# Final decisions and reasons for decisions by delegates of the Secretary to the Department of Health

# October 2014

## Notice under subsections 42ZCZS and 42ZCZX of the Therapeutic Goods Regulations 1990 (the Regulations)

A delegate of the Secretary to the Department of Health hereby gives notice of the delegate's final decisions for amending the Poisons Standard (commonly referred to as the *Standard for the Uniform Scheduling of Medicines and Poisons* – SUSMP) under subsections 42ZCZS and 42ZCZX of the Therapeutic Goods Regulations 1990 (the Regulations). This notice also provides the reasons for each decision and the date of effect (implementation date) of the decision.

The delegate's final decisions and reasons relate to:

- scheduling proposals initially referred to the July 2014 meeting of the Advisory Committee on Medicines Scheduling (ACMS#12);
- scheduling proposals considered as delegate-only matters, i.e. not referred to an expert advisory committee.

## Scheduling proposals referred to the expert advisory committees

### Pre-meeting public notice

A 'pre-meeting' public notice inviting submissions on the scheduling proposals referred to the expert advisory committees was published on 3 April 2014 and the second public notice was published on and 29 May 2014 at http://www.tga.gov.au/newsroom/consult-scheduling-acms-1407.htm and http://www.tga.gov.au/newsroom/consult-scheduling-accs-1407.htm, respectively.

Edited versions of these public submissions received in response to this invitation were published on 18 September 2014 at http://www.tga.gov.au/industry/scheduling-submissions-acms-1407.htm.

### Interim decisions

The delegate's interim decisions on recommendations by the ACMS#12 were published on 18 September 2014 at http://www.tga.gov.au/industry/scheduling-decisions-1409-interim.htm. This public notice also invited further comment from the applicant and from those parties who made a valid submission in response to the original invitation for submissions.

Further submissions from parties other than those who made a valid submission in response to the original invitation or the applicant, or those received after the closing date, may not be considered by the delegate.

Edited versions of valid public submissions received in response to the interim decisions were published on 23 October 2014 and are available at http://www.tga.gov.au/industry/scheduling-decisions-interim.htm.

### Final decisions

In accordance with subsection 42ZCZR of the Regulations, if a delegate makes an interim decision on an application, the delegate may make a final decision either, confirming, varying or setting aside the interim decision, but only after considering any valid submissions received in response to the interim decisions.

## Matters not referred to an advisory committee

A delegate may decide not to refer a scheduling proposal to an expert advisory committee for advice and instead may make a delegate-only decision. When deciding not to refer a matter to a committee, the delegate considers the scheduling guidelines as set out in the *Scheduling Policy Framework for Chemicals and Medicines* (SPF, 2010), available at http:www.tga.gov.au/industry/scheduling-spf.htm**.**

## Publishing of the amendments to the Poisons Standard

The amendments to the Schedules, Appendices or other parts of the Poisons Standard are published electronically on ComLaw as amendments to the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) prior to the date of effect (implementation date) of the final decisions. Further information, including links to the Poisons Standard on ComLaw, is available at http:www.tga.gov.au/industry/scheduling-poisons-standard.htm.

# Glossary

| Abbreviation | Name |
|---|---|
| AAN | Australian Approved Name |
| AC | Active constituent |
| ACCC | Australian Competition and Consumer Commission |
| ACCM | Advisory Committee on Complementary Medicines (formerly Complementary Medicine Evaluation Committee [CMEC]) |
| ACNM | Advisory Committee on Non-prescription Medicines (formerly Medicines Evaluation Committee [MEC]) |
| ACPM | Advisory Committee on Prescription Medicines (formerly Australian Drug Evaluation Committee [ADEC]) |
| ACSOM | Advisory Committee on the Safety of Medicines (formerly Adverse Drug Reactions Advisory Committee [ADRAC]) |
| ADEC | Australian Drug Evaluation Committee (now Advisory Committee on Prescription Medicines [ACPM]) |
| ADI | Acceptable daily intake |
| ADRAC | Adverse Drug Reactions Advisory Committee (now Advisory Committee on the Safety of Medicines [ACSOM]) |
| AHMAC | Australian Health Ministers' Advisory Council |
| APVMA | Australian Pesticides and Veterinary Medicines Authority |
| AQIS | Australian Quarantine and Inspection Service |
| ARfD | Acute reference dose |
| ASCC | Australian Safety and Compensation Council |
| ASMI | Australian Self-Medication Industry |
| ARTG | Australian Register of Therapeutic Goods |
| CAS | Chemical Abstract Service |

| Abbreviation | Name |
|---|---|
| CHC | Complementary Healthcare Council of Australia |
| CMEC | Complementary Medicine Evaluation Committee (now Advisory Committee on Complementary Medicines [ACCM]) |
| CMI | Consumer Medicine Information |
| COAG | Councils of Australian Governments |
| CRC | Child-resistant closure |
| CTFAA | Cosmetic, Toiletry & Fragrance Association of Australia |
| CWP | Codeine Working Party |
| DAP | Drafting Advisory Panel |
| ECRP | Existing Chemicals Review Program |
| EPA | Environmental Protection Authority |
| ERMA | Environmental Risk Management Authority (New Zealand) |
| FAISD | First Aid Instructions and Safety Directions |
| FDA | Food and Drug Administration (United States) |
| FOI | *Freedom of Information Act 1982* |
| FSANZ | Food Standards Australia New Zealand |
| GHS | Globally Harmonised System for Classification and Labelling of Chemicals |
| GIT | Gastro-intestinal tract |
| GP | General practitioner |
| HCN | Health Communication Network |
| IMAP | Inventory Multi-tiered Assessment Prioritisation |

| Abbreviation | Name |
|---|---|
| INN | International Non-proprietary Name |
| ISO | International Standards Organization |
| $LC_{50}$ | The concentration of a substance that produces death in 50 per cent of a population of experimental organisms. Usually expressed as mg per litre (mg/L) as a concentration in air. |
| $LD_{50}$ | The concentration of a substance that produces death in 50 per cent of a population of experimental organisms. Usually expressed as milligrams per kilogram (mg/kg) of body weight. |
| LOAEL | Lowest observed adverse effect level |
| LOEL | Lowest observed effect level |
| MCC | Medicines Classification Committee (New Zealand) |
| MEC | Medicines Evaluation Committee (now Advisory Committee on Non-prescription Medicines [ACNM]) |
| MOH | Ministry of Health (New Zealand) |
| NCCTG | National Coordinating Committee on Therapeutic Goods |
| NDPSC | National Drugs and Poisons Schedule Committee |
| NHMRC | National Health and Medical Research Council |
| NICNAS | National Industrial Chemicals Notification & Assessment Scheme |
| NOAEL | No observed adverse effect level |
| NOEL | No observable effect level |
| NOHSC | National Occupational Health & Safety Commission |
| OCM | Office of Complementary Medicines |
| OCSEH | Office of Chemical Safety and Environmental Health (now Office of Chemical Safety [OCS]) |

| Abbreviation | Name |
|---|---|
| OCS | Office of Chemical Safety (formerly Office of Chemical Safety and Environmental Health [OCSEH]) |
| ODA | Office of Devices Authorisation |
| OMA | Office of Medicines Authorisation (formerly Office of Prescription and Non-prescription Medicines) |
| OOS | Out of session |
| OTC | Over-the-counter |
| PACIA | Plastics and Chemicals Industries Association |
| PAR | Prescription animal remedy |
| PBAC | Pharmaceutical Benefits Advisory Committee |
| PEC | Priority existing chemical |
| PGA | Pharmaceutical Guild of Australia |
| PHARM | Pharmaceutical Health and Rational Use of Medicines |
| PI | Product Information |
| PIC | Poisons Information Centre |
| PSA | Pharmaceutical Society of Australia |
| QCPP | Quality Care Pharmacy Program |
| QUM | Quality Use of Medicines |
| RFI | Restricted flow insert |
| SCCNFP | Scientific Committee on Cosmetic and Non-Food Products |
| SCCP | Scientific Committee on Consumer Products |
| STANZHA | States and Territories and New Zealand Health Authorities |

| Abbreviation | Name |
|---|---|
| SUSDP | Standard for the Uniform Scheduling of Drugs and Poisons |
| SUSMP | Standard for the Uniform Scheduling of Medicines and Poisons |
| SVT | First aid for the solvent prevails |
| TCM | Traditional chinese medicine |
| TGA | Therapeutic Goods Administration |
| TGC | Therapeutic Goods Committee |
| TGO | Therapeutic Goods Order |
| TTHWP | Trans-Tasman Harmonisation Working Party |
| TTMRA | Trans-Tasman Mutual Recognition Agreement |
| WHO | World Health Organization |
| WP | Working party |
| WS | Warning statement |

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# Part A - Final decisions on matters referred to an expert advisory committee

## 1. Scheduling proposals referred to the July 2014 meeting of the Advisory Committee on Medicines Scheduling (ACMS#12)

### 1.1 AMOROLOFINE

***Scheduling proposal***

The medicines scheduling delegate considered a proposal to amend the Schedule 2 amorolfine entry to exempt from scheduling preparations for the treatment of onychomycoses (fungal infections of the nail).

The delegate referred the proposal to the Advisory Committee on Medicines Scheduling (ACMS) for advice.

***Substance summary***

Amorolfine is a morpholine derivative with antifungal activity. It acts by interfering with the synthesis of sterols essential for the functioning of fungal cell membranes. Amorolfine is active *in vitro* against a wide variety of pathogenic and opportunistic fungi including dermatophytes, *Blastomyces dermatitidis*, *Candida* spp., *Histoplasma capsulatum*, and *Sporothrix schenckii*. It also has variable activity against *Aspergillus* spp. However, despite its *in vitro* activity, amorolfine is inactive when given systemically and this limits its use to topical application for superficial infections.

For the treatment of nail infections caused by dermatophytes, yeasts, and moulds a lacquer containing the equivalent of 5% amorolfine is painted onto the affected nail once or sometimes twice weekly until the nail has regenerated. Treatment generally needs to be continued for 6 to 12 months. For skin infections, including dermatophyte infections, a cream containing the equivalent of 0.25% amorolfine is applied once daily for at least 2 to 3 weeks (up to 6 weeks for foot infections) and continued for 3 to 5 days after clinical cure is achieved.

***Scheduling status***

Amorolfine is currently listed in Schedule 2 and Schedule 4 of the SUSMP.

**SCHEDULE 2**

AMOROLFINE for topical use except in preparations for the treatment of tinea pedis.

**SCHEDULE 4**

AMOROLFINE except:

(a) when included in Schedule 2; or
(b) in preparations for the treatment of tinea pedis.

***Scheduling history***

In February 1995, the National Drug and Poisons Scheduling Committee (NDPSC) considered the outcome of the 173rd Australian Drug Evaluation Committee (ADEC) meeting, which approved the registration of amorolfine. Based on this approval, the committee scheduled amorolfine in Schedule 4.

The NDPSC considered a proposal to place amorolfine in Schedule 2 for topical preparations containing 5% or less of the substance for the treatment of nail infections in February 1998. The committee felt that with inadequate safety data regarding the long term use, the ADEC consideration of the product for registration and the concern that consumers could not accurately diagnosis the condition without medical advice, the scheduling remained appropriate as Schedule 4.

The sponsor requested the committee to reconsider the proposal in May 1998. The sponsor provided further information addressing the NDPSC concerns and the committee noted that other aspects of the application were not give adequate consideration. The committee decided to review the application, pending information from the sponsor.

Amorolfine next appeared in the scheduling history records in August 1999. During this time, a Schedule 3 entry for the substance had been either considered or recommended, but no record of this could be located. Based on a recommendation from the Trans-Tasman Harmonisation Working Party (TTHWP), the Schedule 4 and 3 entries were to be amended and a new Schedule 2 entry was to be created for topical preparations containing 0.25% or less of amorolfine. This recommendation was in line with New Zealand's entry for creams treating tinea pedis and the Schedule 3 equivalent for nail lacquers. The committee also agreed on an Appendix H entry for the substance.

During discussions at the November 1999 meeting, the committee noted that the amendments suggested in August 1999 followed the consideration of proposals from the product sponsor and the TTHWP, with the sponsor requesting the Schedule 3 entry and Appendix H listing and the TTHWP recommending the Schedule 2 entry. The NDPSC supported the proposals and the committee accepted the findings of the AHMAC committee in relation to the matters mentioned in subsection 52E (1) of the Act. The Schedule 4 and 3 entries were amended and the Schedule 2 entry outlined in August 1999 was accepted.

In October 2005, the NDPSC reviewed the scheduling of amorolfine, including the TTHWP recommendations. They noted that in NZ, amorolfine products containing 0.25% or less of the substance for the treatment of tinea pedis were general sale (exempt from scheduling). Harmonisation was supported on the basis of history of safe use in NZ and the committee foreshadowed amending the Schedule 2 entry to exempt preparations for the treatment of tinea pedis.

In February 2006, the committee confirmed the foreshadowed decisions outlined in October 2005 on the grounds of harmonisation.

Amorolfine was considered as part of a group item relating to substances that are applied to nails and clarifying their scheduling entries in June 2006. The committee reviewed the history of the scheduling decisions, and discussed substance details and possible amendments to the amorolfine entries, in an effort to be consistent with other substance entries relating to the fungal treatment of nails. The members agreed that an amendment for consistency was not appropriate in this case.

In June 2010 the committee discussed an application from the product sponsor requesting that all topical use preparations of amorolfine, regardless of strength, be rescheduled from Schedule 3 to Schedule 2. The applicant stated that there was low potential for harm from inappropriate use and low abuse potential, low or well characterised incidence of adverse effects, the condition onychomycosis is easily recognisable by the consumer and amenable to short-term treatment and that there are positive benefits for consumers. The committee agreed to remove the Schedule 3 entry and place all topical preparations in Schedule 2 on the grounds the risk posed by the substance was similar to other schedule 2 anti-fungals and that any risk would be addressed by labelling. The exemption for preparations treating tinea pedis remained.

In June 2011, the medicines delegate agreed with an ACMS member's comments that now there was no longer a Schedule 3 entry for the substance, the Appendix H entry was no longer needed and the delegate decided that it would be removed.

### *Pre-meeting public submissions*

Two submissions were received; both did not support the proposal. The first submission was of the belief that access to health professionals is required for correct use of treatments and that underlying or related health conditions associated with onychomycosis are examined and referred to medical practitioners where appropriate. Conveying similar reasons, the second submission felt that consumers using amorolfine should have the opportunity for immediate access to pharmacist advice to support appropriate self-medication practices, tailor therapy and promote optimal outcomes from therapy.

### *ACMS advice to the delegate*

The ACMS recommended that the current scheduling of amorolfine remains appropriate.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the Committee included: b) the purpose for which a substance is to be used and the extent of use of a substance.

The reasons for the recommendation comprised the following:

- The diagnosis of onychomycoses can be difficult and treatment requires long term use of amorolfine. Consequently, the patient will benefit from having access to professional advice in both initiating and maintaining treatment.

### *Delegate's interim decision*

The interim decision is that the current scheduling of amorolfine remains appropriate.

Reasons for the decision are:

- Concerns about the ability to self-diagnosis onychomycosis (or) fungal nail infections, particularly in people with diabetes. The main reason for this is that visible symptoms of fungal infections (discolouration of the nail) could mask those of underlying diabetic issues, such as impaired blood circulation. The minimum treatment period of onychomycoses is six months.
- This interim decision is supported by the applicant's statement that diagnosis of onychomycoses is difficult and that public awareness of onychomycoses is limited.
- No other comparable country has amorolfine available as a general sale product.
- No other antifungal is exempt from scheduling except for the treatment of tinea pedis.

### *Delegate's considerations*

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- Public submissions received;
- ACMS advice;
- Section 52E of the *Therapeutic Goods Act 1989*;

- Scheduling factors[1];
- Other relevant information.

***Public submissions on the interim decision***

One submission was received that did not support delegate's interim decision on the basis that definitive diagnosis any fungal condition is difficult, people with diabetes are usually under care of a medical practitioner/specialist and the Consumer Medicine Information provides relevant advice.

Edited versions of these submissions are available at Public submissions on scheduling matters.

***Delegate's final decision***

The delegate notes the submission received in response to publication of the interim decision and confirms the interim decision as no evidence has been received to alter the interim decision. The delegate has confirmed that the reasons for the final decision are in keeping with those for the interim decision.

## 1.2 CALCIUM HYDROXYLAPAITE

***Scheduling proposal***

The medicines scheduling delegate considered a proposal to include calcium hydroxylapatite in preparations for injection or implantation when used for tissue augmentation or for cosmetic use in Schedule 4.

The delegate referred the proposal to the Advisory Committee on Medicines Scheduling (ACMS) for advice.

***Substance summary***

Hydroxylapatite (also known as hydroxyapatite) is a natural mineral with a composition similar to that of the mineral in bone. For therapeutic purposes, hydroxylapatite is prepared from bovine bone and contains, in addition to calcium and phosphate, trace elements, fluoride and other ions, proteins and glycosaminoglycans. It is given orally to patients requiring both calcium and phosphorus supplementation and hydroxylapatite with tricalcium phosphate has been used in bone grafts.

Hydroxylapatite derived from marine coral has been used in the construction of orbital implants for use after surgical removal of the eye. A form of hydroxyapatite referred to as calcium hydroxyapatite is used for correction of facial lipoatrophy in patients with HIV infection and as a cosmetic filler for moderate to severe facial wrinkles and folds.[2]

***Scheduling status***

Calcium hydroxylapatite is not specifically scheduled.

***Scheduling history***

Calcium hydroxylapatite has not been previously considered for scheduling therefore scheduling history is not available.

[1] Scheduling Policy Framework for Medicines and Chemicals (SPF, 2010) [http://www.tga.gov.au/pdf/scheduling-policy-framework.pdf]
[2] Martindale: The Complete Drug Reference. [online] London: Pharmaceutical Press [www.medicinescomplete.com] [Accessed on 12 June 2014]

### *Pre-meeting public submissions*

One public submission was received, asking the committee and the delegate to consider that the substance is used in dental bone grafting medical devices, entry could potentially impact on these products, suggested exempting the substance for dental use.

### *ACMS advice to the delegate*

The ACMS recommended that calcium hydroxylapatite in preparations for injection or implantation when used for tissue augmentation or for cosmetic use be included in Schedule 4 with an implementation date of 1 February 2015.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the Committee included: 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; d) the dosage, formulation, labelling, packaging and presentation of a substance; and f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the recommendation comprised the following:

- There needs to be appropriate monitoring and reporting of adverse effects.
- There is the potential for inappropriate off-label administration.
- An injectable implant needs to be administered by a health practitioner who has knowledge and training in injection/implantation techniques, uses appropriate infection control procedures and undertakes appropriate follow-up. There is potential for serious adverse effects if the administration of the product is not undertaken by an appropriately trained and qualified practitioner.

There is potential for inappropriate advertising direct to consumers. Concurrent administration of local anaesthetic may be required and this should be administered by an appropriately qualified health practitioner.

### *Delegate's interim decision*

The interim decision is that calcium hydroxylapatite in preparations for injection or implantation when used for tissue augmentation or for cosmetic use be included in Schedule 4 with an implementation date of 1 February 2015.

The reasons for the interim decision are:

- An injectable implant needs to be administered by a health practitioner who has knowledge and training in injection/implantation techniques, uses appropriate infection control procedures and undertakes appropriate follow-up. There is potential for serious adverse effects if the administration of the product is not undertaken by an appropriately trained and qualified practitioner.
- Concurrent administration of local anaesthetic may be required and this should be administered by an appropriately qualified health practitioner.
- There is potential for inappropriate advertising direct to consumers.
- There needs to be appropriate monitoring and reporting of adverse effects.

### *Delegate's considerations*

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- Public submissions received;
- ACMS advice;
- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors[3];
- Other relevant information.

***Public submissions on the interim decision***

No public submissions were received.

***Delegate's final decision***

The delegate has confirmed that the reasons for the final decision are in keeping with those for the interim decision.

***Schedule entry***

**Schedule 4 – New Entry**

CALCIUM HYDROXYLAPATITE in preparations for injection or implantation:

(a) for tissue augmentation; or
(b) for cosmetic use.

**1.3 MACITENTAN**

***Scheduling proposal***

The medicines scheduling delegate considered a proposal to include macitentan in Appendix D, Item 2 and Appendix L.

The delegate referred the proposal to the Advisory Committee on Medicines Scheduling (ACMS) for advice.

***Substance summary***

Macitentan belongs to the same class of pharmaceuticals as bosentan and ambrisentan and the former sitaxentan (withdrawn globally due to liver toxicity) which are orally active endothelin receptor antagonists (ERAs). Macitentan, like bosentan, is a dual endothelin A and B receptor antagonist, which is different to ambrisentan which is specific for endothelin type A receptors.

Macitentan is proposed for the long-term treatment of pulmonary arterial hypertension (PAH) in patients of WHO Functional Class II to IV, as monotherapy or in combination with approved PAH treatments (phosphodiesterase-5 inhibitors or prostanoids) to delay disease progression.

***Scheduling status***

Macitentan is not currently scheduled in Australia. Macitentan has just been considered by the New Zealand Medsafe Committee as a prescription medication. It is also considered a prescription drug in the United States of America (USA), Canada and the European Union. Macitentan is considered

[3] Scheduling Policy Framework for Medicines and Chemicals (SPF, 2010) [http://www.tga.gov.au/pdf/scheduling-policy-framework.pdf]

by the USA as a Pregnancy Category X drug. In Canada and in the EU the substance is contraindicated during pregnancy and for nursing women.

### *Scheduling history*

Macitentan has not been previously considered for scheduling therefore scheduling history is not available.

### *Pre-meeting public submissions*

No submissions were received for this scheduling proposal.

### *ACMS advice to the delegate*

The ACMS recommended that Macitentan be included in Appendix D, Item 6 as well as Appendix L with warning statements 7, 62 and 76 with an implementation date of 1 February 2015.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the Committee included: a) the risks and benefits of the use of a substance and c) the toxicity of the substance.

The reasons for the recommendation comprised the following:

- Teratogenicity which is consistent with other substances in this class

The need for product information containing contraindications during pregnancy.

### *Delegate's interim decision*

The interim decision is to include macitentan in Appendix D, Item 6 as well as Appendix L with warning statements 7, 62 and 76 with an implementation date of 1 February 2015.

The reasons for the interim decision are:

- Its teratogenicity which is consistent with other substances in this class which have this scheduling.
- The need for product information containing contraindications during pregnancy.
- That it is considered by the USA as a Pregnancy Category X drug.

That in Canada and in the EU the substance is contraindicated during pregnancy and for nursing women.

### *Delegate's considerations*

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- Public submissions received;
- ACMS advice;
- Section 52E of the *Therapeutic Goods Act 1989*;

- Scheduling factors4;
- Other relevant information.

***Public submissions on the interim decision***

No public submissions were received.

***Delegate's final decision***

The delegate has confirmed that the reasons for the final decision are in keeping with those for the interim decision.

***Schedule entry***

**Appendix D, Item 6 – New Entry**

MACITENTAN for human use

**Appendix L, Part 2 – New Entry**

| Column 1<br>Substance | Column 2<br>Warning statement |
|---|---|
| Macitentan | 7, 62 and 76 |

## 1.4 POLYCAPROLACTONE

***Scheduling proposal***

The medicines scheduling delegate considered a proposal to include polycaprolactone in preparations for injection or implantation when used for tissue augmentation or for cosmetic use in Schedule 4.

The delegate referred the proposal to the Advisory Committee on Medicines Scheduling (ACMS) for advice.

***Substance summary***

A substance summary for polycaprolactone was not provided for this proposal.

***Scheduling status***

Polycaprolactone is not specifically scheduled.

***Scheduling history***

Polycaprolactone has not been previously considered for scheduling therefore scheduling history is not available.

***Pre-meeting public submissions***

No submissions were received for this scheduling proposal.

[4] Scheduling Policy Framework for Medicines and Chemicals (SPF, 2010) [http://www.tga.gov.au/pdf/scheduling-policy-framework.pdf]

### *ACMS advice to the delegate*

The ACMS recommended that polycaprolactone in preparations for injection or implantation when used for tissue augmentation or for cosmetic use be included in Schedule 4 with an implementation date of 1 February 2015.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the Committee included: 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; d) the dosage, formulation, labelling, packaging and presentation of a substance; and f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the recommendation comprised the following:

- There needs to be appropriate monitoring and reporting of adverse effects.
- There is the potential for inappropriate off-label administration.
- An injectable implant needs to be administered by a health practitioner who has knowledge and training in injection/implantation techniques, uses appropriate infection control procedures and undertakes appropriate follow-up. There is potential for serious adverse effects if the administration of the product is not undertaken by an appropriately trained and qualified practitioner.
- There is potential for inappropriate advertising direct to consumers. Concurrent administration of local anaesthetic may be required and this should be administered by an appropriately qualified health practitioner.

### *Delegate's interim decision*

The interim decision is that polycaprolactone in preparations for injection or implantation when used for tissue augmentation or for cosmetic use is included in Schedule 4 with an implementation date of 1 February 2015.

Reasons for the interim decision are:

- An injectable implant needs to be administered by a health practitioner who has knowledge and training in injection/implantation techniques, uses appropriate infection control procedures and undertakes appropriate follow-up. There is potential for serious adverse effects if the administration of the product is not undertaken by an appropriately trained and qualified practitioner.
- Concurrent administration of local anaesthetic may be required and this should be administered by an appropriately qualified health practitioner.
- There needs to be appropriate monitoring and reporting of adverse effects.
- There is potential for inappropriate advertising direct to consumers.

### *Delegate's considerations*

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- Public submissions received;
- ACMS advice;

- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors[5];
- Other relevant information.

***Public submissions on the interim decision***

No public submissions were received.

***Delegate's final decision***

The delegate has confirmed that the reasons for the final decision are in keeping with those for the interim decision.

***Schedule entry***

**Schedule 4 – New Entry**

POLYCAPROLACTONE in preparations for injection or implantation:

(a) for tissue augmentation; or
(b) for cosmetic use.

## 1.5 RIOCIGUAT

***Scheduling proposal***

The medicines scheduling delegate considered a proposal to include riociguat in Appendix D, Item 2 and Appendix L.

***Substance summary***

Riociguat is a stimulator of soluble guanylate cyclase, an enzyme in the cardiopulmonary system, and increases production of the second messenger cyclic guanosine monophosphate (cGMP).

Adempas (riociguat) is proposed to be used in adult patients with chronic thromboembolic pulmonary hypertension and pulmonary arterial hypertension.

***Scheduling status***

Riociguat is not currently scheduled in Australia or New Zealand. It is, however, a prescription drug in the United States of America (USA), Canada and the European Union. Riociguat is considered by the USA as a Pregnancy Category X drug. In Canada and in the EU the substance is contraindicated during pregnancy and for nursing women.

***Scheduling history***

Riociguat has not been previously considered for scheduling therefore scheduling history is not available.

***Pre-meeting public submissions***

No submissions were received for this scheduling proposal.

[5] Scheduling Policy Framework for Medicines and Chemicals (SPF, 2010) [http://www.tga.gov.au/pdf/scheduling-policy-framework.pdf]

### *ACMS advice to the delegate*

The ACMS recommended that riociguat be included in Appendix D, Item 4 as well as Appendix L with warning statements 7, 62 and 76 with an implementation date of 1 February 2015.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the Committee included: c) the toxicity of the substance.

The reason for the recommendation comprised the following:

- Teratogenic nature of the substance.

### *Delegate's interim decision*

The interim decision is that riociguat is included in Appendix D, Item 4, as well as Appendix L with warning statements 7, 62 and 76 with an implementation date of 1 February 2015.

The reasons for the interim decision are:

- The teratogenic nature of the substance.
- FDA have stipulated a 1 month washout period.
- It is considered by the USA as a Pregnancy Category X drug.
- That in Canada and in the EU the substance is contraindicated during pregnancy and for nursing women.

### *Delegate's considerations*

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- Public submissions received;
- ACMS advice;
- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors[6];
- Other relevant information.

### *Public submissions on the interim decision*

No public submissions were received.

### *Delegate's final decision*

The delegate has confirmed that the reasons for the final decision are in keeping with those for the interim decision.

### *Schedule entry*

**Appendix D, Item 4 – New Entry**

RIOCIGUAT for human use

[6] Scheduling Policy Framework for Medicines and Chemicals (SPF, 2010) [http://www.tga.gov.au/pdf/scheduling-policy-framework.pdf]

**Appendix L, Part 2 – New Entry**

| Column 1<br>Substance | Column 2<br>Warning statement |
|---|---|
| Riociguat | 7, 62 and 76 |

## 1.6 SUVOREXANT

### *Scheduling proposal*

The medicines scheduling delegate considered a proposal to include suvorexant in Appendix K.

The delegate referred the proposal to the Advisory Committee on Medicines Scheduling (ACMS) for advice.

### *Substance summary*

Suvorexant is a dual orexin receptor antagonist and is indicated for the treatment of insomnia, characterised by difficulties with sleep onset and/or sleep maintenance.

### *Scheduling status*

Suvorexant is not currently scheduled in Australia or New Zealand. It is currently under review by the Food and Drug Administration (FDA) in the United States of America (USA). The FDA is yet to approve suvorexant due to concerns regarding the safety and efficacy of the substance.

### *Scheduling history*

Suvorexant has not been previously considered for scheduling therefore scheduling history is not available.

### *Pre-meeting public submissions*

No submissions were received for this scheduling proposal.

### *ACMS advice to the delegate*

The ACMS recommended that suvorexant be included in Appendix K with an implementation date of 1 February 2015.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the Committee included: a) the risks and benefits of the use of a substance and c) the toxicity of the substance.

The reasons for the recommendation comprised the following:

- Pronounced sedation effect
- Entry would be consistent with other sedative drugs in Appendix K
- Long duration of action of the substance may impact on peoples' ability to drive and operate machinery
- Narrow therapeutic margin.

### *Delegate's interim decision*

The interim decision is that suvorexant be included in Appendix K.

Reasons for the interim decision are:

- Pronounced sedation effect
- Entry would be consistent with other sedative drugs in Appendix K
- Long duration of action of the substance may impact on peoples' ability to drive and operate machinery
- Narrow therapeutic margin of the substance.

### *Delegate's considerations*

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- Public submissions received;
- ACMS advice;
- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors[7];
- Other relevant information.

### *Public submissions on the interim decision*

No public submissions were received.

### *Delegate's final decision*

The delegate has confirmed that the reasons for the final decision are in keeping with those for the interim decision.

### *Schedule entry*

**Appendix K – New Entry**

SUVOREXANT

## 1.7 TOFACTINIB

### *Scheduling proposal*

The medicines scheduling delegate considered a proposal to include tofacitinib in Appendix D and Appendix L.

The delegate referred the proposal to the Advisory Committee on Medicines Scheduling (ACMS) for advice.

[7] Scheduling Policy Framework for Medicines and Chemicals (SPF, 2010) [http://www.tga.gov.au/pdf/scheduling-policy-framework.pdf]

### *Substance summary*

Tofacitinib is a JAK1, 2 and 3 kinase inhibitor with some limited inhibitory activity against tyrosine kinase 2 (TyK2).

### *Scheduling status*

Tofacitinib is not currently scheduled in Australia or New Zealand.

### *Scheduling history*

Tofacitinib has not been previously considered for scheduling therefore scheduling history is not available.

### *Pre-meeting public submissions*

No submissions were received for this scheduling proposal.

### *ACMS advice to the delegate*

The ACMS recommended that tofacitinib does not require inclusion in Appendix D or Appendix L.

### *Delegate's interim decision*

The interim decision is that tofacitinib does not require inclusion in Appendix D or Appendix L.

The reasons for the interim decision are:

- Pregnancy is not contraindicated and as tofacitinib is considered pregnancy category D, it would not require an Appendix L listing.
- As Appendix L is not required there is no need for a specialist prescription and hence does not require Appendix D listing.
- USA has classified tofacitinib as Pregnancy Category C under their own classification system.

### *Delegate's considerations*

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- Public submissions received;
- ACMS advice;
- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors[8];
- Other relevant information.

### *Public submissions on the interim decision*

No public submissions were received.

[8] Scheduling Policy Framework for Medicines and Chemicals (SPF, 2010) [http://www.tga.gov.au/pdf/scheduling-policy-framework.pdf]

***Delegate's final decision***

The delegate has confirmed that the reasons for the final decision are in keeping with those for the interim decision.

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

## 2. New chemical entities – medicines for human therapeutic use

### 2.1 BENDAMUSTINE

***Scheduling proposal***

The delegate considered the scheduling of bendamustine, a new chemical entity (a human therapeutic medicine).

***Scheduling status***

Bendamustine is the Internationally Nonproprietary Name (INN) and it is not specifically scheduled in the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP). A related compound, mustine, is listed in the SUSMP No. 3 as follows:

**SCHEDULE 4**

MUSTINE (nitrogen mustard)

***Delegate's consideration***

The delegate considered the following in regards to this application for scheduling.

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

***Delegate's final decision***

The delegate has made a final decision to amend the SUSMP to include bendamustine in Schedule 4, with an implementation date of 1 February 2015.

The delegate decided that the relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of bendamustine; (b) the purpose and the extent of use of bendamustine; (c) the toxicity of bendamustine; d) the dosage, formulation, labelling, packaging and presentation of bendamustine; (e) the potential for abuse of bendamustine.

The delegate decided that the reasons for the final decision comprise the following:

- This is a new chemical entity with limited clinical experience in Australia. The TGA has found a positive benefit-risk balance for bendamustine for specific uses.
- Recommended use is limited to specified haemato-oncology indications.

- Toxicity has been factored into the TGA appraisal of benefit – risk balance and is consistent with S4 scheduling.
- These factors have been considered in the TGA appraisal of benefit – risk balance and are consistent with S4 scheduling.

The potential for abuse of bendamustine is unlikely.

***Schedule entry***

**Schedule 4 – New Entry**

BENDAMUSTINE.

## 2.2 BOSUTINIB

***Scheduling proposal***

The delegate considered the scheduling of bosutinib, a new chemical entity (a human therapeutic medicine).

***Scheduling status***

Bosutinib monohydrate is not specifically scheduled and is not captured by any entry in the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP).

***Delegate's consideration***

The delegate considered the following in regards to this application for scheduling.

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

***Delegate's final decision***

The delegate has made a final decision to amend the SUSMP to include bosutinib in Schedule 4, with an implementation date of 1 February 2015.

The delegate decided that the relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of bosutinib; (b) the purpose and the extent of use of bosutinib; (c) the toxicity of bosutinib; d) the dosage, formulation, labelling, packaging and presentation of bosutinib; and (e) the potential for abuse of bosutinib.

The delegate decided that the reasons for the final decision comprise the following:

- This is a new chemical entity with limited clinical experience in Australia. The TGA has found a positive benefit-risk balance for bosutinib for specific uses.
- Recommended use is limited to specified haemato-oncology indications.
- Toxicity has been factored into the TGA appraisal of benefit – risk balance and is consistent with S4 scheduling.

- These factors have been considered in the TGA appraisal of benefit – risk balance and are consistent with S4 scheduling.
- The potential for abuse of bosutinib is unlikely.

***Schedule entry***

**Schedule 4 – New Entry**

BOSUTINIB.

**2.3 BRENTUXIMAB**

***Scheduling proposal***

The delegate considered the scheduling of brentuximab vedotin, a new chemical entity (a human therapeutic medicine).

***Scheduling status***

Brentuximab vedotin is not specifically scheduled and is not captured by any entry in the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP).

***Delegate's consideration***

The delegate considered the following in regards to this application for scheduling.

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

***Delegate's final decision***

The delegate has made a final decision to amend the SUSMP to include brentuximab vedotin in Schedule 4, with an implementation date of 1 February 2015.

The delegate decided that the relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of brentuximab vedotin; (b) the purpose and the extent of use of brentuximab vedotin; (c) the toxicity of brentuximab vedotin; d) the dosage, formulation, labelling, packaging and presentation of brentuximab vedotin; (e) the potential for abuse of brentuximab vedotin.

The delegate decided that the reasons for the final decision comprise the following:

- This is a new chemical entity with limited clinical experience in Australia. The TGA has found a positive benefit-risk balance for brentuximab vedotin for specific uses.
- Recommended use is limited to specified haemato-oncology indications.
- Toxicity has been factored into the TGA appraisal of benefit – risk balance and is consistent with S4 scheduling.
- These factors have been considered in the TGA appraisal of benefit – risk balance and are consistent with S4 scheduling.

The potential for abuse of brentuximab vedotin is unlikely.

***Schedule entry***

**Schedule 4 – New Entry**

BRENTUXIMAB VEDOTIN.

## 2.4 CARGLUMIC ACID

***Scheduling proposal***

The delegate considered an application from the Therapeutic Goods Administration (TGA) for the scheduling of carglumic acid, a new chemical entity for a human therapeutic medicine.

***Scheduling status***

Carglumic acid is not specifically scheduled and is not captured by any entry in the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP).

***Delegate's consideration***

The delegate considered the following in regards to this application for scheduling.

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

***Delegate's final decision***

The delegate has made a final decision to amend the SUSMP to include carglumic acid in Schedule 4 with an implementation date of 1 February 2015.

The delegate decided that the relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of a substance; (b) the purpose and the extent of use of a substance; and d) the dosage, formulation, labelling, packaging and presentation of a substance.

The delegate decided that the reasons for the final decision comprise the following:

- It is a new chemical entity with no [clinical/marketing] experience in Australia.
- The proposed therapeutic use relates to conditions requiring specialist care including acute care settings.

Labelling needs to comply with requirements of a prescription-only medicine.

***Schedule entry***

**Schedule 4 – New Entry**

CARGLUMIC ACID (*N*-carbomoyl-L-glutamic acid).

## 2.5 ELOSULFASE ALFA

### *Scheduling proposal*

The delegate considered an application from the Therapeutic Goods Administration (TGA) for the scheduling of elosulfase alfa, a new chemical entity for a human therapeutic medicine.

### *Scheduling status*

Elosulfase alfa is not specifically scheduled and is not captured by any entry in the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP).

### *Delegate's consideration*

The delegate considered the following in regards to this application for scheduling.

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

### *Delegate's final decision*

The delegate has made a final decision to amend the SUSMP to include elosulfase alfa in Schedule 4, with an implementation date of 1 February 2015.

The delegate decided that the relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of; (b) the purpose and the extent of use of; (c) the toxicity of; d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse.

The delegate decided that the reasons for the final decision comprise the following:

- It is a new chemical entity with no clinical or marketing experience in Australia.
- It has no previous experience of use in Australia but has recently been approved for use overseas.
- Elosulfase alfa is indicated for the treatment of mucopolysaccharidosis type IVA (MPS IVA; Morquio A).
- It is proposed for hospital use and home based use.
- The risks and benefits of the medicine have been considered and are outlined in the Product Information.
- Treatment should be supervised by a physician or healthcare provider experienced in the management of patients with MPS IVA or other inherited metabolic disorders.
- The use of the medicine requires medical intervention, adjunctive therapy, evaluation and monitoring by a medical practitioner.
- Labelling needs to comply with the requirements for a prescription only medicine.
- It does not appear to produce dependency and the abuse potential appears to be low.

***Schedule entry***

**Schedule 4 – New Entry**

ELOSULFASE ALFA.

## 2.6 MACITENTAN

***Scheduling proposal***

The delegate considered an application from the Therapeutic Goods Administration (TGA) for the scheduling of macitentan, a new chemical entity for a human therapeutic medicine.

Macitentan is a dual endothelin A and B receptor antagonist.

Macitentan, as monotherapy or in combination with approved PAH treatments (phosphodiesterase-5 inhibitors or inhaled prostanoids), is indicated for the treatment of:

- idiopathic pulmonary arterial hypertension
- heritable pulmonary arterial hypertension
- pulmonary arterial hypertension associated with connective tissue disease
- pulmonary arterial hypertension associated with congenital heart disease with repaired shunts in patients with WHO Functional class II, III or IV symptoms.

The delegate decided to make a delegate-only decision to include this to Schedule 4. The Advisory Committee on Medicines Scheduling (ACMS) was consulted due to the pregnancy Category X status of macitentan. The delegate has considered the committee's recommendation and macitentan is to be included in Appendix D and Appendix L (see Part A 1. Scheduling proposals referred to the July 2014 meeting of the Advisory Committee on Medicines Scheduling (ACMS#12) of this document).

***Scheduling status***

Macitentan is not specifically scheduled and is not captured by any entry in the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP).

Macitentan is not classified in New Zealand.

***Delegate's consideration***

The delegate considered the following in regards to this application for scheduling:

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

***Delegates' final decision***

The delegate has made a final decision to amend the SUSMP to include macitentan in Schedule 4, with an implementation date of 1 February 2015.

The delegate decided that the relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of; (b) the purpose and the extent of use of; (c) the toxicity of; d) the dosage, formulation, labelling, packaging and presentation of; and (e) the potential for abuse of macitentan.

The delegate decided that the reasons for the final decision comprise the following:

- Macitentan is a new chemical entity with no clinical experience in Australia.
- Macitentan has risks and benefits which are outlined in the Product Information.
- It is indicated for the treatment of pulmonary arterial hypertension in certain subgroups as either monotherapy or in combination with other treatments and in patients with specific WHO functional classes.
- Experience of its use is limited.
- The drug has specific toxicities related to embryo-fetal risk and therefore is a category X drug and contraindicated in pregnancy or in women who may become pregnant.
- Treatment with macitentan should only be initiated and monitored by a physician experienced in the treatment of pulmonary arterial hypertension. The use of the medicine requires medical intervention and monitoring by a medical practitioner.
- Labelling needs to comply with the requirements for a prescription only medicine.
- It does not appear to produce dependency and the abuse potential appears to be low.

## 2.7 RIOCIGUAT

### *Scheduling proposal*

The delegate considered an application from the Therapeutic Goods Administration (TGA) for the scheduling of riociguat, a new chemical entity for a human therapeutic medicine.

Riociguat is a stimulator of soluble guanylate cyclase, an enzyme in the cardiopulmonary system, and increases production of the second messenger cyclic guanosine monophosphate (cGMP).

Adempas (riociguat) has the following indications:

**Pulmonary arterial hypertension**

Adempas, as monotherapy or in combination with approved PAH treatments (endothelin receptor antagonists or inhaled or subcutaneous prostanoids), is indicated for the treatment of:

- idiopathic pulmonary arterial hypertension
- heritable pulmonary arterial hypertension
- pulmonary arterial hypertension associated with connective tissue diseases or
- pulmonary arterial hypertension associated with congenital heart disease in adult patients with WHO functional Class II, lll or IV symptoms

**Chronic thromboembolic pulmonary hypertension**

Adempas is indicated for the treatment of:

- persistent or recurrent chronic thromboembolic pulmonary hypertension (CTEPH) after surgical treatment or
- inoperable CTEPH in adult patients with WHO functional Class II, III or IV symptoms.

The delegate decided to make a delegate-only decision to include this to Schedule 4. The Advisory Committee on Medicines Scheduling (ACMS) was consulted on the requirement for a sedation warning. The delegate has considered the committee's recommendation and riociguat is to be included in Appendix D and Appendix L (see Part A 1. Scheduling proposals referred to the July 2014 meeting of the Advisory Committee on Medicines Scheduling (ACMS#12) of this document).

***Scheduling status***

Riociguat is not specifically scheduled and is not captured by any entry in the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP).

Riociguat is not classified in New Zealand.

***Delegate's consideration***

The delegate considered the following in regards to this application for scheduling.

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

***Delegate's final decision***

The delegate has made a final decision to amend the SUSMP to include riociguat in Schedule 4, with an implementation date of 1 February 2015.

The delegate decided that the relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of; (b) the purpose and the extent of use of; (c) the toxicity of; d) the dosage, formulation, labelling, packaging and presentation of; and (e) the potential for abuse of riociguat.

The delegate decided that the reasons for the final decision comprise the following:

- Riociguat is a new chemical entity with no clinical experience in Australia.
- The risks and benefits are outlined in the Product Information, Delegate's Request for ACPM advice and the TGA evaluation reports.
- It is proposed to be used in adult patients with pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension in certain subgroups as either monotherapy or in combination with other treatments and in patients with specific WHO functional classes.
- Experience of its use is limited.
- The use of riociguat requires medical intervention, adjunctive therapy and evaluation.

- The drug has specific toxicities related to use in pregnancy and is proposed as a category X drug and contraindicated in pregnancy. It also has safety concerns with hypotension and bleeding and concomitant use with nitrates, nitric oxide donors and PDE-5 inhibitors.
- Treatment with riociguat should only be initiated and monitored by a physician experienced in the treatment of pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension.
- The use of riociguat requires monitoring by a medical practitioner to minimize the risk of using it.
- Medicine is packed as 0.5, 1.0, 1.5, 2.0 and 2.5 mg film-coated tablets in blister packs.
- It does not appear to produce dependency and the abuse potential appears to be low.

***Schedule entry***

**Schedule 4 – New Entry**

RIOCIGUAT

## 2.8 SIMOCTOCOG ALFA

***Scheduling proposal***

The delegate considered the scheduling of simoctocog alfa, a new chemical entity (a human therapeutic medicine).

***Scheduling status***

Simoctocog alfa is not specifically scheduled in the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP).

***Delegate's consideration***

The delegate considered the following in regards to this application for scheduling.

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

***Delegate's final decision***

The delegate has made a final decision that simoctocog alfa falls under Appendix A – General Exemptions under Human Blood Products as it is an equivalent recombinant alternative to a plasma-derived clotting factor.

## 2.9 SUVOREXANT

***Scheduling proposal***

The delegate considered an application from the Therapeutic Goods Administration (TGA) for the scheduling of suvorexant, a new chemical entity for a human therapeutic medicine.

Suvorexant is a dual orexin receptor antagonist.

Suvorexant was proposed to be indicated for the treatment of insomnia, characterised by difficulties with sleep onset and/or sleep maintenance.

The delegate decided to make a delegate-only decision to include this to Schedule 4. The Advisory Committee on Medicines Scheduling (ACMS) was consulted on the requirement for a sedation warning. The delegate has considered the committee's recommendation and suvorexant is to be included in Appendix K (see Part A 1. Scheduling proposals referred to the July 2014 meeting of the Advisory Committee on Medicines Scheduling (ACMS#12) of this document).

### *Scheduling status*

Suvorexant is not specifically scheduled and is not captured by any entry in the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP).

Suvorexant is not classified in New Zealand.

### *Delegate's consideration*

The delegate considered the following in regards to this application for scheduling.

- The new drug application.
- Subsection 52E(1) of the *Therapeutic Goods Act 1989*.
- The Scheduling Policy Framework scheduling factors.

### *Delegate's final decision*

The delegate has made a final decision to amend the SUSMP to include suvorexant in Schedule 4, with an implementation date of 1 February 2015.

The delegate decided that the relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of suvorexant.

The delegate decided that the reasons for the final decision comprise the following:

- Suvorexant is a new chemical entity with no clinical or marketing experience in Australia.
- The substance is intended to cause drowsiness and its effects are additive with alcohol.
- The delegate made an initial decision to reject registration of suvorexant.

### *Schedule entry*

**Schedule 4 – New Entry**

SUVOREXANT.