Australian Government

Department of Health
Therapeutic Goods Administration

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

Final decisions and reasons for New Chemical Entities and medicines and chemicals referred to the November 2018 scheduling meetings

26 April 2019

Scheduling amendments referred to expert advisory committee

Subdivision 3D.2 of the *Therapeutic Goods Regulations 1990* (the Regulations) sets out the procedure to be followed where the Secretary receives an application under section 52EAA of the *Therapeutic Goods Act 1989* (the Act) to amend the current *Poisons Standard* and decides to refer the proposed amendment to an expert advisory committee. These include, under regulation 42ZCZK, that the Secretary publish (in a manner the Secretary considers appropriate) the proposed amendment to be referred to an expert advisory committee, the committee to which the proposed amendment will be referred, and the date of the committee meeting. The Secretary must also invite public submissions to be made to the expert advisory committee by a date mentioned in the notice as the closing date, allowing at least 20 business days after publication of the notice. Such a notice relating to the final decisions herein was made available on the TGA website at Scheduling advisory committees: invitations for public comment on 31 August 2018 and closed on 28 September 2018. Public submissions received on or before this closing date were published on the TGA website at Public submissions on scheduling matters referred to the ACMS #25, ACCS #23 and Joint ACMS-ACCS #20 meetings held in November 2018, in accordance with regulation 42ZCZL.

Under regulation 42ZCZN of the Regulations, the Secretary, after considering the advice or recommendation of the expert advisory committee, must (subject to regulation 42ZCZO) make an interim decision in relation to the proposed amendment. If the interim decision is to amend the current *Poisons Standard*, the Secretary must, in doing so, take into account the matters mentioned in subsection 52E(1) of the Act (including, for example, the risks and benefits of the use of a substance, and the potential for abuse of a substance) and the scheduling guidelines as set out in the *Scheduling Policy Framework for Medicines and Chemicals*.

Under regulation 42ZCZP of the Regulations, the Secretary must, among other things, publish (in a manner the Secretary considers appropriate) the scheduling interim decision, the reasons for that decision and the proposed date of effect (for decisions to amend the current Poisons Standard, this will be the date when it is expected that the current Poisons Standard will be amended to give effect to the decision). Also in accordance with regulation 42ZCZP of the Regulations, the Secretary must invite the applicants and persons who made a submission in response to the original invitation under paragraph 42ZCZK(1)(d), to make further submissions to the Secretary in relation to the interim decisions by a date mentioned in the notice as the closing date, allowing at least 10 business days after publication of the notice. Such a notice relating to the interim decisions of substances initially referred to the November 2018 meetings

of the Advisory Committee on Medicines Scheduling (ACMS #25), the Advisory Committee on Chemicals Scheduling (ACCS #23), and the Joint Advisory Committee on Medicines and Chemicals Scheduling (Joint ACMS-ACCS #20) was made available on the TGA website at Publication of interim decisions amending, or not amending, the current Poisons Standard, February 2019 on 7 February 2019 and closed on 7 March 2019. Public submissions received on or before this closing date will be published on the TGA website at Public submissions on scheduling matters in accordance with regulation 42ZCZQ.

Under regulation 42ZCZR of the Regulations, the Secretary may make a final decision by confirming, varying or setting aside the interim decision, but only after considering all relevant submissions and any advice received under request 42ZCZQ(2)(a). In accordance with 42ZCZS the Secretary publishes here the scheduling final decision, the reasons for that decision and the date of effect (for decisions to amend the current *Poisons Standard*, this will be the date when it is expected that the current Poisons Standard will be amended to give effect to the decision). These Secretary's final decisions and reasons related to:

- scheduling proposals initially referred to the November 2018 meeting of the Advisory Committee on Medicines Scheduling (ACMS #25);
- scheduling proposals initially referred to the November 2018 meeting of the Joint meeting of the Advisory Committees on Chemicals and Medicines Scheduling (ACCS-ACMS #20); and
- scheduling proposals initially referred to the November 2018 meeting of the Advisory Committee on Chemicals Scheduling (ACCS #23).

Scheduling amendments not referred to expert advisory committee

Subdivision 3D.3 of the *Therapeutic Goods Regulations 1990* (the Regulations) sets out the procedure to be followed where the Secretary receives an application under section 52EAA of the *Therapeutic Goods Act 1989* (the Act) to amend the current *Poisons Standard* and decides not to refer the proposed amendment to an expert advisory committee. These include, under regulation 42ZCZU, that the Secretary decides to make a final decision in relation to the proposed amendment without an interim decision. If the final decision is to amend the current Poisons Standard, the Secretary must, in doing so, take into account the matters mentioned in subsection 52E(1) of the Act (including, for example, the risks and benefits of the use of a substance, and the potential for abuse of a substance) and the scheduling guidelines as set out in the *Scheduling Policy Framework for Medicines and Chemicals*.

In accordance with 42ZCZX of the Regulations, the Secretary publishes here the scheduling final decision, the reasons for that decision and the date of effect (for decisions to amend the current *Poisons Standard*, this will be the date when it is expected that the current *Poisons Standard* will be amended to give effect to the decision). These Secretary's final decisions and reasons related to:

- New therapeutic Prescription Only medicines known as New Chemical Entities (NCEs).

Privacy and your personal information

The Therapeutic Goods Administration (TGA) will not publish information it considers confidential, including yours/other individuals' personal information (unless you/they have consented to publication) or commercially sensitive information. Also, the TGA will not publish information that could be considered advertising or marketing (e.g. logos or slogans associated with products), information about any alleged unlawful activity or that may be defamatory or offensive.

For general privacy information, go to Privacy. The TGA is part of the Department of Health and the link includes a link to the Department's privacy policy and contact information if you have a query or concerns about a privacy matter.

The TGA may receive submissions from the public on a proposed amendment to the *Poisons Standard* where there has been an invitation to the public for submissions on the proposal in accordance with the *Therapeutic Goods Regulations 1990*. These submissions may contain personal information of the individual making the submissions and others.

The TGA collects this information as part of its regulatory functions and may use the information to contact the individual who made the submissions if the TGA has any queries.

As set out above, the TGA is required to publish these submissions unless they contain confidential information.

If you request for your submission to be published in full, including your name and any other information about you, then the TGA will publish your personal information on its website. However, if at any point in time, you change your mind and wish for your personal information to be redacted then please contact the Scheduling Secretariat at medicines.scheduling@health.gov.au so that the public submissions can be updated accordingly.

Please note that the TGA cannot guarantee that updating the submissions on the TGA website will result in the removal of your personal information from the internet.

Please note that the TGA will not publish personal information about you/others without your/ their consent unless authorised or required by law.

Enquiries

Any questions relating to submissions should be directed by email to medicines.scheduling@health.gov.au (for substances referred to the ACMS or Joint ACCS-ACMS) or chemicals.scheduling@health.gov.au (for substances referred to the ACCS).

Contents

Part A - Final decisions on matters referred to an expert advisory committee (November 2018)

1. Advisory Committee on Medicines Scheduling (ACMS #25)

1.1. Nabiximols

Delegate's final decision

Final decision

The delegate's final decision under regulation 42ZCZR of the *Therapeutic Goods Regulations 1990* (the Regulations) is not to amend the current Poisons Standard in relation to nabiximols.

Reasons

The delegate has confirmed that the reasons for the final decision align with those for the interim decision.

Additional reasons, including consideration of the public submission on the interim decision:

The delegate acknowledges that the WHO Expert Committee on Drug Dependence has recently made a recommendation to ease the international restrictions on preparations containing delta-9-tetrahydrocannabinol (dronabinol) by down scheduling it to Schedule III in the United Nations Single Convention on Narcotic Drugs of 1961. Should this occur it would mean that one of the scheduling factors under the Scheduling Policy Framework for Schedule 8 would not be met. However it would not automatically mean that Schedule 4 is appropriate. However, the United Nations Commission on Narcotic Drugs (CND) has postponed their vote on the WHO recommendations to reschedule delta-9-tetrahydrocannabinol-containing preparations. This means that, under the current Scheduling Policy Framework, [redacted] is still required to be classified as a Schedule 8 poison. Not only is the current scheduling of nabiximols consistent with international restrictions on narcotics, but I believe that the current scheduling controls for nabiximols in Australia are comparable to those overseas countries, as evidenced by the information provided by the applicant.

Overall conclusions

On balance, the delegate considers that the risk of misuse and abuse of nabiximols cannot be accurately quantified based of the current level of clinical evidence. In addition, amending the scheduling of nabiximols as proposed would be inconsistent with current scheduling policy and with the Schedule 8 status of other THC/CBD combinations for therapeutic use. As the United Nations Commission on Narcotic Drugs (CND) has postponed their vote on the WHO's recommendation to reschedule delta-9-tetrahydrocannabinol-containing preparations, the delegate considers that the loss of the current Schedule 8 regulatory controls over the prescribing of nabiximols would be premature, and therefore has made the final decision not to amend its current scheduling.

Public submissions on the interim decision

One (1) public submission was received before the second closing date in response to an invitation published on 7 February 2019 under regulation 42ZCZP of the Regulations. The submission opposed the interim decision.

The main points provided in opposition of the amendment were:

- on the balance of risks, the benefit to those limited numbers of Australian patients in medical need of a prescription medicine containing nabiximols such as [redacted] is far outweighed by the perceived risks intended to be controlled by retaining this specific pharmaceutical product in S8 and Appendix D.
- the proposed change is specifically only applicable to nabiximols as contained in prescription medicines on the ARTG. This means that the attendant regulatory controls of a registered prescription medicine apply now, and would continue to apply regardless of whether it is down scheduled to Schedule 4 or removed from Appendix D
- post-marketing experience internationally and within Australia demonstrate that [redacted] as a nabiximols registered medicine is not associated with problems of abuse, dependence or diversion
- [redacted] is available as a prescription-only medicine in major European countries, with scheduling similar to the proposed Australian Schedule 4
- The World Health Organisation (WHO) Expert Committee on Drug Dependence made a recommendation to ease the international restrictions on preparations containing delta-9-tetrahydrocannabinol (dronabinol) by down scheduling it to Schedule III in the U.N. Single Convention on Narcotic Drugs of 1961. This would potentially remove the requirement for the inclusion of [redacted] in the SUSMP Schedule 8 under the Scheduling Policy Framework.

Interim decision

The interim decision was published on the TGA website on 7 February 2019 at Scheduling delegates' interim decisions and invitation for further comment: ACMS #25, November 2018 – 1.1. Nabiximols.

Scheduling proposal

The pre-meeting scheduling proposal was published on the TGA website on 31 August 2018 at Consultation: Proposed amendments to the Poisons Standard - ACCS, ACMS and Joint ACCS-ACMS meetings, November 2018.

1.2. Racetams

Delegate's final decision

Final decision

The delegate's final decision under regulation 42ZCZR of the *Therapeutic Goods Regulations 1990* (the Regulations) is to amend the current Poisons Standard in relation to racetams as follows:

Schedule 4 – New Entries

RACETAMS except when separately specified in these Schedules.

ANIRACETAM.

COLURACETAM.

DIMIRACETAM.

FASORACETAM.

METHYLPHENYLPIRACETAM.

NEBRACETAM.

NEFIRACETAM.

OMBERACETAM.

OXIRACETAM.

PHENYLPIRACETAM.

PRAMIRACETAM.

ROLZIRACETAM.

SELETRACETAM.

SUNIFIRAM.

UNIFIRAM.

Appendix K – New entry

SELETRACETAM

Index – New Entries

RACETAMS

Schedule 4

ANIRACETAM
cross reference: RACETAMS

Schedule 4

COLURACETAM
cross reference: RACETAMs

Schedule 4

DIMIRACETAM
cross reference: RACETAMS

Schedule 4

FASORACETAM
cross reference: RACETAMS

Schedule 4

METHYLPHENYLPIRACETAM
cross reference: RACETAMS

Schedule 4

NEBRACETAM
cross reference: RACETAMS

Schedule 4

NEFIRACETAM
cross reference: RACETAMS

Schedule 4

OMBERACETAM
cross reference: RACETAMS

Schedule 4

OXIRACETAM
cross reference: RACETAMS

Schedule 4

PHENYLPIRACETAM
cross reference: RACETAMS

Schedule 4

PRAMIRACETAM
cross reference: RACETAMS

Schedule 4

ROLZIRACETAM
cross reference: RACETAMS

Schedule 4

SELETRACETAM
Cross reference RACETAMS

Schedule 4

Appendix K

Schedule 4

SUNIFIRAM
cross reference: RACETAMS

Schedule 4

UNIFIRAM
cross reference: RACETAMS

Index – Amended Entries

BRIVARACETAM

cross reference: RACETAMS

Schedule 4

Appendix K

LEVETIRACETAM
cross reference: RACETAMS

Schedule 4

Appendix K

PIRACETAM
cross reference: RACETAMS

Schedule 4

Implementation date: *1 June 2019*

Reasons

The reasons for the final decision remain the same as for the interim decision.

Public submissions on the interim decision

Nil received

Interim decision

The interim decision was published on the TGA website on 7 February 2019 at Scheduling delegates' interim decisions and invitation for further comment: ACMS #25, November 2018 – 1.2 Racetams.

Scheduling proposal

The pre-meeting scheduling proposal was published on the TGA website on 31 August 2018 at Consultation: Proposed amendments to the Poisons Standard - ACCS, ACMS and Joint ACCS-ACMS meetings, November 2018.

2. Joint meeting of the Advisory Committee on Chemicals and Medicines Scheduling (ACCS-ACMS #20)

2.1. Salts of boric acid

Delegate's final decision

Final decision

The delegate's final decision under regulation 42ZCZR of the *Therapeutic Goods Regulations 1990* (the Regulations) is to amend the current Poisons Standard in relation to boric acid and its salts. The amendments relate to the delegate's final decision (published on 10 April 2018) to amend the Schedule 5 entry for boric acid aligning it with the European Union cut-off concentrations for cosmetics, to create new entries in Schedule 5 for the salts of boric acid (due to be implemented on 1 June 2019) and to create new Appendix F, Part 3 entries, as follows:

Schedule 5

BORIC ACID **except**:

a) when included in Schedule 4; or

b) in ~~preparations, other than insect baits, containing 1 per cent or less calculated as boron; or; c)~~ cosmetic hand cleaning preparations when labelled with a warning to the following effect:

NOT TO BE USED FOR CHILDREN UNDER 3 YEARS OF AGE; and if the concentration of free soluble borates exceeds 1.5 per cent (as boric acid), with the words: NOT TO BE USED ON PEELING OR IRRITATED SKIN; or

c) in cosmetic talc preparations containing 5 ~~%~~ per cent or less calculated as ~~boron~~ boric acid when labelled with a warning to the following effect:

~~DO~~ NOT TO BE USED ~~(*THIS PRODUCT/INSERT NAME OF PRODUCT*) IN~~ FOR CHILDREN UNDER 3 YEARS OF AGE ~~OR LESS~~; and if the concentration of free soluble borates exceeds 1.5 per cent (as boric acid), with the words: NOT TO BE USED ON PEELING OR IRRITATED SKIN; or

d) in cosmetic oral hygiene preparations containing 0.1~~%~~ per cent or less calculated as ~~boron~~ boric acid when labelled with a warning to the following effect:

NOT TO BE SWALLOWED. ~~DO~~ NOT TO BE USED ~~(*THIS PRODUCT/INSERT NAME OF PRODUCT*) IN~~ FOR CHILDREN UNDER 3 YEARS OF AGE ~~OR LESS~~; or

e) in other cosmetic preparations containing 3~~%~~ per cent or less calculated as ~~boron~~ boric acid when labelled with a warning to the following effect:

~~DO~~ NOT TO BE USED ~~(*THIS PRODUCT/INSERT NAME OF PRODUCT*) IN~~ FOR CHILDREN UNDER 3 YEARS OF AGE ~~OR LESS~~; and if the concentration of free soluble borates exceeds 1.5 per cent (as boric acid), with the words: NOT TO BE USED ON PEELING OR IRRITATED SKIN; or

f) in preparations, other than insect baits, containing 6 per cent or less calculated as boric acid.

~~Schedule 5 – New Entries~~

~~SODIUM BORATE (CAS No. 1330-43-4)~~ **~~except~~**~~:~~

~~a) in talc preparations containing 5% or less of sodium borate when labelled with a warning to the following effect:~~

~~DO NOT USE (THIS PRODUCT/*INSERT NAME OF PRODUCT*) IN CHILDREN 3 YEARS OF AGE OR LESS; or~~

~~b) in oral preparations containing 0.1% or less of sodium borate when labelled with a warning to the following effect:~~

~~DO NOT USE (THIS PRODUCT/INSERT NAME OF PRODUCT) IN CHILDREN 3 YEARS OF AGE OR LESS; or~~

~~c) in other preparations containing 3% or less of sodium borate when labelled with a warning to the following effect:~~

~~DO NOT USE (THIS PRODUCT/*INSERT NAME OF PRODUCT*) IN CHILDREN 3 YEARS OF AGE OR LESS.~~

~~POTASSIUM BORATE (CAS No. 1332-77-0)~~ **~~except~~**~~:~~

~~a) in talc preparations containing 5% or less of potassium borate when labelled with a warning to the following effect:~~

~~DO NOT USE (THIS PRODUCT/*INSERT NAME OF PRODUCT*) IN CHILDREN 3 YEARS OF AGE OR LESS; or~~

~~b) in oral preparations containing 0.1% or less of potassium borate when labelled with a warning to the following effect:~~

~~DO NOT USE (THIS PRODUCT/INSERT NAME OF PRODUCT) IN CHILDREN 3 YEARS OF AGE OR LESS; or~~

~~c) in other preparations containing 3% or less of potassium borate when labelled with a warning to the following effect:~~

~~DO NOT USE (THIS PRODUCT/*INSERT NAME OF PRODUCT*) IN CHILDREN 3 YEARS OF AGE OR LESS.~~

~~MEA-borate (CAS No. 26038-87-9)~~ **~~except~~**~~:~~

~~a) in talc preparations containing 5% or less of MEA-borate when labelled with a warning to the following effect:~~

~~DO NOT USE (THIS PRODUCT/*INSERT NAME OF PRODUCT*) IN CHILDREN 3 YEARS OF AGE OR LESS; or~~

~~b) in oral preparations containing 0.1% or less of MEA-borate when labelled with a warning to the following effect:~~

~~DO NOT USE (THIS PRODUCT/INSERT NAME OF PRODUCT) IN CHILDREN 3 YEARS OF AGE OR LESS; or~~

~~c) in other preparations containing 3% or less of MEA-borate when labelled with a warning to the following effect:~~

~~DO NOT USE (THIS PRODUCT/*INSERT NAME OF PRODUCT*) IN CHILDREN 3 YEARS OF AGE OR LESS.~~

~~MIPA-BORATE (CAS No. 26038-90-4 and 68003-13-4)~~ **~~except~~**~~:~~

~~a) in talc preparations containing 5% or less of MIPA-borate when labelled with a warning to the following effect:~~

~~DO NOT USE (THIS PRODUCT/*INSERT NAME OF PRODUCT*) IN CHILDREN 3 YEARS OF AGE OR LESS; or~~

~~b) in oral preparations containing 0.1% or less of MIPA-borate when labelled with a warning to the following effect:~~

~~DO NOT USE (THIS PRODUCT/INSERT NAME OF PRODUCT) IN CHILDREN 3 YEARS OF AGE OR LESS; or~~

~~c) in other preparations containing 3% or less of MIPA-borate when labelled with a warning to the following effect:~~

~~DO NOT USE (THIS PRODUCT/*INSERT NAME OF PRODUCT*) IN CHILDREN 3 YEARS OF AGE OR LESS.~~

~~**Index – New Entries**~~

~~**SODIUM BORATE (CAS No. 1330-43-4)**~~
~~Schedule 5~~

~~**POTASSIUM BORATE (CAS No. 1332-77-0)**~~

~~Schedule 5~~

~~**MEA-BORATE (CAS No. 26038-87-9)**~~

~~Schedule 5~~

~~**MIPA-BORATE (CAS No. 26038-90-4 and 68003-13-4)**~~

~~Schedule 5~~

Appendix E, Part 2

BORIC ACID

First aid instructions: A.

Appendix F, Part 3 – New Entry

BORIC ACID when included in Schedule 5

Warning statements: **25**, **26**.

Index – Amend Entry

BORIC ACID cross reference: BORAX, SODIUM BORATE, POTASSIUM BORATE, MEA-BORATE, MIPA-BORATE

Schedule 5

Schedule 4

Appendix E, Part 2

Appendix F, Part 3

Implementation date: *1 February 2021*

Reasons

The delegate has confirmed that the reasons for the final decision align with those for the interim decision.

Additional reasons, including consideration of the public submission on the interim decision:

Having considered the public submission on the interim decision, to further clarify which substances are captured by the boric acid entry and to facilitate compliance, the index entry will be further amended to include cross references to the additional compounds, sodium borate, potassium borate, meta-borate and mipa-borate.

Public submissions on the interim decision

One (1) public submission was received before the second closing date in response to an invitation published on 7 February 2019 under regulation 42ZCZP of the Regulations. While the submission was generally supportive, it did request minor changes to the interim decision to provide clarity and reduce the regulatory burden on industry.

The main points raised in the submission were:

- It was previously indicated that there was a preference for the scheduling of the four salts specifically (i.e. by CAS number). If separate entries by CAS number are not supported in this case, other ways of easily identifying the substances intended to be captured by the Schedule entry should be considered i.e. by adding the four borate salts (sodium borate, potassium borate, MEA-borate, MIPA-borate) to the index with cross-references to the boric acid entry.
- The concentration cut-off for the exemption for non-cosmetic preparations (other than insect baits) is now expressed as a percentage of boric acid instead of boron, though the effective concentration remains the same. This change provides consistency with the exemptions for cosmetic products, based on the European Union Cosmetics Regulation.
- An adequate transition period of at least 12 months, preferably 24 months, is necessary to accommodate these changes as there is no evidence that would suggest immediate action is required for the risk management of these substances.

Interim decision

The interim decision was published on the TGA website on 7 February 2019 at Scheduling delegates' interim decisions and invitation for further comment: ACCS/ACMS #20, November 2018 – 2.1 Salts of boric acid.

Scheduling proposal

The pre-meeting scheduling proposal was published on the TGA website on 31 August 2018 at Consultation: Proposed amendments to the Poisons Standard - ACCS, ACMS and Joint ACCS-ACMS meetings, November 2018.

2.2. Naphthalene

Delegate's final decision

Final decision

The delegate's final decision under regulation 42ZCZR of the *Therapeutic Goods Regulations 1990* (the Regulations) is to amend the current Poisons Standard in relation to naphthalene as follows:

Schedule 10 – New Entry

NAPHTHALENE (excluding derivatives) in preparations in block, ball, disc, pellet or flake form for domestic use **except** when enclosed in a device which, in normal use, prevents removal or ingestion of its contents.

Schedule 6 – Amend Entry

NAPHTHALENE (excluding its derivatives) **except** in liquid hydrocarbons ~~as an impurity.~~

Index – Amend Entry

NAPHTHALENE

Schedule 10

Schedule 6

Appendix E, Part 2

Appendix F, Part 3

Appendix G

Implementation date: *1 June 2019*

Reasons

The delegate has confirmed that the reasons for the final decision align with those for the interim decision.

Additional reasons, including consideration of the public submissions on the interim decision:

The purpose of the Schedule 10 entry is to address public health risks associated with the importation, retail and use of non-compliant naphthalene in domestic situations for the control of moths and larvae which are destructive to natural-fibre textiles. However, having considered the public submissions on the interim decision, the interim decision has been qualified to ensure that legitimate domestic uses of naphthalene are not inadvertently captured.

Public submissions on the interim decision

Four (4) public submissions were received before the second closing date in response to an invitation published on 7 February 2019 under regulation 42ZCZP of the Regulations. All four submissions were not supportive of the proposed amendments.

The main points provided in opposition of the amendment were:

- The proposed Schedule 10 entry should be qualified as it is not currently clear as to what products would potentially be incorporated under the proposed entry.
- By extension, clarification is required as to what is meant by the Schedule 6 statement 'except in liquid hydrocarbons as an impurity'. Industry have been able to quantify the benzene content in fuels and solvents and schedule high boiling aromatic hydrocarbon solvents with particular exclusions, yet industry has been left in a state of unknown compliance in respect to when naphthalene should be considered to be an impurity. It would be useful to resolve the issue of what is a naphthalene solvent impurity at this stage to minimise the uncertainty to the manufacturing industry.
- Naphthalene in each Schedule needs to be considered on its own individual merit as presented, as there is no link or reference between the schedules. Consequently, anything that meets the Schedule 10 definition of naphthalene will be prohibited from sale and supply for domestic use and this will lead to prohibition of critical products from the market place, beyond the intention of the review.
- The proposal would have substantial and widespread impacts on the economy. If the decision is to maintain the current interim decision, the proposal is likely to have a measurable impact on business, community or individuals. Under such circumstances it is considered that a RIS (Regulatory Impact Statement) would be required to ensure the net impact is fully evaluated as recommended.

Interim decision

The interim decision was published on the TGA website on 7 February 2019 at Scheduling delegates' interim decisions and invitation for further comment: ACCS/ACMS, November 2018 – 2.2 Naphthalene.

Scheduling proposal

The pre-meeting scheduling proposal was published on the TGA website on 31 August 2018 at Consultation: Proposed amendments to the Poisons Standard - ACCS, ACMS and Joint ACCS-ACMS meetings, November 2018.

3. Advisory Committee on Chemicals Scheduling (ACCS #23)

3.1. 2-chloro-p-phenylenediamine/2-chloro-p-phenylenediamine sulfate

Delegate's final decision

Final decision

The delegate's final decision under regulation 42ZCZR of the *Therapeutic Goods Regulations 1990* (the Regulations) is to amend the current Poisons Standard in relation to 2-chloro-p-phenylenediamine/2-chloro-p-phenylenediamine sulfate as follows:

Schedule 6 – Amend Entry

PHENYLENEDIAMINES including alkylated, arylated, halogenated and nitro derivatives not elsewhere specified in these Schedules:

a) in preparations packed and labelled for photographic purposes;

b) in preparations packed and labelled for testing water except tablets containing 10 mg or less of diethyl-para-phenylenediamine or dimethyl-para-phenylenediamine in opaque strip packaging provided the directions for use include the statement, "Do not discard testing solutions into the pool";

c) in hair dye preparations except when the immediate container and primary pack are labelled with the following statements:

KEEP OUT OF REACH OF CHILDREN, and

WARNING – This product contains ingredients which may cause skin irritation to certain individuals. A preliminary test according to the accompanying directions should be made before use. This product must not be used for dyeing eyelashes or eyebrows; to do so may be injurious to the eye.

written in letters not less than 1.5 mm in height; or

d) in eyelash and eyebrow tinting products when the immediate container and primary pack are labelled with the following statement:

WARNING – This product contains ingredients which may cause skin irritation to certain individuals, and when used for eyelash and eyebrow tinting may cause injury to the eye. A preliminary test according to the accompanying directions should be made before use.

written in letters not less than 1.5 mm in height.

Schedule 10 – Amend Entry

PHENYLENEDIAMINES, including alkylated, arylated, halogenated and nitro derivatives, in preparations for skin colouration, tattooing and dyeing of eyelashes or eyebrows **except** when included in Schedule 6.

Appendix E Part 2 – Amend Entry

PHENYLENEDIAMINES, including alkylated, arylated, halogenated and nitro derivatives

- Standard statements when used in hair dyes: **A**, **E1**.

- Standard statements when used in preparations other than hair dyes: **A**, **G1, G3**, **E1**, **S1**.

Appendix F Part 3 – Amend Entry

PHENYLENEDIAMINES including alkylated, arylated, halogenated and nitro derivatives

- Warning statements when used in hair dyes: **21.**
- Warning statements when used in in preparations other than hair dyes: **28.**
- Safety directions when used in preparations other than hair dyes: **1, 4**, **8.**

Index – Amend entry

PHENYLENEDIAMINES cross reference: ~~ALKYLATED PHENYLENEDIAMINES~~, ALKYLATED, ARYLATED, HALOGENATED and NITRO- PHENYLENEDIAMINES, DIETHYL-PARA-PHENYLENEDIAMINE, DIMETHYL-PARA-PHENYLENEDIAMINE

INDEX

Schedule 10

Schedule 6

Appendix E, Part 2

Appendix F, Part 3

Implementation date: *1 June 2019*

Reasons

The reasons for the final decision remain the same as for the interim decision. It is noted that the public submission received in response to the interim decision, did not present any new evidence.

Public submissions on the interim decision

One public submission was received before the second closing date in response to an invitation published on 7 February 2019 under regulation 42ZCZP of the Regulations. The submission supported the interim decision.

The main points provided in support of the amendment were:

- The proposed amendment will clarify that halogenated derivatives are captured by the existing scheduling entries for phenylenediamines; and
- The clarification is not expected to result in any regulatory impact.

Interim decision

The interim decision was published on the TGA website on 7 February 2019 at Scheduling delegates' interim decisions and invitation for further comment: ACCS #23, November 2018 – 3.1 2-chloro-p-phenylenediamine.

Scheduling proposal

The pre-meeting scheduling proposal was published on the TGA website on 31 August 2018 at Consultation: Proposed amendments to the Poisons Standard - ACCS, ACMS and Joint ACCS-ACMS meetings, November 2018.

Part B - Final decisions on matters not referred to an expert advisory committee

4. New Chemical Entities – medicines for human therapeutic use

4.1. Galcanezumab

Delegate's final decision

Final decision

The delegate's final decision is to amend the Poisons Standard to include galcanezumab in Schedule 4 as follows:

Schedule 4 – New Entry

GALCANEZUMAB

Index – New Entry

GALCANEZUMAB

Schedule 4

Implementation date: *1 June 2019*

Reasons

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate for the decision include:

a. the risks and benefits of the use of a substance:

It is a new chemical entity with no clinical or marketing experience in Australia.

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

Migraine prophylaxis requires medical assessment and monitoring.

c. the toxicity of a substance:

Potential toxicity is not known.

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

Substance requires subcutaneous injection

e. the potential for abuse of a substance:

Nil

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

Nil

Scheduling proposal

The delegate of the Secretary proposed to amend the Poisons Standard with respect to galcanezumab, a new chemical entity (NCE) for a human therapeutic medicine.

Scheduling status

Galcanezumab is not specifically scheduled in the Poisons Standard but as it is a monoclonal antibody, galcanezumab is captured by the Schedule 4 entry for monoclonal antibodies as follows:

> **Schedule 4**
>
> MONOCLONAL ANTIBODIES for therapeutic use **except**:
>
> a) in diagnostic test kits; or
>
> b) when separately specified in these Schedules.

Delegate's considerations

- Section 52E(1) of the *Therapeutic Goods Act 1989*;
- Scheduling Policy Framework (SPF 2018); and
- Advice on the place in therapy of this NCE.

4.2. Doravirine

Delegate's final decision

Final decision

The delegate's final decision is to amend the Poisons Standard to include doravirine in Schedule 4 as follows:

Schedule 4 – New Entry

DORAVIRINE

Index – New Entry

DORAVIRINE

Schedule 4

Implementation date: *1 June 2019*

Reasons

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate for the decision include:

a. the risks and benefits of the use of a substance:

It is a New Chemical Entity with no clinical or marketing experience in Australia. The risk-benefit requires appropriate selection of patients by the treating physician.

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

Used in the treatment of a serious infection (HIV) requiring specialised medical oversight and monitoring.

c. the toxicity of a substance:

Doravirine is a HIV-1 non-nucleoside reverse transcriptase inhibitor (NNRTI). Toxicity typical of NNRTI agents is expected. Drug interactions are also a safety concern.

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

Presentation and packaging consistent with the labelling requirements for prescription medicine.

e. the potential for abuse of a substance:

Nil

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

Nil

Scheduling proposal

The delegate of the Secretary proposed to amend the Poisons Standard with respect to doravirine, a new chemical entity (NCE) for a human therapeutic medicine.

Scheduling status

Doravirine is not specifically scheduled and is not captured by any entry in the Poisons Standard.

Delegate's considerations

- Section 52E(1) of the *Therapeutic Goods Act 1989*;
- Scheduling Policy Framework (SPF 2018); and
- Advice on the place in therapy of this NCE.

4.3. Abemaciclib

Delegate's final decision

Final decision

The delegate's final decision is to amend the Poisons Standard to include abemaciclib in Schedule 4 as follows:

Schedule 4 – New Entry

ABEMACICLIB

Index – New Entry

ABEMACICLIB

Schedule 4

Implementation date: *1 June 2019*

Reasons

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate for the decision include:

a. the risks and benefits of the use of a substance:

As per palbociclib which is Schedule 4.

Benefit: Improvement in PFS (Progression Free Survival - length of time during and after the treatment of a disease, such as cancer, that a patient lives with the disease without it getting worse).

Risks: VTE (Venous thromboembolism), diarrhoea, neutropenia.

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

Abemaciclib is indicated for the treatment of women with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant as initial endocrine-based therapy, or in women who have received prior endocrine therapy (MONARCH-2,3).

In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinising hormone-releasing hormone (LHRH) agonist.

c. the toxicity of a substance:

Nil

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

Nil

e. the potential for abuse of a substance:

Nil

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

Nil

Scheduling proposal

The delegate of the Secretary proposed to amend the Poisons Standard with respect to abemaciclib, a new chemical entity (NCE) for a human therapeutic medicine.

Scheduling status

Abemaciclib is not specifically scheduled and is not captured by any entry in the Poisons Standard.

Delegate's considerations

- Section 52E(1) of the *Therapeutic Goods Act 1989*;
- Scheduling Policy Framework (SPF 2018); and
- Advice on the place in therapy of this NCE.

4.4. Plitidepsin

Delegate's final decision

Final decision

The delegate's final decision is to amend the Poisons Standard to include plitidepsin in Schedule 4 as follows:

Schedule 4 – New Entry

PLITIDEPSIN

Appendix L – New Entry

PLITIDEPSIN

Warning statements: 7 (WARNING – Causes birth defects), 62 (Do not use if pregnant), 63 (See a doctor if you are pregnant or diabetic), 76 (Do not become pregnant during use or within 6 months of stopping treatment), 87 (Plitidepsin remains in the body for many months after treatment has stopped. Do not become pregnant or father a child before consulting your doctor)

Index - New Entry

PLITIDEPSIN

Schedule 4

Appendix L

Implementation date: *1 June 2019*

Reasons

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate for the decision include:

a. the risks and benefits of the use of a substance:

It is a new cytotoxic chemical entity with no marketing experience in Australia.

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

Plitidepsin is used for the treatment of patients with relapsed or refractory multiple myeloma who have received at least three prior treatment regimens, including both a proteasome inhibitor and an immunomodulator. Aplidin may be used after two prior lines of therapy if refractory and/or intolerant to both a proteasome inhibitor and an immunomodulator.

c. the toxicity of a substance:

Reported adverse effects from plitidepsin exposure include cytopaenias, elevation of creatine phosphokinase, liver enzyme derangement, cardiac rhythm disturbance and fatigue.

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

Plitidepsin is presented as a powder for reconstitution and administered by intravenous injection.

e. *the potential for abuse of a substance:*

There is no identified risk of abuse of plitidepsin outside the registered indication.

f. *any other matters that the Secretary considers necessary to protect public health:*

Nil.

Scheduling proposal

The delegate of the Secretary proposed to amend the Poisons Standard with respect to plitidepsin, a new chemical entity (NCE) for a human therapeutic medicine.

Scheduling status

Plitidepsin is not specifically scheduled and is not captured by any entry in the Poisons Standard.

Delegate's considerations

- Subsection 52E(1) of the *Therapeutic Goods Act 1989*;
- The Scheduling Policy Framework (2018) scheduling factors;
- The TGA evaluation report;
- The advice of the Advisory Committee Medicines; and
- The new drug application.

4.5. Isavuconazole

Delegate's final decision

Final decision

The delegate's final decision is to amend the Poisons Standard to include isavuconazole in Schedule 4 as follows:

Schedule 4 – New Entry

ISAVUCONAZOLE

Appendix L – New Entry

ISAVUCONAZOLE

Warning statement: 53 (CAUTION – Isavuconazole should not be used by pregnant women)

Index – New Entries

ISAVUCONAZOLE

Schedule 4

Appendix L

Implementation date: *1 June 2019*

Reasons

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate for the decision include:

a. the risks and benefits of the use of a substance:

Isavuconazole is a new chemical entity with no clinical or marketing experience in Australia.

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

Isavuconazole is used for the treatment of invasive aspergillosis and mucormycosis in patients for whom amphotericin B is inappropriate.

c. the toxicity of a substance:

Safety issues include hepatotoxicity and the potential for drug-drug interactions.

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

Isavuconazole should be prescribed by medical professionals who are familiar with the management of invasive fungal infections. Patients need to be instructed to follow the dosing regimens.

e. the potential for abuse of a substance:

Nil

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

The Australian Pregnancy Categorisation for isavuconazonium is D, as reproductive toxicity studies showed an increased incidence of bone abnormalities in rats and rabbits.

Scheduling proposal

The delegate of the Secretary proposed to amend the Poisons Standard with respect to isavuconazole, a new chemical entity (NCE) for a human therapeutic medicine.

Scheduling status

Isavuconazole is not specifically scheduled and is not captured by any entry in the Poisons Standard.

Delegate's considerations

- Section 52E(1) of the *Therapeutic Goods Act 1989*;
- Scheduling Policy Framework (SPF 2018); and
- Advice on the place in therapy of this NCE.

4.6. Semaglutide

Delegate's final decision

Final decision

The delegate's final decision is to amend the Poisons Standard to include semaglutide in Schedule 4 as follows:

Schedule 4 – New Entry

SEMAGLUTIDE

Index - New Entry

SEMAGLUTIDE

Schedule 4

Implementation date: *1 June 2019*

Reasons

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate for the decision include:

a. the risks and benefits of the use of a substance:

It is a new biological entity with no clinical or marketing experience in Australia.

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

Semaglutide is a long-acting glucagon like peptide-1 (GLP-1) receptor agonist (GLP=1RA), with suggested indication for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise:

- as monotherapy when metformin is considered inappropriate due to intolerance or contraindications
- in addition to other medicinal products for the treatment of type 2 diabetes

c. the toxicity of a substance:

No known major/serious toxicities

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

No specific requirements over existing regulations and guidelines

e. the potential for abuse of a substance:

Unlikely

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

Nil

Scheduling proposal

The delegate of the Secretary proposed to amend the Poisons Standard with respect to semaglutide, a new chemical entity (NCE) for a human therapeutic medicine.

Scheduling status

Semaglutide is not specifically scheduled and is not captured by any entry in the Poisons Standard.

Delegate's considerations

- Advice on the place in therapy of this NCE;
- Scheduling Policy Framework (SPF 2018); and
- Section 52E(1) of the *Therapeutic Goods Act 1989*.

4.7. Cenegermin

Delegate's final decision

Final decision

The delegate's final decision is to amend the Poisons Standard to include cenegermin in Schedule 4 as follows:

Schedule 4– New Entry

CENEGERMIN

Index- New Entry

CENEGERMIN

Schedule 4

Implementation date: *1 June 2019*

Reasons

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate for the decision include:

a. the risks and benefits of the use of a substance:

Cenegermin is a new biological medicine not currently captured under an existing schedule.

In clinical trials, treatment with cenegermin resulted in healing of corneal epithelial defects, improvement of corneal sensation, and improvement in vision. There were no major adverse effects.

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

Cenegermin is indicated for the treatment of neurotrophic keratitis.

The diagnosis of neurotrophic keratitis requires a detailed clinical assessment and ongoing assessment by an ophthalmologist. This is a prescription medicine.

c. the toxicity of a substance:

Clinical trials did not show any evidence of toxicity when used as directed in the clinical trial protocol.

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

Eye drop. given as 1 drop 6 times a day

e. the potential for abuse of a substance:

Low

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

Nil

Scheduling proposal

The delegate of the Secretary proposed to amend the Poisons Standard with respect to cenegermin, a new chemical entity (NCE) for a human therapeutic medicine.

Scheduling status

Cenegermin is not specifically scheduled and is not captured by any entry in the Poisons Standard.

Delegate's considerations

- Advice on the place in therapy of this NCE;
- Scheduling Policy Framework (SPF 2018); and
- Section 52E(1) of the *Therapeutic Goods Act 1989*.