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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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 of the *Therapeutic Goods Regulations 1990* (the **Regulations**). In accordance with regulations 42ZCZS, this notice comprises:

- the decisions made by a delegate[1] of the Secretary of the Department of Health and Aged Care (the Delegate) pursuant to regulations 42ZCZR
- 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 #43, November 2023)

Final decision in relation to glycopyrronium

Proposal

The applicant proposed the creation of an Appendix H entry for glycopyrronium to allow advertising of Pharmacist only medicine (Schedule 3) glycopyrronium preparations. Glycopyrronium is currently Prescription only medicine (Schedule 4) when in preparations for injections, and Pharmacist only medicine (Schedule 3) for all other preparations. The proposal aims to allow advertising of a topical glycopyrronium preparation which would be classified as a Schedule 3 medicine under the current scheduling.

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 glycopyrronium as follows:[2]

Schedule 4 – Amend Entry

GLYCOPYRRONIUM ~~in preparations for injection~~.

Schedule 3 – Delete Entry

~~GLYCOPYRRONIUM except when included in Schedule 4.~~

Index – Amend Entry

GLYCOPYRRONIUM

Schedule 4
~~Schedule 3~~

[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 material:

- the application to amend the current Poisons Standard with respect to glycopyrronium (the Application)
- the 28 public submissions received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations
- the advice received from the 43rd meeting of the Advisory Committee on Medicines Scheduling (the Committee)[3]
- the interim decision relating glycopyrronium and the materials considered as part of the interim decision, as published on 3 April 2024
- the 2 public submissions received in response to the interim decision consultation under regulation 42ZCZP of the Regulations (the Submissions)
- 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.[4]

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 glycopyrronium. My reasons for making the final decision are in alignment with those set out in the interim decision. In making my final decision, I have considered the material in the interim decision and the 2 public submissions that were received in response to the interim decision consultation. Both submissions were not in support of the interim decision.

The reasons set out in the interim decision address the proposal to permit advertising of glycopyrronium under the current scheduling. The proposal would permit glycopyrronium in all preparations, except those for injection, to be advertised regardless of indication. I have considered the request in the submissions in response to the interim decision to confine the Schedule 3 entry and Appendix H entry to topical preparations of glycopyrronium.

I note one of the submissions argued that symptoms of primary axillary hyperhidrosis, a condition that involves excessive sweating, can be managed by patients without close medical supervision after diagnosis. However, it is specified in the Therapeutic Guidelines that management of primary hyperhidrosis may involve referral to a specialist, such as a dermatologist or neurologist with expertise in sweating disorders.[5] It is common for those with primary axillary hyperhidrosis to have severe sweating or experience excessive sweating in other areas including the head and face.[6,7] These factors can make medical assessment, treatment and management more complex, which support my view that Schedule 4 is most appropriate.

I acknowledge that due to the localised application and reduced systemic drug exposure, topical preparations of glycopyrronium are likely to be better tolerated when compared to other glycopyrronium preparations, such as oral preparations. However, the use of topical preparations of

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

[4] https://www.tga.gov.au/sites/default/files/scheduling-handbook-guidance-amending-poisons-standard.pdf

[5] https://www.tg.org.au/

[6] https://www.sweathelp.org/pdf/IHHS%20-%20Prevalence.pdf

[7] https://onlinelibrary.wiley.com/doi/full/10.1111/1346-8138.16908

glycopyrronium is not without potential risk of adverse effects. Topical glycopyrronium preparations have never been available in Australia, and, therefore, there is a lack of experience and real-world data regarding topical glycopyrronium use in Australia. These elements are consistent with the factors for prescription medicines (Schedule 4, factor 8).

I note that topical glycopyrronium has been registered with the US FDA as a prescription medicine. Qbrexza®, a glycopyrronium preparation in cloth form was registered in 2018. Based on the FDA Adverse Events Reporting System (FAERS)[8], as of May 2024, there were over 735 cases of adverse events associated with the use of Qbrexza®, where 77 of them were reported to be serious cases.

More recently sofpironium, a muscarinic acetylcholine, M3 receptor ligand that closely resembles glycopyrronium in chemical structure, has been registered with the US FDA as prescription medicine (Sofdra™). It is a topical gel containing sofpironium, and was approved by the FDA to treat primary axillary hyperhidrosis (excessive underarm sweating) in June 2024.[9]

I retain concerns that Schedule 3 availability of such preparations circumvents the need for medical diagnosis of hyperhidrosis and identification of any underlying causes. Inappropriate use of glycopyrronium may mask symptoms, delay diagnosis and treatment of underlying conditions, which could lead to serious health outcomes. The risk of inappropriate use could be exacerbated by advertising of topical glycopyrronium preparations. Consumers may form their own opinion about the suitability of the preparation based on product marketing prior to consulting with a health professional. This may negatively impact a health professionals' ability to determine genuine therapeutic need for patients.

Having considered one of the submission's (in response to the interim decision) approach to addressing the scheduling factors, I find it important to note scheduling decisions follow the cascading principle, where more restrictive schedules are considered first, as a precautionary principle for protecting public health. As a systematic approach, it is also used to facilitate the reclassification process when an application for rescheduling is received.

I remain of the opinion that the current scheduling of topical glycopyrronium preparations is not appropriate and should not be supplied as a Pharmacist only medicine (Schedule 3) at this stage. Concurring with my interim decision and reasoning, I have decided on an implementation date of 1 October 2024. As there are no glycopyrronium products currently marketed in Australia under Schedule 3, no products will be affected by the changes to the scheduling of glycopyrronium. This decision will not impact consumers in accessing existing glycopyrronium medicines.

Implementation date

1 October 2024

[8] https://www.fda.gov/drugs/drug-approvals-and-databases/fda-adverse-event-reporting-system-faers

[9] https://www.fda.gov/drugs/novel-drug-approvals-fda/novel-drug-approvals-2024

Final decisions on proposed amendments referred to the Advisory Committee on Medicines and Chemicals Scheduling in joint session (Joint ACMS-ACCS #35, November 2023)

Final decision in relation to palmitoylethanolamide (PEA)

Proposal

The applicant has proposed a new Poisons (Schedule 6) entry for palmitoylethanolamide (PEA) with an exemption for use in listed human medicines. The proposal would require products containing PEA that are not listed as human medicines, such as veterinary products, to have distinctive packaging with strong warnings and safety directions on the label.

Final decision

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

Schedule 6 – New entry

PALMITOYLETHANOLAMIDE (excluding derivatives) **except:**

a) in preparations for therapeutic use; or

b) in preparations for dermal cosmetic use containing 1% or less of palmitoylethanolamide.

Index – New entry

PALMITOYLETHANOLAMIDE
cross reference: PALMIDROL

Schedule 6

Materials considered

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

- the application to amend the current Poisons Standard with respect to PEA (the Application)
- the 19 public submissions received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations
- the advice received from the 35th meeting of the Advisory Committees on Medicines and Chemicals Scheduling in joint session (the Committee)
- the interim decision relating to palmitoylethanolamide and the materials considered as part of the interim decision, as published on 3 April 2024
- the 2 public submissions received in response to the interim decision consultation under regulation 42ZCZP of the Regulations (the Submissions)
- 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

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and presentation of a substance; and (f) any other matters considered necessary to protect public health.

- Safety Assessment of Ethanolamides as Used in Cosmetics - International Journal of Toxicology
- Palmitoylethanolamide in the Treatment of Chronic Pain: A Systematic Review and Meta-Analysis of Double-Blind Randomized Controlled Trials – Nutrients
- Palmitoylethanolamide: A Natural Compound for Health Management – International Journal of Molecular sciences.
- 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 palmitoylethanolamide (PEA). I have decided that PEA will not be included in any Schedule to the Poisons Standard when in preparations for dermal cosmetic use containing 1% or less of PEA. My reasons for making the final decision are in alignment those set out in the interim decision and the reasons for exempting certain dermal cosmetic preparations are set out below. In making my final decision, I have taken into account the 3 public submissions which were received in response to the interim decision, of which 2 were supportive and one did not support the interim decision. The submission that did not support the interim decision provided information on the use of PEA within products for dermal cosmetic use in Australia and relevant safety data.

In considering 52E(a)(b) and (d) of the Act, I have reviewed the use of PEA in cosmetics applied dermally and its risk profile in these types of formulations. PEA is alternatively referred to as palmitamide MEA in cosmetic products. It is used in dermal cosmetic preparations for its properties as a skin conditioning agent, foam boosting surfactant and to increase formulation viscosity. A submission in response to the interim decision reported PEA to be present in concentrations varying from 0.3% to 1.0% in dermal cosmetic products.

I have reviewed the safety assessment of ethanolamides, a class of compounds that include PEA, by the Cosmetic Ingredient Review (CIR) Expert Panel, in accordance with 52E(c) of the Act.[11] There were minimal to no adverse effects reported in repeat dose toxicity studies of related ethanolamides applied dermally. I find this to be consistent with the post market adverse event data of a dermal cosmetic product containing 0.3% PEA. The post market adverse event data indicates local toxicity is very rare.[12]

Based on the available safety data, I have concluded that dermal cosmetic preparations that do not exceed 1% PEA should be exempt from scheduling as there is an acceptable margin of safety. This means access to dermal cosmetic products that contain 1% or less of PEA will remain unimpacted, as they will not be captured by the new Schedule 6 entry for PEA. Following 2 rounds of consultation, I have not been made aware of any dermal cosmetic preparations with concentrations greater than 1% of PEA in the market. I have formed the view the cosmetic industry is unlikely to be impacted by this change and have therefore decided on an early implementation date of 1 October 2024.

Implementation date

1 October 2024

[11] Fiume MM et al, 2015. Safety assessment of ethanolamides as used in cosmetics. *Int J Toxicology* 34(Suppl 1): 18S-34S. https://journals.sagepub.com/doi/full/10.1177/1091581815586599

[12] Based on post market adverse event data on a low concentration PEA product provided by a public submission

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