.

The use of nicotinic acid in animals in Australia is to treat vitamin B deficiencies or to restore lost energy during strenuous exercise, particularly in dogs and horses. There are 4 products listed on the Public Chemical Registration Information System (PubCRIS) database. They are available as oral supplements or injections. Two of these products are administered by intramuscular injection, one of which is also labelled for slow intravenous injection. Injecting animals requires specialised handling for administration e.g. precise vein access, accurate control of the injection rate and needle stability which are consistent with Scheduling Factor 2 for Schedule 4 of the SPF. Injecting horses or dogs without appropriate training present risks to the user, including bites, kicks, or sudden movements that can cause physical injury. Risks to humans includes needle stick injuries that present infection risks. Improper preparation or technique can also harm the animal by causing infection or injecting into blood vessels or striking nerves. Therefore, I am of the view veterinary medicines that contain nicotinic acid and are administered by injection should be restricted to Schedule 4.

Following the human health risk assessment conducted by the APVMA in relation to a proposed nicotinic acid product for agricultural use, I have decided to create a Schedule 5 entry for nicotinic acid when it is packed and labelled for use as an agricultural chemical. Based on the available toxicity data and use patterns, I concur with the APVMA that it is appropriate to limit the access of veterinary medicines containing nicotinic acid that are administered by injection to Schedule 4.

Implementation date

1 February 2025

Therapeutic Goods Administration

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