Australian Government

Department of Health and Aged Care

Therapeutic Goods Administration

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

3 May 2023

Version 2.0

TGA Health Safety Regulation

Contents

1 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 42ZCZX, 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 42ZCZR and 42ZCZU;
- 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 be defined for individual decisions.

2 Final decisions on proposed amendments referred to the Advisory Committee on Medicines Scheduling (ACMS #40, November 2022)

2.1 Final decision in relation to paracetamol

CONTENT WARNING

The Department of Health (the 'Department') recognises that each of the numbers reported within this document represents an individual. The Department acknowledges the devastating effects associated with acts of self-harm on individuals, their families, friends and communities. A list of support services and information sources is provided below.

The information below contains details of self-poisonings some people may find distressing. If you or someone you know needs additional support, please contact any of the below crisis support helplines:

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

Support services and information sources

Adult

- Lifeline: 13 11 14
- Suicide Call Back Service: 1300 659 467
- Beyond Blue: 1800 512 348
- MensLine Australia: 1300 789 978

Youth

- Kids Helpline (5-25 years): 1800 551 800
- Headspace: 1800 650 890
- ReachOut

Proposal

The Delegate proposed changes to the entries for paracetamol in Schedules 2, 3 and 4 of the Poisons Standard. The changes would reduce the maximum size of packs of immediate release paracetamol from:

- 20 tablets/capsules to 16 for unscheduled products,
- 100 tablets/capsules to 32 for Schedule 2 products, and
- mandate blister or strip packaging for all tablet/capsule products containing paracetamol that are unscheduled or included in Schedule 2 (the Proposal).

Equivalent and proportionate changes would also apply to preparations of wrapped powders and sachets of granules that contain paracetamol.

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 paracetamol as follows:

Schedule 4

PARACETAMOL:

a) when combined with aspirin or salicylamide or any derivative of these substances **except** when separately specified in these Schedules; or

b) when combined with ibuprofen in a primary pack containing more than 30 dosage units; or

c) in modified release tablets or capsules containing more than 665 mg paracetamol; or

d) in non-modified release tablets or capsules containing more than 500 mg paracetamol; or

e) in individually wrapped powders or sachets of granules each containing more than 1000 mg paracetamol; or

f) in tablets or capsules enclosed in a primary pack containing more than 100 tablets or capsules **except** in ~~Schedule 2 or~~ Schedule 3; or

g) in individually wrapped powders or sachets of granules enclosed in a primary pack containing more than 50 wrapped powders or sachets of granules **except** when included in Schedule ~~2~~3; or

h) for injection; or

i) for the treatment of animals.

Schedule 3

PARACETAMOL:

a) when combined with ibuprofen in a primary pack containing 30 dosage units or less **except** when included in Schedule 2; or

b) in modified release tablets or capsules containing 665 mg or less paracetamol enclosed in a primary pack containing not more than 100 tablets or capsules; or

c) in modified release-tablets or capsules containing 665 mg or less paracetamol enclosed in a primary pack containing more than 100 tablets or capsules intended only as a bulk medicine and labelled 'For dispensing only' and 'This pack is not to be supplied to a patient'; or

d) in non-modified release tablets or capsules containing not more than 500 mg paracetamol and in a primary pack containing not more than 100 tablets or capsules **except** when included in or expressly excluded from Schedule 2; or

e) in tablets or capsules enclosed in a primary pack containing more than 100 tablets or capsules intended only as a bulk medicine pack and labelled 'For dispensing only' and 'This pack is not to be supplied to a patient'; or

f) in individually wrapped powders or sachets of granules enclosed in a primary pack containing not more than 50 wrapped powders or sachets of granules **except** when included in or expressly excluded from Schedule 2; or

g) in individually wrapped powders or sachets of granules enclosed in a primary pack containing more than 50 wrapped powders or sachets of granules intended only as a bulk medicine pack and labelled 'For dispensing only' and 'This pack is not to be supplied to a patient'; or

h) in liquid preparations for oral use **except** when in Schedule 2.

Schedule 2

PARACETAMOL for therapeutic use:

a) in liquid preparations for oral use containing a maximum of 10 g of paracetamol per container; or

b) when combined with ibuprofen in preparations for oral use when labelled with a recommended daily dose of 1200 mg or less of ibuprofen in divided doses in a primary pack containing no more than 12 dosage units per pack; or

c) in tablets or capsules in blister or strip packaging enclosed in a primary pack containing not more than 50 ~~100~~ tablets or capsules; or

~~d) in tablets or capsules enclosed in a primary pack containing more than 100 tablets or capsules intended only as a bulk medicine pack and labelled 'For dispensing only' and 'This pack is not to be supplied to a patient'; or~~

e) in individually wrapped powders or sachets of granules enclosed in a primary pack containing not more than 25 ~~50~~ wrapped powders or sachets of granules; or

~~f) in individually wrapped powders or sachets of granules enclosed in a primary pack containing more than 50 wrapped powders or sachets of granules intended only as a bulk medicine pack and labelled 'For dispensing only' and 'This pack is not to be supplied to a patient'; or~~

g) in other preparations **except**:

i) when included in Schedule 3 or 4; or

ii) in individually wrapped powders or sachets of granules each containing 1000 mg or less of paracetamol as the only therapeutically active constituent (other than caffeine, phenylephrine and/or guaifenesin or when combined with effervescent agents) when:

(A) enclosed in a primary pack that contains not more than 10 such powders or sachets of granules,

(B) compliant with the requirements of the Required Advisory Statements for Medicine Labels,

(C) not labelled for the treatment of children 6 years or age or less, and

(D) not labelled for the treatment of children under 12 years of age when combined with caffeine, phenylephrine and/or guaifenesin; or

iii) in tablets or capsules each containing 500 mg or less of paracetamol as the only therapeutically active constituent (other than caffeine, phenylephrine and/or guaifenesin or when combined with effervescent agents) when:

(A) packed in blister or strip packaging ~~or in a container with a child-resistant closure~~,

(B) in a primary pack containing not more than 16 ~~20~~ tablets or capsules,

(C) complaint with the requirements of the Required Advisory Statements for Medicine Labels,

(D) not labelled for the treatment of children 6 years of age or less, and

(E) not labelled for the treatment of children under 12 years of age when combined with caffeine, phenylephrine and/or guaifenesin.

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PARACETAMOL
cross reference: ASPIRIN, IBUPROFEN, METOCLOPRAMIDE, SALICYLAMIDE, CAFFEINE

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Appendix H, clause 1

Materials considered

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

- The delegate-initiated proposal to amend the current Poisons Standard with respect to paracetamol (the **Proposal**);
- The 190 public submissions received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice received from the 40th meeting of the Advisory Committee on Medicines Scheduling (the **Committee**);
- The 201 public submissions received in response to the interim decision consultation under regulation 42ZCZP of the Regulations;
- The findings and recommendations in the independent expert report of the risks of intentional self-poisoning with paracetamol, published on the TGA website on 14 September 2022 (the **Report**);
- 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;
- The Therapeutic Guidelines;
- The Pharmacy Guild pharmacy and dispensary assistant S2/S3 training summary;
- The Explanatory Note for The Medicines (Sale or Supply) (Miscellaneous Provisions) Amendment (No. 2) Regulations 1997;
- Further data from the New South Wales Poison Information Centre (NSW PIC);
- Two journal articles on paracetamol overdose as cited in the reasons below;
- 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 and amend the current Poisons Standard to reduce pack sizes and mandate blister packs in the manner detailed above. My final decision departs from my interim decision by:

- Reducing the maximum size of Pharmacy Only (Schedule 2) packs of paracetamol tablets and capsules from 100 to 50 instead of 32
- Reducing the maximum size of Pharmacy Only (Schedule 2) packs of paracetamol powders or sachets of granules from 50 to 25 instead of 16; and
- Leaving the maximum size of general sale (not scheduled) packs of paracetamol in sachets as they currently are instead of reducing them to 8.

Consistent with my interim decision, I have decided to not introduce or change purchasing or access restrictions related to the number of packs that can be sold in a single transaction, sales from behind the counter, modified release (MR) paracetamol preparations, or purchaser age.

In reaching my final decision, I have considered all the 201 public submissions received between 3 February and 3 March 2023. I note that over 80% of organisations, including peak bodies representing consumers, healthcare practitioners and industry, partially or fully supported the interim decision.

There was consensus among submissions to not implement limits on the number of packs that can be purchased in a single transaction, sales from behind the counter and purchaser age restrictions. In contrast, there were divergent views in relation to restrictions on pack sizes and MR formulations. Several submissions emphasised the differing characteristics and purchasing trends of cough and cold products containing paracetamol compared to those for pain relief containing paracetamol as the only active ingredient, with the maximum pack sizes of both having been proposed in my interim decision to be reduced. Finally, most submissions from individuals expressed opposition to any changes to paracetamol purchasing or access controls.

The factors that I have considered in accordance with s 52E(1) of the Act and my reasons in reaching my final decision are those in my interim decision except:

- In weighing up the spectrum of views from the public consultation, I am persuaded that access to paracetamol in a pharmacy setting should be slightly less restrictive than proposed in my interim decision.
- In response to concerns raised in the submissions, and with regard to s 52E(1)(a) and (d) of the Act and additional intentional overdose data, I have specifically reconsidered the likelihood of the involvement of paracetamol in sachet form in intentional overdose.

I am satisfied that the changes between my interim and final decisions attain the appropriate balance between addressing intentional paracetamol overdose and ensuring appropriate access for legitimate therapeutic use that I expressed in my interim decision.

My detailed reasons for these changes and other comments are as follows. I also elaborate, given the public consultation submissions, on my reasons for those matters that are unchanged between my interim and final decisions.

Reasons for reducing the maximum size of paracetamol packs, including varying my interim decision

I maintain the view, despite some submissions, that reductions in maximum pack sizes of both general sale and Pharmacy Only paracetamol is generally appropriate. However, I have decided to vary the interim decision in relation to the degree to which Pharmacy Only pack sizes should be reduced, and I will now set out further reasoning to support this amendment.

Most peak bodies expressed some level of support for reducing the maximum pack size of products containing only paracetamol as the active ingredient. There were recurring concerns that a limit of 32 for Pharmacy Only (Schedule 2) medicine was disproportionately restrictive with numerous counterproposals for maximum pack sizes to be reduced instead to 50 tablets or capsules (or equivalent). I also note that a survey conducted by Pain Australia showed that only 25% of those who live with chronic pain agreed with the reduced maximum pack sizes in the interim decision. Moreover, the overwhelming majority of individual submissions did not support any reduction.

On the other hand, the Australian Medical Association (AMA) expressed support for a limit of 32 and the Royal Australian College of General Practitioners (RACGP) were in favour of even lower pack sizes, consistent with those available via general sale, to adequately reduce the amount of paracetamol in the home.

In light of these views and pursuant to s 52E(1)(a) of the Act, I have reconsidered the relative risks of overdosing with 25 g compared to 16 g of paracetamol (equivalent to 50 versus 32 tablets or capsules of 500 mg paracetamol). In particular, I note that the Therapeutic Guidelines[2] and the Report state that ingestion of 30 g of immediate-release paracetamol is the threshold of increasing risk of acute liver injury even when current antidote therapy starts within 8 hours of ingestion, with treatments for overdoses <30 g being effective particularly if patients present earlier than 8 hours.[3,4] I find this distinction particularly important considering most of those that overdose on paracetamol present within 8 hours.[5]

Moreover, I have considered, pursuant to s 52E(1)(b) of the Act, the need highlighted by the Australian Commission on Safety and Quality in Health Care to align with the National Medicines Policy of fair, timely, safe and reliable access to medicines.

I acknowledge the concerns raised by the RACGP, but for the reasons outlined in the interim decision and in light of further information, I am not swayed that maximum Pharmacy Only pack sizes of less than 32 tablets or capsules would fairly consider the many Australians that safely use paracetamol.

For the purposes of s 52E(1)(f) of the Act, I have also taken into account that over 94% of community pharmacies in Australia are QCPP accredited, requiring all staff who supply Pharmacy Only (Schedule 2) medicine to be trained via a recognised and accredited course.[6] Due to this widespread training, and with the option to refer to a pharmacist, I am satisfied these safeguards will allow for pack sizes of 50 to be appropriately managed as Pharmacy Only (Schedule 2) medicine.

On the basis of the above, I have formed the view that limiting pack sizes of Pharmacy Only (Schedule 2) immediate release paracetamol to 50 units of 500 mg tablets and capsules,

[2] Therapeutic Guidelines. Melbourne: Therapeutic Guidelines Limited; accessed 24 April 2023. https://www.tg.org.au

[3] Paracetamol poisoning: immediate-release preparations [published August 2020]. In: Therapeutic Guidelines. Melbourne: Therapeutic Guidelines Limited; accessed 24 April 2023. https://www.tg.org.au

[4] the Report p. 16

[5] the Report p. 38

[6] https://www.guild.org.au/training/pharmacy-and-dispensary-assistant/s2s3-training

equivalent to 25 g total paracetamol, will achieve the fine balance between the risks and benefits that I sought in making my interim decision.

Consistent with my concerns in the interim decision, I am reassured that my final decision will continue to support access to those in rural and remote areas and will alleviate the major impacts on industry that were raised again by Consumer Healthcare Products (CHP) Australia.

In contrast, consistent with my interim decision and with a high level of support from submissions, I am assured that reducing pack sizes to 16 in a general retail setting is appropriate and necessary to protect the public.

Combination tablets or capsules. Consumer Healthcare Products (CHP) Australia and several pharmaceutical companies advocated against changes to maximum pack sizes of cough and cold products containing paracetamol along with other active ingredients. These products are currently available on general sale[7] or as Pharmacy Only (Schedule 2) preparations. They argued that these products are unlikely to be used in intentional paracetamol overdose due to their comparatively higher cost, unique patterns of purchase and use by consumers and a paucity of data of their use in intentional paracetamol overdose.

However, I note that the Report's data on intentional paracetamol combination product overdose exposures included some cough and cold preparations.[8] Given these data, in April 2023 I obtained further information from the New South Wales Poisons Information Centre (NSW PIC).[9] They advised that the proportion of intentional exposure events they recorded as being specifically attributed to paracetamol-containing cough and cold products in the year 2022 was 6.5% of intentional exposure events. In this light, I am concerned that these products, like single ingredient paracetamol products, pose a risk from intentional overdose.

In addition, I have considered that changes to maximum paracetamol pack sizes that were introduced in the United Kingdom (UK) that effectively reduced the rates of overdose. Cough and cold products containing paracetamol and in the form of tablets or capsules were not exempted from these changes.[10] I am therefore disinclined to treat these differently in regard to maximum pack sizes.

While I have considered the rationale provided by industry in accordance with s 52E(1)(a) and (d) of the Act, I therefore remain satisfied that the maximum pack sizes of these paracetamol-containing cough and cold products should be reduced to 16 in general retail and 50 as Pharmacy Only (Schedule 2) medicine. That is, they should not be treated differently in relation to maximum pack sizes from single active ingredient paracetamol products.

Powders or sachets of granules. Several submissions presented the view that, in contrast to the interim decision, no changes should be made to the scheduling of powders or sachets of granules for similar reasons to those presented for cough and cold products in tablets or capsules. It was argued in submissions that the way in which these formulations are prepared and consumed, and the presentation of the goods, impede or discourage their use in intentional paracetamol overdose. This led me to reassess, pursuant to s 52E(1)(a) and (d) of the Act, the scheduling of powders or granules in sachets, considering their distinct presentation and formulation.

In brief, the benefits of tightening the maximum size of packs of these products outweigh the risks for Pharmacy Only products but not general sale products, as follows.

[7] Combination products available for general sale are captured in Schedule 2 exceptions in the Poisons Standard

[8] the Report, Figure 16.

[9] Email communication - <11/04/2023 – 19/04/2023>

[10] Explanatory Note, The Medicines (Sale or Supply) (Miscellaneous Provisions) Amendment (No. 2) Regulations 1997. https://www.legislation.gov.uk/uksi/1997/2045/made

I recognise that the UK excluded these preparations from the tightening of restrictions on maximum pack sizes of paracetamol in general retail in 1998. Moreover, NSW PIC has advised me that these products are rarely recorded as being involved in overdose.[9] In this light, my view is that there is likely to be minimal benefit in addressing the incidence of intentional overdose with paracetamol from reducing pack sizes of these formulations, and less so for general sale than Pharmacy Only products.

On the other hand, there will be risks associated with reducing pack sizes, namely the potential for reduced access to these products for legitimate therapeutic use. I note these formulations are typically for the relief of temporary cough or cold and for those otherwise used for pain are likely to attract select individuals, such as those with difficulty swallowing tablets, rather than a need for catering for groups of people such as families where larger quantities may be required.

The risks in reducing maximum pack sizes of sachet products available as Pharmacy Only (Schedule 2) medicine in line with tablets and capsules (by paracetamol quantity per pack) are outweighed by the benefits for minimising intentional overdose, as the products containing paracetamol currently on the Australian Register of Therapeutic Goods (ARTG) in this form all provide a total amount of paracetamol in a pack that is less than 25 g (equivalent to 50 tablets or capsules of 500 mg paracetamol). That is, it appears there are no sachet products that are currently Schedule 2 medicines that would be affected by changing the maximum permissible pack size.

Conversely, there are sachet products currently available on general sale, access to which may be affected by a change in maximum pack size. In this case, the risks from such a change would outweigh the benefits in relation to minimising harm from intentional overdose.

Having considered s 52E(1) paragraphs (a), (b) and (d) of the Act, I am compelled to exclude these products from tightened restrictions on general sale only, but I am content with bringing Pharmacy Only products in line with the tightening of restrictions of Pharmacy Only paracetamol tablets or capsules as a precautionary means of reducing future harm.

Review of submissions in relation to blister packaging

I affirm that my reasons for implementing this change are those set out in my interim decision with the following additional comments.

Overall, blister packs were well supported in the submissions on the interim decision. However, one industry stakeholder expressed concerns about the lack of effectiveness and evidence of blister packaging, and another questioned the advantage of loose fill products for those with hand mobility issues.

Consistent with the interim decision and in accordance with s 52E(1)(a) and (d) of the Act, I give significant weight in maintaining my position on blister packaging to the implementation of paracetamol blister packs in the United Kingdom (UK), following which there was a 21% reduction in all paracetamol overdoses and a 64% reduction in severe overdoses. This experience in the UK satisfies me that mandating blister packaging where there is no pharmacist supervision over access is an effective way forward.[11]

However, I also recognise the limited options in product packaging for those with compromised hand mobility, and the challenge for industry to satisfy opposing objectives—supporting accessibility on the one hand and minimising harm from intentional overdose on the other. In the context of these competing forces and considering s 52E(1)(b) and (d) of the Act, I consider

[11] https://www.sciencedirect.com/science/article/pii/S0140673600023552

that it is appropriate for loose fill paracetamol products to continue to be available without a prescription, but only as Schedule 3 preparations.

Options not adopted in my interim or final decisions

Submissions on my interim decision also touched on options that I sought comment on in the first round of consultation but did not incorporate into my interim decision, but few expressed concerns about my decision to exclude them.

However, there were strongly divergent views on my interim decision to not amend the scheduling of MR paracetamol. For this reason, I will further explain why changes to MR paracetamol scheduling are still not warranted at this time, and then briefly touch on why I am not incorporating the remaining options into my final decision.

Modified release paracetamol. Pain Australia supported the interim decision not to up-schedule, citing concerns for the 3.4 million Australians with chronic pain, particularly those in rural areas and with lower incomes. However, the AMA and RACGP were not supportive and suggested consultation with GPs and repeat prescriptions as options to minimise issues concerning access for legitimate use. The RACGP also expressed concerns about the overuse of MR paracetamol for conditions with little benefit, while another submission raised concerns about children and adolescents continuing to access these formulations for overdose.

As previously stated in my interim decision, I remain of the view that up-scheduling MR paracetamol at this time would be premature and disproportionately impact upon the management of chronic pain. In considering s 52E(1)(f) of the Act, I have taken into account that the coming into effect of the up-scheduling of MR paracetamol from Schedule 2 to Schedule 3 coincided with the emergence of the COVID-19 pandemic. While there has been a slight reduction in average dose consumed in overdose, the effects since up-scheduling have not been significant.[12] It is unclear, however, to what extent the incidence of overdosing with these preparations since then has been influenced by factors such as lockdowns and potential stockpiling of these products.

For this reason, I have carefully considered the proportion of overall poisonings that have occurred due to MR formulations since up-scheduling. It is important to acknowledge that against the backdrop of large increases in overdose across young age groups, it is evident that these concerning increases are not being driven by MR ingestions.[13] In light of these trends, while I acknowledge that 34% of overdoses with MR paracetamol are still being observed in children and adolescents, the same age groups are more concerningly accounting for approximately 50% of cases involving immediate-release preparations with rapidly increasing and much higher rates overall.[14]

While I acknowledge the concerns of the AMA and RACGP, I must emphasise that MR paracetamol remains a first line therapy for certain chronic pain conditions such as osteoarthritis where safe and accessible pharmacological alternatives are lacking.[3] Prescription only restrictions would lead to increased costs, wait times and workload, limiting access to those in need. Given the prevalence of chronic pain in Australia, there remains a need to prioritise maintaining access to pain management options.

For the reasons outlined above and consistent with the interim decision, I am not persuaded to include further restrictions to MR formulations at this time.

[12] https://pubmed.ncbi.nlm.nih.gov/36941110/
[13] the Report p. 34 (Figure 20)
[14] the Report p. 33, 34 & 49 (Figure 18, 20 & 29)

Pack limits, sales behind the counter and age restrictions. The AMA maintained the view that measures other than these would be more appropriate, and Pain Australia pointed out that excluding them would continue to enable access for young people that are independent or hold carer responsibilities. There were no major concerns or resistance to exclude both age restrictions and placing paracetamol behind the counter in general sale. I am reassured by the absence of concerns and affirm the reasons for excluding these measures are adequately justified by those set out in the interim decision.

Implementation date

Having reconsidered the potential impact of my decision, I acknowledge the need for an appropriate transition period that does not excessively postpone the implementation of changes aimed at safeguarding vulnerable Australians, while allowing a reasonable period for industry to adapt their manufacturing processes.

Based on feedback from industry, I acknowledge the numerous steps involved for end-to-end implementation, including redesign and retooling to accommodate blister reconfigurations. I am satisfied a period of 21 months is sufficient and will ensure supply chains of this essential medicine are not disrupted as a result of these scheduling changes.

Therefore, I confirm an implementation date of **1 February 2025**.

Concluding statements

In conclusion, my final decision reflects that I am satisfied that there must be changes to access to paracetamol through amending its scheduling in the manner detailed above to address the increasing incidence of deliberate overdose. However, I reiterate the comments in my interim decision that measures beyond the remit of scheduling can have a role in reducing the incidence of deliberate overdosing, including addressing its root causes.

Implementation date

1 February 2025

2.2 Final decision in relation to ivermectin

Proposal

The applicant proposed deletion of the Appendix D entry relating to ivermectin (the **Proposal**). This would remove the current restrictions on the prescribing of ivermectin for unapproved indications by medical specialists in nominated fields. The restrictions were originally implemented due to concerns regarding the significant increase in off-label prescribing of ivermectin for the prevention and treatment of COVID-19 and the risk of shortages of ivermectin for its approved indications.

Final decision

Pursuant to regulation 42ZCZR of the Regulations, the Delegate has made a final decision to set aside the interim decision and amend the current Poisons Standard in relation to ivermectin.

The final decision is to delete the Appendix D entry, with no changes to the entries for ivermectin in Schedules 4, 5 or 7 as follows:[15,16]

Appendix D – delete entry

~~10.~~	~~**Poisons available only when prescribed or authorised for:**~~	
	~~(1)~~	~~an indication that is accepted by the Secretary of the Australian Government Department of Health in relation to the inclusion of ivermectin in tablet dosage form in the Australian Register of Therapeutic Goods (an ***approved indication***); or~~ ~~Note: Approved indications are shown in the public summary of the Australian Register of Therapeutic Goods on the Therapeutic Goods Administration website at www.tga.gov.au.~~
	~~(2)~~	~~an indication that is not an approved indication, when the preparation is prescribed or authorised by a medical practitioner registered under State or Territory legislation that forms part of the Health Practitioner Regulation National Law, as a specialist in any of the following specialties or fields of specialty practices:~~ ~~(a) dermatology;~~ ~~(b) gastroenterology and hepatology;~~ ~~(c) infectious diseases;~~ ~~(d) paediatric gastroenterology and hepatology;~~ ~~(e) paediatric infectious diseases; or~~
	~~(3)~~	~~use in a clinical trial that is approved by, or notified to, the Secretary of the Australian Government Department of Health under the Therapeutic Goods Act 1989.~~
		~~IVERMECTIN in preparations for oral administration for human use.~~

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IVERMECTIN

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[15] 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.
[16] Only parts or schedules of the Poisons Standard that were proposed to be amended by the Proposal are depicted—refer to the pre-meeting public notice for a comprehensive view of entries for ivermectin in the Poisons Standard

Materials considered

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

- The reasons for the amendment outlined in Notice of an amendment to the current Poisons Standard under paragraph 52D(2)(a) of the Therapeutic Goods Act 1989 to create a new Appendix D entry in the Poisons Standard in relation to ivermectin published on 10 September 2021 (the **2021 decision**);
- The application to amend the current Poisons Standard with respect to ivermectin (the **Application**);
- The 17 public submissions received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**);
- The advice received from the 40th meeting of the Advisory Committee on Medicines Scheduling (the **Committee**);
- The 7 public submissions received in response to the interim decision consultation 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 (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 set aside my interim decision and amend the current Poisons Standard with respect to ivermectin. Specifically, I have decided to remove the Appendix D entry as set out above because the prescribing of ivermectin for unapproved indications should no longer be restricted to certain specialists (infectious disease physicians, dermatologists, gastroenterologists and hepatologists). In brief, this is because I am satisfied that the risks to public health that the Appendix D entry sought to address are now otherwise mitigated so there is no longer sufficient justification to warrant retaining the entry with respect to ivermectin.

My final decision departs from the recommendation of the Committee and my interim decision. This is not a result of new data or issues having come to light. Rather, in reconsidering the information I took into account in making the interim decision and the Committee recommendation, I have come to a different conclusion as to the balance of the risks and benefits of removing the Appendix D controls on ivermectin. My detailed reasoning is as follows.

The 2021 decision to create a new Appendix D entry for ivermectin was based on three main concerns of particular urgency in the face of the COVID-19 pandemic, which I will now address with regard to the current health climate.

Firstly, the 2021 decision was made following reports of increased personal importation and off-label prescribing of oral ivermectin as a potential therapy for prophylaxis and treatment of COVID-19. There is now an overwhelming weight of evidence against the use of ivermectin in

patients either as a prophylaxis or as a treatment of patients with COVID-19 with no benefit in large clinical studies.[17,18,19,20,21,22,23]

As outlined in my interim decision, key national and international institutions strongly advise against the use of ivermectin for the treatment and prophylaxis of COVID-19. Most importantly, the National Covid Evidence Taskforce (NCET) advises against the use of ivermectin for COVID-19 treatment, and strongly discourages the use of ivermectin for the prevention or treatment of COVID-19.[24] In addition, the Cochrane Collaboration (last updated in July 2022) concluded that ivermectin has no demonstrated beneficial effect for treatment or prevention of COVID-19, as the available evidence of efficacy is of low to very low quality, and remained uncertain whether ivermectin increased adverse events associated with COVID-19.[25,26]

The Committee advice and my interim decision made the argument that this state of the evidence warranted the retention of the Appendix D restrictions on the prescribing of ivermectin. However, while I am not dismissing this argument, when looking at these data through a different lens, I am now of the view that the consequence of such a body of clinical evidence is that medical practitioners are now well informed of the risks of prescribing ivermectin for such off-label indications. I have confidence that the volume of published studies demonstrating the lack of efficacy of ivermectin for the prophylaxis and treatment of COVID-19 enables all medical practitioners to exercise sound judgement when considering the specific use of ivermectin for COVID-19.

The second concern that prompted the 2021 decision was the likelihood that persons prescribed ivermectin for COVID-19 would believe themselves protected and would not get vaccinated, and would not seek the appropriate medical care if symptoms developed. This would pose a significant risk to the community through the spread of the disease as well as the risks to individuals using ivermectin for this purpose.

Since the making of the interim decision, I note the recent publication by Naggie *et al.* showing that at higher doses of ivermectin for a longer period of administration than previous clinical studies, 600 ug/kg daily for 6 days, showed no therapeutic benefit of ivermectin in COVID-19 patients, and did not associate ivermectin with serious adverse events. [23] I am of the view that

[17] Naggie S, Boulware DR, Lindsell CJ, et al. Effect of Ivermectin vs Placebo on Time to Sustained Recovery in Outpatients With Mild to Moderate COVID-19: A Randomized Clinical Trial. JAMA. 2022;328(16):1595–1603. doi:10.1001/jama.2022.18590

[18] Reis G, Silva EASM, Silva DCM, et al. TOGETHER Investigators. Effect of Early Treatment with Ivermectin among Patients with Covid-19. N Engl J Med. 2022 May 5;386(18):1721-1731. doi: 10.1056/NEJMoa2115869. Epub 2022 Mar 30. PMID: 35353979; PMCID: PMC9006771.

[19] https://www.medscape.com/viewarticle/971936

[20] Reis G, Silva EASM, Silva DCM, et al; TOGETHER Investigators. Effect of early treatment with ivermectin among patients with Covid-19. *N Engl J Med*. 2022;386(18):1721-1731. doi:10.1056/NEJMoa2115869

[21] Bramante CT, Huling JD, Tignanelli CJ, et al; COVID-OUT Trial Team. Randomized trial of metformin, ivermectin, and fluvoxamine for Covid-19. *N Engl J Med*. 2022; 387(7):599-610. doi:10.1056/NEJMoa2201662

[22] Naggie S, Boulware DR, Lindsell CJ, et al; Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV-6) Study Group and Investigators. Effect of ivermectin vs placebo on time to sustained recovery in outpatients with mild to moderate COVID-19: a randomized clinical trial. *JAMA*. 2022;328(16):1595-1603. doi:10.1001/jama.2022.18590

[23] Naggie S, Boulware DR, Lindsell CJ, et al; for the Accelerating Covid-19 Therapeutic Interventions and Vaccines (ACTIV)-6 Study Group and Investigators. Effect of higher-dose ivermectin for 6 days vs placebo on time to sustained recovery in outpatients with COVID-19: a randomized clinical trial. *JAMA*. Published online February 20, 2023. doi:10.1001/jama.2023.1650

[24] COVID - National Clinical Evidence Taskforce

[25] Popp M, Reis S, Schießer S, et al. Ivermectin for preventing and treating COVID-19. *Cochrane Database Syst Rev*. 2022;6(6):CD015017. doi:10.1002/14651858.CD015017.pub3

[26] Popp M, Stegemann M, Metzendorf MI, Gould S, Kranke P, Meybohm P, Skoetz N, Weibel S. Ivermectin for preventing and treating COVID-19. Cochrane Database Syst Rev. 2021 Jul 28;7(7):CD015017. doi: 10.1002/14651858.CD015017.pub2. Update in: Cochrane Database Syst Rev. 2022 Jun 21;6:CD015017. PMID: 34318930; PMCID: PMC8406455. https://doi.org/10.1002/14651858.CD015017.pub2

the risks to public health that prompted the 2021 decision are now appropriately mitigated through the high vaccination rate and immunity conferred by both prior infection and vaccination (hybrid immunity) in Australia, and that the investigated doses, frequency and duration of ivermectin use, demonstrate a low-risk of toxicity.

Regarding the risk of persons remaining unvaccinated, I have reflected on the publicly available data on vaccination rates in Australia. With over 19.8 million persons aged 16 and over (of a total population aged 16 and over of 20.6 million) having received at least 2 doses of a COVID-19 vaccine and over 14 million having received 3 doses (as of 24 March 2023), I am satisfied that the community has been initially vaccinated to a reasonable level and that there is low risk of individuals seeking ivermectin as an alternative treatment or prophylactic measure.[27]

Regarding risk to the individual, I note that many of the large clinical trials demonstrating no benefit of ivermectin in patients with COVID-19 also show a low risk of adverse reactions resulting from the doses of ivermectin administered in these trials. However, a generally well-tolerated therapy that lacks efficacy can still present risks to patient health, particularly if it results in patients forgoing other interventions with proven efficacy such as evidence-based COVID-19 treatments.[28] Moreover, higher doses of ivermectin still carry significant risk of adverse effects, including severe nausea, vomiting, and neurological effects such as dizziness, seizures and coma. I also note the submission from the Pharmacy Guild of Australia, which states that it is important to retain the current Appendix D entry for ivermectin to ensure patients continue to utilise vaccination for the prevention of COVID-19 infection, and access COVID-19 treatments that are safe and effective. However, in weighing these risks, I am of the view that the risk of medical professionals prescribing ivermectin at higher doses, or for use against COVID-19, is low given the overwhelming evidence against ivermectin use for this indication.

The final concern outlined in the 2021 decision was the significant increase in sales of ivermectin products in Australia potentially resulting in shortages in their supply and access issues. This was of particular concern in relation to access for the treatment of approved indications such as river blindness (onchocerciasis), threadworm of the intestines (intestinal strongyloidiasis) and scabies, as such shortages may disproportionately impact vulnerable communities, including Aboriginal and Torres Strait Islander communities.

I have reviewed the current supply data of ivermectin since the making of the 2021 decision and consider that there is now a minimal risk of an ivermectin shortage, even with the removal of the Appendix D restrictions on the prescribing of the medicine.

In making my final decision, I have considered the material detailed in the 7 public submissions, 5 with a written component, received before the second closing date in response to the call for further submissions published on 3 February 2023 under regulation 42ZCZP of the Regulations. I gave particular notice to the submission from the Australian Medical Association, which did not oppose the interim decision, but stated that stronger justification is required to continue the restriction on the prescribing of ivermectin.

To conclude, I would like to emphasise that that the decision to remove the Appendix D entry is not an endorsement of the off-label prescribing of ivermectin for the treatment or prevention of COVID-19. This decision has been made on the consideration of the risks of ivermectin use in the current health climate in Australia, in particular the high rate of vaccination and hybrid immunity against COVID-19 as well as the large volume of clinical evidence—which will be

[27] COVID-19 vaccination – vaccination data – 24 March 2023 | Australian Government Department of Health and Aged Care

[28] Gandhi RT, Malani PN, Del Rio C. COVID-19 therapeutics for nonhospitalized patients. *JAMA*. 2022;327(7):617-618. doi:10.1001/jama.2022.0335

widely known among medical professionals—that is now available demonstrating the lack of effectiveness of ivermectin in this regard.

Implementation date

1 June 2023

2.3 Final decision in relation to brimonidine

Proposal

The applicant proposed the creation of a new Schedule 2 entry for ophthalmic preparations containing not more than 0.025 per cent of brimonidine for adult use (the **Proposal**). The new entry would provide pharmacy access to certain ophthalmic products for the treatment of eye redness and minor irritations in adults aged 18 years and over.

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 brimonidine as follows:[29]

Schedule 4 – Amend entry

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

Schedule 2 – New entry

BRIMONIDINE in ophthalmic preparations for adult use containing not more than 0.025% of brimonidine.

Index – Amend Entry

BRIMONIDINE

Schedule 4
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 brimonidine (the **Application**);
- The 3 public submissions received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**);
- The advice received from the 40th meeting of the Advisory Committee on Medicines Scheduling (the **Committee**);
- The 2 public submissions received in response to the interim decision consultation under regulation 42ZCZP of the Regulations;

[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.

- 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 (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 brimonidine. My reasons for making the final decision are those set out in the interim decision. I have noted that two public submissions were received before the second closing date in response to the call for further submissions published on 3 February 2023 under regulation 42ZCZP of the Regulations. One of these submissions supported the interim decision, while the other opposed the decision but did not include any written component.

Implementation date

1 June 2023

2.4 Final decision in relation to fexofenadine

Proposal

The applicant has proposed an amendment to the Schedule 2 entry for fexofenadine to increase the pack size available for general sale from 5 dosage units to 10 dosage units, when labelled for the treatment of seasonal allergic rhinitis in adults and children aged 12 years and above (the **Proposal**).

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 fexofenadine as follows:[30]

Schedule 4 – Amend entry

FEXOFENADINE **except**:

a) when included in Schedule 2;

b) in divided preparations for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:

i) in a primary pack containing 20 dosage units or less and not more than 10 days' supply; and

[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.

ii) labelled with a recommended daily dose not exceeding 120 mg of fexofenadine;

c) for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:

i) in a primary pack containing 10~~5~~ dosage units or less and not more than 10~~5~~ days' supply; and

ii) labelled with a recommended daily dose not exceeding 180 mg of fexofenadine; or

d) for the treatment of seasonal allergic rhinitis and children 6 years of age and over when:

i) in a primary pack containing 20 dosage units or less and not more than 10 days' supply; and

ii) labelled with a recommended daily dose not exceeding 60 mg of fexofenadine.

Schedule 2

FEXOFENADINE in preparations for oral use **except** in divided preparations:

a) for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:

i) in a primary pack containing 20 dosage units or less and not more than 10 days' supply; and

ii) labelled with a recommended daily dose not exceeding 120 mg of fexofenadine;

b) for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:

i) in a primary pack containing 10~~5~~ dosage units or less and not more than 10~~5~~ days' supply; and

ii) labelled with a recommended daily dose not exceeding 180 mg of fexofenadine; or

c) for the treatment of seasonal allergic rhinitis and children 6 years of age and over when:

i) in a primary pack containing 20 dosage units or less and not more than 10 days' supply; and

ii) labelled with a recommended daily dose not exceeding 60 mg of fexofenadine.

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FEXOFENADINE

Schedule 4
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 fexofenadine (the **Application**);
- The 2 public submissions received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**);
- The advice received from the 40th meeting of the Advisory Committee on Medicines Scheduling (the **Committee**);
- The 2 public submissions received in response to the interim decision consultation 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; 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)

I have made a final decision to confirm my interim decision to amend the current Poisons Standard with respect to fexofenadine. My reasons for making the final decision are those set out in the interim decision. I have noted that two public submissions were received before the second closing date in response to the call for further submissions published on 3 February 2023 under regulation 42ZCZP of the Regulations. Both submissions opposed the interim decision, however, only one submission included a written component.

I have considered the opposing submission from the Pharmacy Guild of Australia stating that fexofenadine may not be appropriate for use by all individuals, and thus health professional advice should be available due to the associated risks, making reference to the B2 pregnancy category for the substance. I note, however, that numerous preparations of fexofenadine are already available as unscheduled medicines on the basis that the substance can be accessed with 'reasonable safety' as outlined in the Handbook. I have also taken into account how this amendment aligns with the scheduling of cetirizine, another antihistamine in the B2 pregnancy category, which is also available for general sale in preparations containing 10 dosage units or less in the primary pack.

I therefore of the view that the amendment to the Schedule 2 entry for fexofenadine has minimal impact on the overall risk profile of the substance whilst providing benefit to the public through increased pack sizes at general sale.

Implementation date

1 June 2023

2.5 Final decision in relation to ibuprofen

Proposal

The applicant proposed the rescheduling from Schedule 3 to Schedule 2 of modified release ibuprofen in divided preparations containing 400 mg or less of ibuprofen, in a primary pack containing not more than 12 dosage units, when labelled with a recommended daily dose of 1200 mg or less of ibuprofen (the **Proposal**). This would enable patients over 12 years of age to access some preparations of modified release ibuprofen without prior consultation with a pharmacist.

Final decision

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

Current scheduling

Editorial note: IBUPROFEN is currently listed in Schedules 2, 3 and 4 of the Poisons Standard as follows.[31] An error in the previous Poisons Standard update was noted that excludes >400 mg and < 600 mg of ibuprofen from Schedule 3 through the omission of "or less" from the scheduling entry. No substantive change will be made to the scheduling entry in relation to the proposal, however, a minor editorial change will be implemented in the upcoming Standard update in June 2023:

Schedule 4

IBUPROFEN **except**:

a) when included in or expressly excluded from Schedule 2 or 3; or

b) in preparations for dermal use.

Schedule 3

IBUPROFEN:

a) in divided preparations, each containing 400 mg or less of ibuprofen in a primary pack containing not more than 50 dosage units, when labelled:

   i) with a recommended daily dose of 1200 mg or less of ibuprofen; and

   ii) not for the treatment of children under 12 years of age; or

b) in a modified release dosage form, each containing 600 mg or less of ibuprofen in a primary pack containing not more than 32 dosage units, when labelled:

   i) with a recommended daily dose of 1200 mg or less of ibuprofen; and

   ii) not for the treatment of children under 12 years of age;

[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.

except when included in or expressly excluded from Schedule 2.

Schedule 2

IBUPROFEN in preparations for oral use when labelled with a recommended daily dose of 1200 mg or less of ibuprofen:

a) in liquid preparations when sold in the manufacturer's original pack containing 8 g or less of ibuprofen; or

b) in divided preparations, each containing 200 mg or less of ibuprofen, in packs of not more than 100 dosage units **except** when:

i) as the only therapeutically active constituent (other than phenylephrine or when combined with an effervescent agent);

ii) packed in blister or strip packaging or in a container with a child-resistant closure;

iii) in a primary pack containing not more than 25 dosage units;

iv) compliant with the requirements of the Required Advisory Statements for Medicine Labels;

v) not labelled for the treatment of children 6 years of age or less; and

vi) not labelled for the treatment of children under 12 years of age when combined with phenylephrine; or

c) in divided immediate release preparations, each containing 400 mg or less of ibuprofen in a primary pack containing not more than 12 dosage units, when labelled not for the treatment of children under 12 years of age.

It is also included under the entry IBUPROFEN in Appendix F, part 3 as follows:

Warning statements

101. Don't use [this product/name of the product]:

If you have a stomach ulcer.

In the last 3 months of pregnancy. [This statement may be omitted in preparations used exclusively for the treatment of dysmenorrhoea.]

If you are allergic to (name of substance) or anti-inflammatory medicines.

104. Unless a doctor has told you to, don't use [this product/name of the product]:

For more than a few days at a time.

With other medicines containing (name of substance) or other anti-inflammatory medicines.

If you have asthma.

If you are pregnant. [This statement may be omitted in preparations used exclusively for the treatment of dysmenorrhoea.]

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IBUPROFEN
cross reference: PARACETAMOL

Schedule 4
Schedule 3
Schedule 2
Appendix F, Part 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 ibuprofen (the **Application**);
- The 5 public submissions received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**);
- The advice received from the 40th meeting of the Advisory Committee on Medicines Scheduling (the **Committee**);
- The 6 public submissions received in response to the interim decision consultation 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 (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 not to amend the current Poisons Standard with respect to ibuprofen. 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 detailed in the interim decision and the 6 public submissions received before the second closing date in response to the call for further submissions published on 3 February 2023 under regulation 42ZCZP of the Regulations. Of the submissions received, 3 submissions were supportive and three were opposed to the interim decision. One submission in opposition to the interim decision did not provide a written component.

I acknowledge the amended wording proposed by the applicant through the interim decision consultation to amend the proposal to preparations containing 300 mg modified release (MR) ibuprofen on the basis that this would address the concern raised regarding the lack of safety data for preparations containing more than 300 mg of MR ibuprofen. Despite this, I have chosen to not amend the Poisons Standard to down-schedule 300 mg MR preparations, as my key concern regarding toxicity relates also to the recommended daily dose of 1200 mg, as proposed by the applicant.

To permit a Schedule 2 entry for preparations with a recommended daily dose of 1200 mg of MR ibuprofen would contradict the final decision published in December 2021, which was in relation to a proposal to down schedule 600 mg MR ibuprofen with a recommended daily dose of 1200 mg from Schedule 3 to Schedule 2.

I retain the view that the risks of adverse events and concerns of inappropriate use associated with the MR preparations require the intervention of a pharmacist, consistent with the Scheduling Factors of a Schedule 3 classification. Consultation with a pharmacist to assist the consumer in identifying their pain as either 'chronic' or 'persistent' continues to be the safest way to mitigate accidental misuse of the substance and provides the best quality use of the medicine, as per factors 1, 3 and 4 for Schedule 3 of the SPF. Again, I find that the MR ibuprofen 300 mg formulation does not fit the Schedule 2 scheduling factors set out in the SPF, as:

- The quality use of the medicine cannot be achieved by labelling, packaging, or provision of other information; advice from a pharmacist is required.
- Risks of dosing errors cannot be managed by a consumer through appropriate packaging and labelling.
- The use of the medicine is substantially safe for short term use. However, modified release formulations may facilitate longer term use of the substance, for the treatment of ailments that would require pharmacist or, more commonly, medical practitioner oversight.

My concerns regarding administration and dosage errors have not been assuaged by data provided by the applicant through the interim decision consultation. In contrast to the consumer statistics provided, the Consumers Health Forum of Australia published in 2020 a report on the Health Literacy and Quality Use of Medicines in Australia.[32] In this literature review, they referred to published literature demonstrating that a significant cohort of patients are unable to accurately dose out a medication regime, and more than two million Australians may have exceeded the recommended daily dose of widely used medicines, including ibuprofen, and specifically, as many as 1.5 million Australians exceed the recommended dosage of six tablets in a 24-hour period for ibuprofen + codeine tablets.[33,34]

Another independent study published in the Australian and New Zealand Journal of Public Health found that only 60.4% of participants could accurately identify the correct dose for ibuprofen containing products. [35] In addition, of those consumers that could not identify the correct dose of ibuprofen, 18% believed that administration of more than 10 ibuprofen tablets in a 24-hour period was safe.

Another study performed in South Australia and the Northern Territory found that 66% of participants rarely, or never read the manufacturers printed warning instructions on the potential drug interactions or adverse effects associated with the use of ibuprofen products.[36]

I am therefore of the opinion that the current state of Australian consumer health literacy, specifically in relation to recommended daily dosages for ibuprofen products, requires that pharmacist oversight is available when selecting MR ibuprofen.

I have also reflected on the statement provided in opposition to the interim decision that consumers are able to determine the difference between 'chronic pain' and 'persistent pain'. I

[32] Final-Literature-Review-Report_at.pdf (nps.org.au)

[33] McManus, E., S. McCarthy, R. Carson, and L. J. Sahm. 2018. 'Impact of a Universal Medication Schedule on rationalising and understanding of medication; a randomised controlled trial', Res Social Adm Pharm, 14: 831-38.

[34] Survey finds millions of Australians misuse their medicines - NPS MedicineWise

[35] https://onlinelibrary.wiley.com/doi/epdf/10.1111/1753-6405.12589

[36] https://academic.oup.com/ijpp/article/18/1/63/6130463

strongly disagree with this view. There are numerous publications emphasising the clinical use of the term 'chronic pain', and highlighting the inappropriate use of the term.[37] The International Association for the Study of Pain defines chronic pain as 'pain that persists[38] or recurs for longer than 3 months'.[39] Additionally, 'chronic pain' and 'persistent pain' is used interchangeably on several government health websites,[40,41,42] international health websites,[43] and private organisations pages, including Pain Australia.[44] Consequently, I consider that my concern regarding consumers' ability to determine the difference between chronic and persistent pain is legitimate.

On balance, I acknowledge that the use of the MR ibuprofen is safe for short-term use. However, dosage and administration errors pose a significant risk to public health, particularly for the elderly and those with cardiovascular disease, renal disease, and asthma. These concerns are shared by several peak bodies including the Pharmacy Guild of Australia and the Pharmaceutical Society of Australia. I therefore remain of the opinion that the risk of down-scheduling 300 mg MR ibuprofen, with different indications and patterns of use to immediate-release ibuprofen, greatly outweighs the benefit of increased access to these formulations.

2.6 Final decision in relation to melatonin

Proposal

The applicant proposed the rescheduling of immediate release melatonin from Schedule 4 to Schedule 3 for the treatment of jetlag. The rescheduling would apply to divided preparations containing 5 mg or less of melatonin, in packs of no more than 10 dosage units, for adults aged 18 and over (the **Proposal**). This would allow access to melatonin for this indication, without a prescription, after consulting with a pharmacist.

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 melatonin as follows:[45]

Schedule 4

MELATONIN for human use **except** when included in Schedule 3.

Schedule 3 – Amend Entry

MELATONIN in:

a) modified release tablets containing 2 mg or less of melatonin for monotherapy for the short-term treatment of primary insomnia

[37] The use of the term 'chronic pain' in clinical practice | JPR (dovepress.com)

[38] Underline added for emphasis

[39] Definitions of Chronic Pain Syndromes - International Association for the Study of Pain (IASP) (iasp-pain.org)

[40] https://www.aihw.gov.au/reports/chronic-disease/chronic-pain-in-australia/summary

[41] https://www.betterhealth.vic.gov.au/health/conditionsandtreatments/Living-with-persistent-pain

[42] https://www.healthdirect.gov.au/chronic-pain

[43] https://www.nhsinform.scot/illnesses-and-conditions/brain-nerves-and-spinal-cord/chronic-pain

[44] https://www.painaustralia.org.au/about-pain/painaustralia-what-is-pain

[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.

characterised by poor quality of sleep for adults aged 55 or over, in packs containing not more than 30 tablets; or

b) immediate release preparations containing 5 mg or less of melatonin for the treatment of jet lag in adults aged 18 or over, in a primary pack containing no more than 10 dosage units.

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MELATONIN

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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 melatonin (the **Application**);
- The 6 public submissions received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**);
- The advice received from the 40th meeting of the Advisory Committee on Medicines Scheduling (the **Committee**);
- The 5 public submissions received in response to the interim decision consultation 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 (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 melatonin. 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 detailed in the interim decision and the 5 public submissions that were received in response to the call for further submissions published on 3 February 2023 under regulation 42ZCZP of the Regulations. I note that of the submissions received in response to the interim decision 2 were supportive, 2 were partially supportive, and one was opposed (however, this submission had no written component).

I have made this decision on the basis that the proposed Schedule 3 entry for melatonin immediate-release preparations is consistent with the Australian Therapeutic Guidelines, and note that the 5 mg dose is also consistent with the therapeutic guidelines in the United Kingdom.

I note the two partially supportive submissions suggesting that the proposed melatonin preparations for jet lag could be further down-scheduled to Schedule 2. While I acknowledge that there is minimal toxicity at recommended dosages, and that jet lag is a condition that can be

easily self-diagnosed and managed safely with the advice from a pharmacist, availability of these formulations at Schedule 3 under pharmacist oversight is needed to prevent use of these melatonin preparations with benzodiazepines, and to reduce the risk of use for other indications other than jet lag. Schedule 3 is the appropriate schedule for melatonin to support the quality use of medicines and patient safety, taking into account the relatively low risk when used for treatment of jet lag in adults.

I am of the view that, as these preparations will be available to the public for the first time outside of Schedule 4 (Prescription Only Medicines), it is important to allow consumers and pharmacists time to adjust and assess the impact of this scheduling change, and therefore my final decision is to down-schedule to Schedule 3, not Schedule 2. If there is emerging evidence that supports the use of melatonin for a broader range of indications that considers it suitable for inclusion in Schedule 2, such evidence should be presented in a proposal that is the subject of a separate application to amend the Poisons Standard.

Implementation date

1 June 2023

3 Final decisions on proposed amendments referred to the Advisory Committee on Medicines and Chemicals Scheduling (ACMS-ACCS #32, November 2022)

The final decision on the proposal for a new Schedule 2 entry in the Poisons Standard for green tea extract that was considered at the November 2022 meeting of the Joint Advisory Committee on Medicines and Chemicals Scheduling is not published in this notice. The decision has been deferred pending further consultation and consideration by the Delegate.

4 Final decisions on proposed amendments referred to the Advisory Committee on Chemicals Scheduling (ACCS #35, November 2022)

4.1 Final decision in relation to ethalfluralin

Proposal

The applicant proposed new entries in Schedule 6 and Schedule 7 of the Poisons Standard for ethalfluralin (the **Proposal**). Specifically, the Proposal includes:

- A Schedule 6 entry for preparations containing ethalfluralin that are packed in bulk containers for specific use in closed mixing and loading agricultural equipment with a nominal capacity of 400 L or more; and
- A Schedule 7 entry for all other preparations.

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 ethalfluralin as follows:[46]

Schedule 7 – New entry

ETHALFLURALIN.

Index – New Entry

ETHALFLURALIN

Schedule 7

Materials considered

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

- The application to amend the current Poisons Standard with respect to ethalfluralin (the **Application**);
- The public submission received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**);
- The advice received from the 35th Meeting of the Advisory Committee on Chemicals Scheduling (the **Committee**);
- The 2 public submissions received in response to the interim decision consultation 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 (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 ethalfluralin. 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 detailed in the interim decision and the 2 public submissions received before the second closing date in response to the call for further submissions published on 3 February 2023 under regulation 42ZCZP of the Regulations. One of these submissions was supportive of the interim decision, while the other was opposed to the interim decision, however, neither submission provided a written component to their submission to support their stance.

Implementation date

1 June 2023

[46] 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.

4.2 Final decision in relation to tigolaner

Proposal

The applicant has proposed the creation of two new entries in the Poisons Standard for the new veterinary pest control agent tigolaner (the **Proposal**). The Proposal is specifically comprised of a new Schedule 5 entry for preparations containing 10 per cent or less of tigolaner, and a Schedule 6 entry for all other preparations.

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 tigolaner as follows:[47]

Schedule 6 – New Entry

TIGOLANER **except** when in Schedule 5.

Schedule 5 – New Entry

TIGOLANER in preparations containing 10% or less of tigolaner.

Index – New Entry

TIGOLANER

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 tigolaner (the **Application**);
- The public submission received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations (the **Submissions**);
- The advice received from the 35th Meeting of the Advisory Committee on Chemicals Scheduling (the **Committee**);
- The public submission received in response to the interim decision consultation 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; and (d) the dosage, formulation, labelling, packaging and presentation of a substance;
- Pursuant to paragraph 52E(2)(a) of the Act, the SPF; and

[47] 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)

I have made a final decision to confirm my interim decision to amend the current Poisons Standard with respect to tigolaner. 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 detailed in the interim decision. I have noted the single public submission received before the second closing date in response to the call for further submissions published on 3 February 2023 under regulation 42ZCZP of the Regulations was opposed to the interim decision, but did not include any written reasoning to support their stance.

Implementation date

1 June 2023

5 Amendments to the Poisons Standard made as delegate-only decisions

5.1 Final decision in relation to spiromesifen

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 spiromesifen as follows:

Schedule 5 – New entry

SPIROMESIFEN for agricultural use.

Index – New Entry

SPIROMESIFEN

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 spiromesifen (the **Application**);
- 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; (e) the potential for abuse of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.
- Pursuant to paragraph 52E(2)(a) of the Act, the SPF; and
- The Handbook.

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

In determining that this matter will be a delegate-only decision I have taken into account the information provided in the application from the Applicant, the Australian Veterinary and Pesticides Authority (APVMA), and the matters outlined under s 52E of the Act and the SPF. In particular, I note:

- In relation to s 52E(1)(a) of the Act, the proposed amendment of the Poisons Standard is to include a new entry for spiromesifen in Schedule 5, based upon benefits to the agricultural industry as a miticide and insecticide.

- Regarding s 52E(1)(b) of the Act, the intended use of the substance is to control mites, specifically two spotted mites, Byrobia mite and European red mite in pome and stone fruits in a suspension concentrate (SC) formulation. The intended formulation will contain 240 g/L of spiromesifen as the technical grade active constituent (TGAC).

- In relation to s 52E(1)(c) of the Act, the APVMA provided a Human Health Risk Assessment (HHRA) for the TGAC and the intended formulation containing spiromesifen at 240 g/L. The findings from the HHRA indicated that there was no known exposure scenarios which would result in an unacceptable occupational exposure. The APVMA concluded that the risks to human health and safety posed by this substance are acceptable according to the criteria stipulated in Section 5A of the *Agricultural and Veterinary Chemicals Code Act* (1994). The application for Scheduling consideration did not request or provide information in support of a concentration cut-off for the substance to be unscheduled.

- In review of the HHRA, I find that the levels for acute oral, dermal and inhalational toxicity align with the SPF factors for inclusion in Schedule 5. Spiromesifen has low acute oral (LD_{50} >2000 mg/kg bw), low acute dermal (LD_{50} >2000 mg/kg bw) and low acute inhalational toxicity levels (LC_{50} >4.9 mg/L). I note that the acute inhalational toxicity data provided for the proposed SC formulation aligns with the SPF factors for Schedule 6 with and LC_{50} >2500 mg/m^3/4h). However, I am of the mind that an adequate review of the TGAC and proposed product has been conducted by the product regulator, and that the toxicity profile in general is more aligned with Schedule 5.

- Spiromesifen is not a skin or eye irritant in rabbits, however, the substance demonstrated positive Magnusson and Kligman tests for skin sensitisation in guinea pigs. I also note that the SC formulation did not produce evidence of skin irritation, eye irritation or skin sensitisation. Consequently, I am of the view that the substance meets SPF factor 2 for Schedule 5, and that the risk of skin sensitisation can be mitigated through appropriate packaging and labelling.

- I note that spiromesifen is unlikely to pose a carcinogenic risk to humans as chronic repeat dose toxicity studies found no evidence of carcinogenicity in rats or mice. In reference to reproductive and developmental toxicity in rats and rabbits, spiromesifen did not adversely affect reproduction or offspring survival and development at doses that induced adverse effects in the maternal animal. On this basis, spiromesifen is not considered a reproductive toxicant or a teratogen. In addition, there was no evidence that spiromesifen had effects on neurotoxicity or immunotoxicity.

- Pursuant to s 52E(1)(f) of the Act, I have considered the statement made by the applicant that the toxicological database of spiromesifen has been evaluated by the United States Environmental Protection Agency (US EPA), Joint FAO/WHO Meeting on Pesticide Residues (JMPR), European Food Safety Authority (EFSA) and Health Canada Pest Management Regulatory Agency (PMRA). Similar to the APVMA, these international regulatory agencies have considered that spiromesifen containing products can be used

safely in agricultural applications, by adherence to product label instructions. The APVMA has established an Acceptable Daily Intake (ADI) for spiromesifen (0.03 mg/kg bw/d) consistent with the JMPR.

- I am satisfied that, for the purposes of s 52E(1)(d) of the Act, the APVMA, as the product regulator of any commercial products, will consider their dosage (application rate), formulation, labelling, packaging, and presentation.
- In relation to s 52E(1)(e) of the Act, the substance has no human therapeutic value or significant pharmacological effect that would indicate a risk for diversion, misuse, or abuse.

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

Implementation date

1 June 2023

6 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 2023.

6.1 Andexanet alfa

Schedule 4 – New Entry

ANDEXANET ALFA

Index – New Entry

ANDEXANET ALFA

Schedule 4

6.2 Avatrombopag

Schedule 4 – New Entry

AVATROMBOPAG

Index – New Entry

AVATROMBOPAG

Schedule 4

6.3 Difelikefalin

Schedule 4 – New Entry

DIFELIKEFALIN

Appendix K – New Entry

DIFELIKEFALIN

Index – New Entry

DIFELIKEFALIN

Schedule 4

Appendix K, clause 1

6.4 Ivosidenib

Schedule 4 – New Entry

IVOSIDENIB

Index – New Entry

IVOSIDENIB

Schedule 4

6.5 Pralsetinib

Schedule 4 – New Entry

PRALSETINIB

Index – New Entry

PRALSETINIB

Schedule 4

7 Version history

Version	Date	Description of changes
1.0	3 May 2023	Original document
2.0	11 February 2025	On p. 7, the amendments to the Schedule 2 entry for paracetamol incorrectly showed under clause g) iii) (A) the retention of the existing wording 'or in a container with a child-resistant closure'. However, as reflected in the reasons, the decision is that these words are to be removed, to require tablet and capsule preparations on general sale to be in blister packaging. The paracetamol Schedule 2 entry, clause g) iii) (A) has been corrected as: 'packed in blister or strip packaging ~~or in a container with a child-resistant closure~~'