Australian Government
Department of Health
Therapeutic Goods Administration

Final scheduling decisions and reasons for decisions by delegates of the Secretary to the Department of Health for matters not referred to an advisory committee (Delegate-Only decisions)

25 January 2018

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 if the Secretary decides to amend the current Poisons Standard in the manner set out in such an application, the Secretary may make a final decision without making an interim decision. Following publication of the final decision in accordance with regulation 42ZCZX, if the final decision is to amend the current Poisons Standard, the delegate 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 Chemicals and Medicines* (SPF, 2015), available on the TGA website.

Under 42ZCZX of the Regulations, the Secretary must, among other things, publish (in a manner the Secretary considers appropriate) the final scheduling decision, the reasons for that decision and the date of effect of the decision (for final 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. The *Poisons Standard* is published electronically on the Federal Register of Legislation (FRL). Further information, including links to the *Poisons Standard* on FRL, is available on the TGA website.

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1.1. Alectinib

Scheduling proposal

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

Substance summary

Alectinib is a second generation oral drug that selectively inhibits the activity of anaplastic lymphoma kinase (ALK) tyrosine kinase. It is specifically used in the treatment of non-small cell lung cancer (NSCLC) expressing the ALK-EML4 (echinoderm microtubule-associated protein-like 4) fusion protein that causes proliferation of NSCLC cells. Inhibition of ALK prevents phosphorylation and subsequent downstream activation of STAT3 and AKT resulting in reduced tumour cell viability.

Alectinib is indicated for the treatment of patients with ALK-positive locally advanced or metastatic non-small cell lung cancer (NSCLC), who have progressed on or are intolerant to crizotinib.

Scheduling status

Alectinib is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

Alectinib is classified as a prescription only medicine in New Zealand, the United States of America and Canada.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors;
- The TGA evaluation report;
- The advice of the Advisory Committee on Prescription Medicines; and
- The new drug application.
- The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include alectinib in Schedule 4, with an implementation date of 1 February 2018.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

ALECTINIB.

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; and (c) the toxicity of a substance.

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

- Alectinib is a new chemical entity with limited marketing experience in Australia.
- Alectinib has significant capacity for toxicity without benefit outside its proposed usage.

1.2. Apalutamide

Scheduling proposal

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

Substance summary

Apalutamide is a potent androgen receptor (AR) antagonist that targets the AR ligand-binding domain and prevents AR nuclear translocation, DNA binding, and transcription of AR gene targets.

Unlike bicalutamide, apalutamide antagonised AR-mediated signalling in ARs overexpressing human castration-resistant prostate cancer cell lines. In mice bearing human castration-resistant prostate cancer xenografts, apalutamide produced dose-dependent tumor regressions superior to those achieved with bicalutamide or enzalutamide.

Apalutamide is intended to be indicated for the treatment of patients with castration-resistant prostate cancer at risk of developing metastases.

Scheduling status

Apalutamide is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

Apalutamide does not appear to be scheduled internationally.

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 (2015) scheduling factors;
- The new drug application

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include apalutamide in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

APALUTAMIDE.

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.

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

- Apalutamide is an NCE with no clinical/marketing experience in Australia.

1.3. Bictegravir

Scheduling proposal

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

Substance summary

Bictegravir is an integrase strand-transfer inhibitor and will be presented in a single tablet fixed dose combination with emtricitabine and tenofovir alafenamide.

Bictegravir is indicated for the treatment of HIV-1 infection in adults without any known mutations associated with resistance to the individual components of the fixed dose combination and for the treatment of chronic hepatitis B in adults coinfected with HIV-1.

Scheduling status

Bictegravir is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

Bictegravir not classified in New Zealand, Canada or the United States of America.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors;
- The TGA clinical evaluation report; and
- The new drug application.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include bictegravir in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

BICTEGRAVIR.

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; (c) the toxicity 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:

- Bictegravir is an NCE with no clinical or marketing experience in Australia.
- Requires specialised clinical use.

- Presentation will be in compliance with the prescription medicines labelling requirements.

1.4. Binimetinib

Scheduling proposal

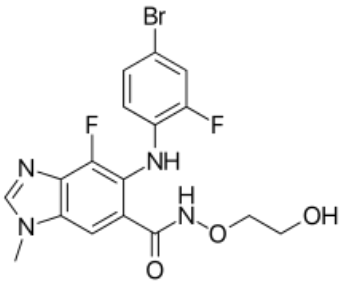
The delegate considered an application from the Therapeutic Goods Administration (TGA) for the scheduling of binimetinib, a new chemical entity (NCE) for a human therapeutic medicine.

Substance summary

Binimetinib is an orally available, ATP-uncompetitive, reversible inhibitor of mitogen-activated extracellular signal regulated kinase 1 (MEK1) and MEK2 activation (162-Enz-1). MEK proteins are upstream regulators of the extracellular signal-related kinase (ERK) pathway, which promotes cellular proliferation. Binimetinib has demonstrated potent activity against MEK 1/2 enzyme and possesses broad anti-proliferative activity *in vitro* and *in vivo*.

Binimetinib is indicated for the treatment of adult patients with unresectable or metastatic melanoma, with NRAS Q61 mutation.

Table A: Binimetinib chemical information and naming

Property	Binimetinib
CAS number	606143-89-9
Chemical structure	
Molecular formula	$C_{17}H_{15}BrF_2N_4O_3$
Molecular weight	441.2 g/mol
Chemical names	5-[(4-bromo-2-fluorophenyl)amino]-4-fluoro-*N*-(2-hydroxyethoxy)- 1-methyl-1*H*-benzimidazole-6-carboxamide
Other names	111235 (AAN); 10288191 (CID)

Scheduling status

Binimetinib is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

- Application for approval of binimetinib was submitted to the United States of America Food and Drug Administration (FDA) for approval (2016). However, binimetinib is not yet FDA approved.

- The European Medicines Agency granted a deferral for binimetinib in 2016, agreeing on an investigation plan.
- Binimetinib is not classified in New Zealand and Canada.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors; and
- The TGA evaluation report.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include binimetinib in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

BINIMETINIB.

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.

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

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

1.5. Cabozantinib

Scheduling proposal

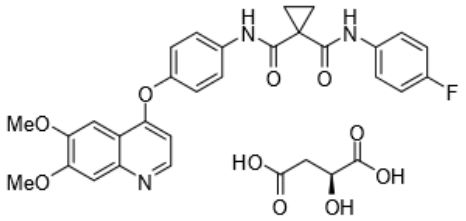
The delegate considered an application from the Therapeutic Goods Administration (TGA) for the scheduling of cabozantinib, a new chemical entity (NCE) for a human therapeutic medicine.

Substance summary

Cabozantinib is a small molecule that inhibits multiple receptor tyrosine kinases (RTKs) implicated in tumour growth and angiogenesis, pathologic bone remodelling, drug resistance, and metastatic progression of cancer. Cabozantinib was evaluated for its inhibitory activity against a variety of kinases and was identified as an inhibitor of MET (hepatocyte growth factor receptor protein) and VEGF (vascular endothelial growth factor) receptors. In addition, cabozantinib inhibits other tyrosine kinases including the GAS6 receptor (AXL), RET, ROS1, TYRO3, MER, the stem cell factor receptor (KIT), TRKB, Fms-like tyrosine kinase-3 (FLT3), and TIE-2.

Cabozantinib is indicated for the treatment of advanced renal cell carcinoma (RCC) in adults following prior therapy.

Table B: Cabozantinib chemical information and naming

Property	Cabozantinib
CAS number	1140909-48-3
Chemical structure	
Molecular formula	$C_{28}H_{24}FN_3O_5 \cdot C_4H_6O_5$
Molecular weight	635.6 Daltons as malate salt
Chemical name	*N*-(4-(6,7-dimethoxyquinolin-4-yloxy)phenyl)-*N*'-(4fluorophenyl)cyclopropane-1,1-dicarboxamide, (2*S*)-hydroxybutanedioate
Other names	111248 (eBS ID); cabozantinib (*S*)-malate (ANN and IIN (modified))

Scheduling status

Cabozantinib is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

Cabozantinib is classified as a prescription only medicine in the United States of America, the European Union and the United Kingdom and is not classified in New Zealand or Canada.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors;
- The TGA evaluation report; and
- The new drug application.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include cabozantinib in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

CABOZANTINIB.

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; and (c) the toxicity of a substance.

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

- Cabozantinib is an NCE with no marketing experience in Australia.
- Cabozantinib has significant capacity for toxicity without benefit outside its proposed usage.

1.6. Cinnarizine

Scheduling proposal

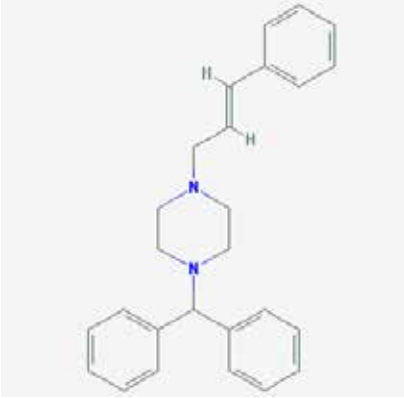
The delegate considered an application from the Therapeutic Goods Administration (TGA) for the scheduling of cinnarizine, a new chemical entity (NCE) for a human therapeutic medicine.

Substance summary

Cinnarizine is a selective calcium channel antagonist that acts mainly as a vestibular sedative through inhibition of the calcium influx into the vestibular sensory cells. Cinnarizine thus acts predominantly on the peripheral vestibular system. Cinnarizine was discovered in 1955 and is used to treat vestibular disorders including motion sickness, tinnitus and Meniere's disease.

Cinnarizine is used in a fixed dose combination product with dimenhydrinate and is intended for the short term treatment of vertigo in adults.

Table C: Cinnarizine chemical information and naming

Property	Cinnarizine
CAS number	298-57-7
Chemical structure	
Molecular formula	$C_{26}H_{28}N_2$
Molecular weight	368.5 g/mol
Chemical name	(*E*)-1-(Diphenylmethyl)-4-(3-phenylprop-2-enyl)piperazine

Scheduling status

Cinnarizine is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

Cinnarizine is not classified or marketed in Canada, New Zealand or the United States of America.

Cinnarizine is classified as a non-prescription medicine in the United Kingdom (UK) in 15 mg tablets.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors;
- The TGA evaluation report; and
- The new drug application.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include cinnarizine in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

CINNARIZINE.

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; (c) the toxicity 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 delegate decided that the reasons for the final decision comprise the following:

- Cinnarizine is an NCE with no marketing experience in Australia.
- Long term use without doctor supervision, particularly by older patients for chronic conditions associated with vertigo, may be put at unacceptable risk of extrapyramidal adverse effects, particularly Parkinsonism, which may be irreversible.
- Cinnarizine should not be taken long term due to its potential side effects.
- Limiting pack size may reduce the likelihood of long term use.
- Cinnarizine has been submitted for use in combination with dimenhydrinate, an antihistamine that was available in both Schedule 2 and Schedule 3 products. However, it was withdrawn from the Australian Register of Therapeutic Goods in June 2017.
- Both actives in the proposed fixed dose combination are available without prescription in the UK. It is not yet clear if this combination is also available without prescription in the UK.
- Cinnarizine has been associated with extrapyramidal effects that are not predictable in severity or time of onset after starting cinnarizine but are more likely in the elderly and individuals taking long term treatments.
- There is concern that if cinnarizine were available without prescription that it may be taken long term, particularly by elderly people and put them at risk of extrapyramidal effects which may be permanent.
- It is being proposed at this stage that the fixed dose combination would be acceptable for short term use e.g. recommended maximum duration of use 4 weeks. It should not be made available

without prescription in order to limit long term use. Limiting pack size may reduce the likelihood of chronic use with its increased risk of extrapyramidal side effects. It is considered that only pack sizes consistent with no more than 4 weeks continuous use will be approved.

1.7. Encorafenib

Scheduling proposal

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

Substance summary

Encorafenib is a highly selective ATP-competitive small-molecule RAF kinase inhibitor acting on the RAS/RAF/MEK/ERK pathway in tumour cells expressing *BRAF* V600 mutations, including melanoma cell lines.

Encorafenib is indicated for use in combination with binimetinib for the treatment of adult patients with unresectable or metastatic melanoma, with *BRAF* V600 mutation.

Scheduling status

Encorafenib is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

Encorafenib is unclassified in New Zealand, Canada and the United States of America.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors;
- The TGA designation evaluation report; and
- The new drug application.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include encorafenib in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

ENCORAFENIB.

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; and (c) the toxicity of a substance.

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

- Encorafenib is an NCE with no marketing experience in Australia.

- Outside of the proposed usage, toxicity may result in a negative risk-benefit balance.

1.8. Erenumab

Scheduling proposal

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

Substance summary

Erenumab is a human immunoglobulin G2 (IgG2) monoclonal antibody that has high affinity binding to the calcitonin gene-related peptide (CGRP) receptor. CGRP is a neuropeptide that modulates nociceptive signalling and a vasodilator that has been associated with migraine pathophysiology.

Erenumab is indicated for the prophylaxis of migraine in adults.

Scheduling status

Erenumab is not specifically scheduled but is captured by the Schedule 4 class entry for monoclonal antibodies in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)) as follows:

Schedule 4

MONOCLONAL ANTIBODIES for therapeutic us **except**:

a) in diagnostic test kits; or

b) when separately specified in these Schedules.

International regulations

Erenumab does not appear to be classified internationally.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors;
- The TGA evaluation report; and
- The new drug application.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include erenumab in Schedule 4 with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

ERENUMAB.

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; (c) the toxicity 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:

a. the risks and benefits of the use of a substance
   - Erenumab is an NCE 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
   - Erenumab 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.

NCEErenumab

1.9. Ertugliflozin

Scheduling proposal

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

Substance summary

Ertugliflozin is a sodium-glucose co-transporter 2 (SGLT2) inhibitor. It reduces blood glucose levels by increasing renal excretion of glucose.

Ertugliflozin is indicated for the treatment of type 2 diabetes.

Scheduling status

Ertugliflozin is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)). However, there are a number of other similar medicines of this class of agents known as SGLT-2 inhibitors in Schedule 4, e.g. empagliflozin, canagliflozin and dapagliflozin.

International regulations

Ertugliflozin is classified as a prescription medicine in the United States of America.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors;
- The TGA evaluation report;
- The advice of the Advisory Committee on Prescription Medicines; and
- The new drug application.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include ertugliflozin in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

ERTUGLIFLOZIN.

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; (c) the toxicity of a substance; (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:

- Ertugliflozin is an NCE with no clinical or marketing experience in Australia.
- There are a number of other similar medicines of this class of agents known as SGLT-2 inhibitors in Schedule 4.
- Ertugliflozin will be prescribed by medical practitioners for the management of type 2 diabetes when metformin and dietary measures and/or other medicines are unable to control blood glucose levels.
- There are no major serious toxicities.
- No specific requirements over existing regulations and guidelines.

1.10. Ferric derisomaltose

Scheduling proposal

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

Substance summary

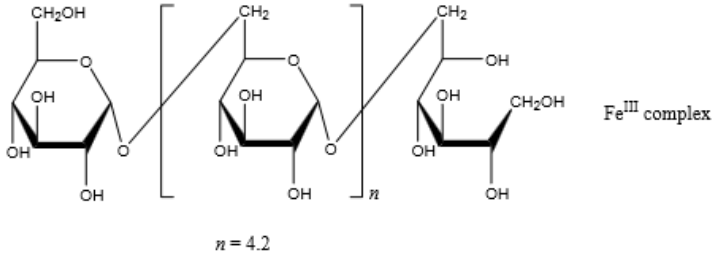
Ferric derisomaltose is a colloid (intended to be intravenously injected or infused) with bound iron in spheroidal iron-carbohydrate particles. This complex enables release of bioavailable iron to iron-binding proteins.

Ferric derisomaltose is indicated for the treatment of iron deficiency in adults, under the following conditions:

- when oral preparations are ineffective or cannot be used; and
- when there is a clinical need to deliver iron rapidly.

The diagnosis must be based on laboratory tests.

Table D: Ferric derisomaltose chemical information and naming

Property	Ferric derisomaltose
CAS Number	1345510-43-1
Chemical structure	
Molecular formula	$(C_6H_{11}O_5)(C_6H_{10}O_5)_n(C_6H_{13}O_5).Fe^{III}$ complex (n = 4.2)
Molecular weight	562.3 g/mol
Chemical name	Iron (III) hydroxide isomaltoside 1000; (1⟶6)-α-D-glucopyranan-(1⟶6)-α-D-glucitol iron(III) complex
Other names	Ferric derisomaltose (ANN and INN); iron isomaltoside, iron isomaltooligosaccharide, iron oligosaccharide, iron isomaltopentaoside 100

Scheduling status

Ferric derisomaltose is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

Ferric derisomaltose is unclassified in New Zealand, the United States of America, Canada and Europe. In the United Kingdom, ferric derisomaltose is a prescription only medicine.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors;
- The TGA evaluation report;
- The advice of the Advisory Committee on Prescription Medicines;
- The new drug application; and
- Other.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include ferric derisomaltose in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

FERRIC DERISOMALTOSE.

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; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse; and (f) any other matters that the Secretary considers necessary to protect public health.

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

- Ferric derisomaltose is an NCE with no marketing experience in Australia.
- The risks and benefits of use have been considered in the evaluation for product registration.
- All matters under subsections 52E(1) have been considered as part of the evaluation and approval process.

1.11. Insulin degludec

Scheduling proposal

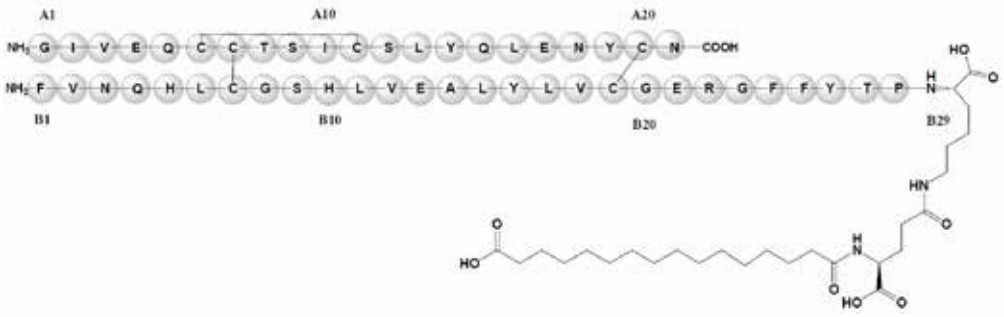
The delegate considered an application from the Therapeutic Goods Administration (TGA) for the scheduling of insulin degludec, a new chemical entity (NCE) for a human therapeutic medicine.

Substance summary

Insulin degludec is a basal insulin with a slow and distinct absorption mechanism resulting in an ultra-long, flat, and stable pharmacokinetic profile in patients with diabetes mellitus.

Insulin degludec is indicated to improve glycaemic control in adult patients with diabetes mellitus.

Table E: Insulin degludec chemical information and naming

Property	Insulin degludec
CAS number	844439-96-9
Chemical structure	
Molecular formula	$C_{274}H_{411}N_{65}O_{81}S_6$
Molecular weight	6103.97 Da
Chemical name	(1*A*-21*A*),(1*B*-29*B*)-Insulin (human), 29*B*-(*N*6-(*N*-(15-carboxy-1-oxopentadecyl)-*L*-gamma- glutamyl)-*L*-lysine)-
Other names	Insulin degludec (human) (INN); Insulin degludec (ABN)

Scheduling status

Insulin degludec is not specifically scheduled but is captured by the Schedule 4 class entry for insulins in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)) as follows:

Schedule 4

INSULINS.

The similar substance, insulin glargine, is in Schedule 4 of the Poisons Standard as follows:

Schedule 4

INSULIN GLARGINE.

International regulations

Insulin degludec is not classified in New Zealand. Insulin degludec is listed under Schedule D in Canada and is listed as a prescription only medicine in the United States of America (USA) and the European Union (EU).

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors; and
- The TGA evaluation report.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include insulin degludec in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

INSULIN DEGLUDEC.

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; (c) the toxicity of a substance; and (e) the potential for abuse.

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

- Insulin degludec is an NCE with no clinical or marketing experience in Australia.
- Insulin degludec has had clinical and marketing experience in the EU and USA.
- Insulin degludec is similar to other long acting insulins available in Australia such as insulin glargine.
- Insulin degludec is indicated to improve glycaemic control in adult patients with diabetes mellitus.
- The toxicity of insulin degludec is minimal if used appropriately with blood glucose monitoring. Like other insulins if used inappropriately there is a risk of hypoglycaemia.
- The potential for abuse of insulin degludec is unlikely.

1.12. Letermovir

Scheduling proposal

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

Substance summary

Letermovir is an inhibitor of cytomegalovirus viral terminase and will be presented as a concentrated injection solution for infusion.

Letermovir has been requested for the indication of "*prophylaxis of cytomegalovirus (CMV) infection or disease in adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT).*"

Scheduling status

Letermovir is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

Letermovir is classified as a prescription only medicine in Canada and the United States of America, and is unclassified in New Zealand.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors;
- The TGA clinical evaluation report; and
- The new drug application.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include letermovir in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

LETERMOVIR.

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; (c) the toxicity 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:

- Letermovir is an NCE with no clinical or marketing experience in Australia.
- Letermovir is for highly specialised clinical use.

- Requires use under specialised clinical supervision.
- Presentation will be in compliance with the prescription medicines labelling requirements.

1.13. Nusinersen

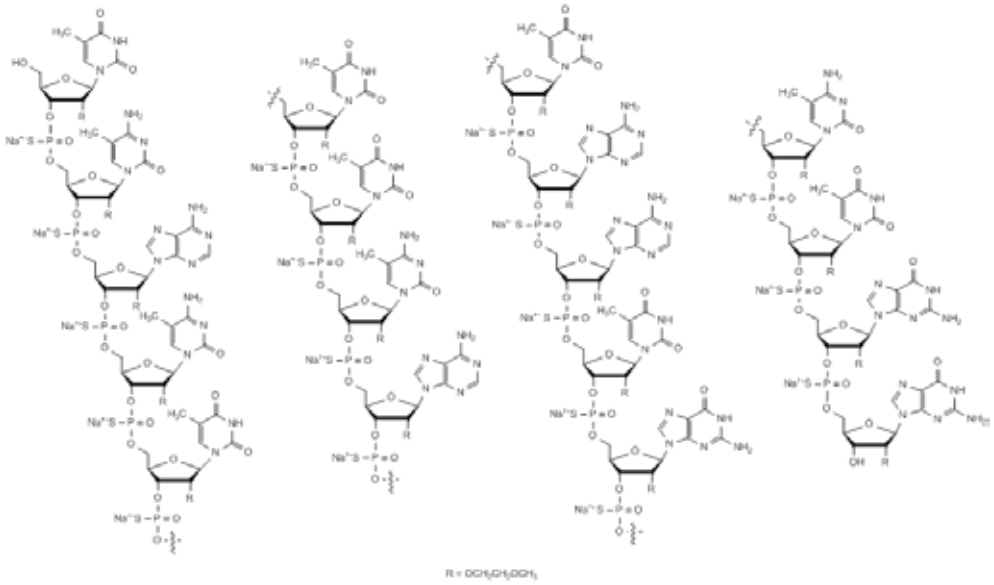
Scheduling proposal

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

Substance summary

Nusinersen is an antisense oligonucleotide (ASO) indicated for the treatment of spinal muscular atrophy, an autosomal recessive progressive neuromuscular disease caused by mutation or deletion of the survival motor neuron 1 (SMN1) gene on the q arm of chromosome 5. This results in a deficiency of SMN protein. The SMN2 gene, also present on the same chromosome, transcribes a similar but generally truncated SMN protein that is unstable and defective. Fully functioning SMN protein is essential for normal function of the anterior horn cell. Its deficiency results in progressive loss of skeletal muscle. Nusinersen promotes the transcription of a full length SMN protein.

Table F: Nusinersen chemical information and naming

Property	Nusinersen
CAS Number	1258984-36-9
Chemical structure	
Molecular formula	$C_{234}H_{323}N_{61}O_{128}P_{17}S_{17}Na_{17}$
Molecular weight	7501.0 g/mol
Chemical name	Nusinersen (as heptadecasodium)

Scheduling status

Nusinersen (as heptadecasodium) is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

Nusinersen is not classified in New Zealand. Nusinersen is a prescription only medicine in Canada, the European Union and the United States of America.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors;
- The TGA evaluation report; and
- The new drug application.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include nusinersen in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

NUSINERSEN.

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; (c) the toxicity of a substance; (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:

- Nusinersen is an NCE with no marketing experience in Australia.
- The benefits and risks of nusinersen have been considered and are outlined in the Product Information.
- Nusinersen should be prescribed under the supervision of medical practitioners with experience in the diagnosis and management of spinal muscular atrophy.
- Nusinersen is proposed for use in hospitals.
- The use of nusinersen has risks that may require clinical evaluation, intervention and monitoring by a medical practitioner.
- Labelling needs to comply with the requirements for an injectable prescription medicine.
- Nusinersen does not appear to produce dependency and the abuse potential appears to be low.

1.14. Patiromer sorbitex calcium

Scheduling proposal

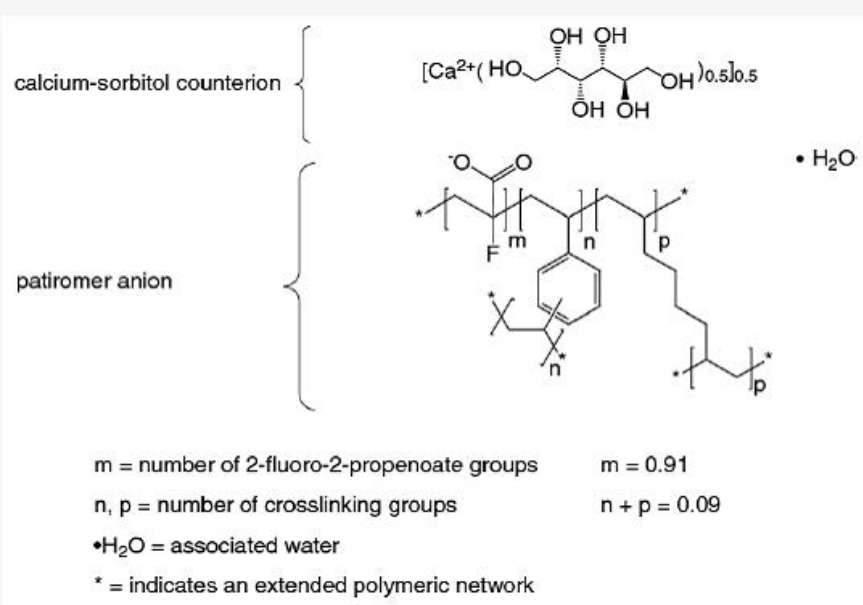
The delegate considered an application from the Therapeutic Goods Administration (TGA) for the scheduling of patiromer sorbitex calcium, a new chemical entity (NCE) for a human therapeutic medicine.

Substance summary

Patiromer sorbitex calcium is a crosslinked polymer anion of 2-propenoic acid, 2-fluoro-, polymer with diethenylbenzene and 1,7-octadiene with calcium-sorbitol counterion. Patiromer sorbitex calcium is an amorphous, free-flowing powder that is composed of individual spherical beads.

Patiromer sorbitex calcium is indicated for the treatment of hyperkalaemia in adults.

Table G: Patiromer sorbitex calcium chemical information and naming

Property	Patiromer sorbitex calcium
CAS number	1415477-49-4
Chemical structure	
Molecular formula	$C_{613}H_{765}F_{114}O_{399}Ca_{57}$
Molecular weight	5.6 × 1017 g/mol[1]
Chemical name	Hydrolyzed divinylbenzene-Me 2-fluoro-2-propenoate-1,7-octadiene polymer sorbitol complexes calcium
Other names	Patiromer sorbitex calcium (AAN)

[1] The molecular weight of a 100 micrometre patiromer sorbitex calcium bead is calculated using an experimentally derived value for density and the theoretical calculated value for volume.

Scheduling status

Patiromer sorbitex calcium is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

Patiromer sorbitex calcium is not classified in New Zealand and Canada, but is listed as a prescription only medicine in the United States of America and the European Union.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors; and
- The TGA evaluation report.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include patiromer sorbitex calcium in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

PATIROMER SORBITEX CALCIUM.

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; (c) the toxicity of a substance; (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:

- Patiromer sorbitex calcium is an NCE with no clinical/marketing experience in Australia.
- The toxicity of patiromer sorbitex calcium is of low risk.
- The potential for abuse of patiromer sorbitex calcium is minimal.

1.15. Peramivir

Scheduling proposal

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

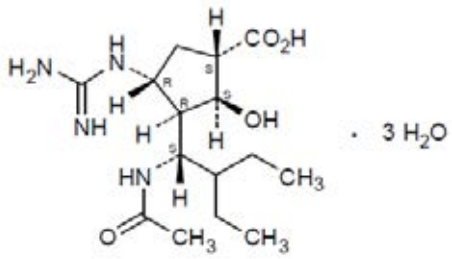
Substance summary

Peramivir is an inhibitor of influenza virus neuraminidase, an enzyme that releases viral particles from the plasma membrane of infected cells and is also important for viral entry into uninfected cells, which causes further spread of infectious virus in the body.

The antiviral activity of peramivir against laboratory strains and clinical isolates of influenza virus was determined in cell culture. The concentrations of peramivir required for inhibition of influenza virus in cell culture varied depending on the assay method used and the virus tested.

Peramivir is indicated for the treatment of infections due to influenza A and B viruses in adults and children 2 years and older. Treatment should commence as soon as possible, but no later than 2 days after the onset of the initial symptoms of infection.

Table H: Peramivir chemical information and naming

Property	Peramivir
CAS number	330600-85-6
Chemical structure	
Molecular formula	$C_{15}H_{28}N_4O_4$
Molecular weight	382.5 g/mol
Chemical names	(1S,2S,3R,4R)-3-[(1*S*)-1-(acetylamino)-2-ethylbutyl]-4-(carbamimidoylamino)-2hydroxycyclopentanecarboxylic acid,trihydrate
Other names	111346 (eBS ID); Peramivir (ANN/INN)

Scheduling status

Peramivir is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

Peramivir is classified as a prescription medicine in Canada, United States of America and the European Union.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors;
- The TGA evaluation report; and
- The new drug application.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include peramivir in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

PERAMIVIR.

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; (c) the toxicity 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:

- Peramivir is a new chemical entity with no clinical or marketing experience in Australia.
- Peramivir is to be used for the treatment of infections due to influenza A and B viruses. Treatment should commence as soon as possible, but no later than 2 days after the onset of the initial symptoms of infection.
- The adverse events include insomnia, liver function abnormality, abnormal behaviour, skin reactions, hypertension, etc.
- Peramivir is for intravenous infusion.

1.16. Recombinant varicella zoster virus glycoprotein E antigen

Scheduling proposal

The delegate considered an application from the Therapeutic Goods Administration (TGA) for the scheduling of recombinant varicella zoster virus glycoprotein E antigen, a new chemical (biological) entity (NCE) for a human therapeutic medicine.

Substance summary

Recombinant varicella zoster virus glycoprotein E antigen is a varicella zoster virus antigen based on recombinant technology and will be presented as powder for suspension for injection 50 micrograms.

Recombinant varicella zoster virus glycoprotein E antigen is indicated for the prevention of herpes zoster (HZ) and HZ-related complications, such as post-herpetic neuralgia (PHN), in adults 50 years of age or older.

Scheduling status

Recombinant varicella zoster virus glycoprotein E antigen is not specifically scheduled but is captured by the Schedule 4 class entry for vaccines in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)) as follows:

Schedule 4

VACCINES.

International regulations

Recombinant varicella zoster virus glycoprotein E antigen is classified as a biological product in Canada and a prescription medicine in New Zealand.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors;
- The TGA clinical evaluation report; and
- The new drug application.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include recombinant varicella zoster virus glycoprotein E antigen in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

RECOMBINANT VARICELLA ZOSTER VIRUS GLYCOPROTEIN E ANTIGEN.

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; (c) the toxicity 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:

- Recombinant varicella zoster virus glycoprotein E antigen is an NCE with no clinical or marketing experience in Australia.
- Active immunisation against herpes zoster.
- Usage needs to be based on clinical assessment.
- Presentation will be in compliance with the prescription medicines labelling requirements.

1.17. Reslizumab

Scheduling proposal

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

Substance summary

Reslizumab is a humanized anti-human interleukin 5 monoclonal antibody (anti IL-5 mAb) of the immunoglobulin-G4-kappa (IgG4/k) isotope, produced in mouse myeloma cells (NS0) by recombinant DNA technology. Reslizumab works by binding to IL-5, thereby preventing binding of IL-5 to the IL-5 receptor and consequently reduces circulating and tissue eosinophils.

Reslizumab is indicated as an add-on treatment in adult patients with severe eosinophilic asthma.

Table I: Reslizumab chemical information and naming

Property	Reslizumab
CAS number	241473-69-8
Molecular weight	147 kDa
Australian Biological Name (ABN)	Reslizumab
Other names	Immuoglobulin G4; anti-(human interleukin 5) (human-rat monoclonal SCH 55700 γ4-chain); disulphide with human-rat monoclonal SCH 55700 light chain dimer

Scheduling status

Reslizumab is not specifically scheduled but is captured by the Schedule 4 class entry for monoclonal antibodies in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)) as follows:

Schedule 4

MONOCLONAL ANTIBODIES for therapeutic us **except**:

c) in diagnostic test kits; or

d) when separately specified in these Schedules.

International regulations

Reslizumab is not classified in New Zealand. Reslizumab is classified as a prescription only medicine in the United States of America and the European Union. In Canada, reslizumab is classified as a prescription medicine and is also in Schedule D (drugs listed in Schedule D of the *Food and Drugs Act*, i.e. biological products).

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors; and
- The TGA evaluation report.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include reslizumab in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

RESLIZUMAB.

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 (e) the potential for abuse.

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

- Reslizumab is an NCE with no clinical or marketing experience in Australia, but shares some similarities with the currently marketed medicine mepolizumab.
- Reslizumab is for severe eosinophilic asthma in patients inadequately controlled on maximum dose ICS and another preventative medicine. It is likely to be prescribed only by specialist physicians.
- The potential for abuse of reslizumab is unlikely.

1.18. Ribociclib

Scheduling proposal

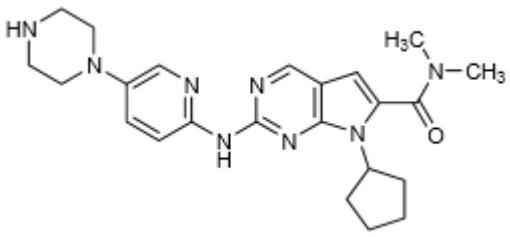
The delegate considered an application from the Therapeutic Goods Administration (TGA) for the scheduling of ribociclib, a new chemical entity (NCE) for a human therapeutic medicine.

Substance summary

Ribociclib is an orally available cyclin-dependent kinase (CDK) inhibitor targeting cyclin D1/CDK4 and cyclin D3/CDK6 cell cycle pathway, with potential antineoplastic activity.

Ribociclib is indicated for advanced breast cancer.

Table J: Ribociclib chemical information and naming

Property	Ribociclib
CAS number	1211441-98-3
Chemical structure	
Molecular formula	$C_{23}H_{30}N_8O$
Molecular weight	434.6 g/mol
Chemical names	7-cyclopentyl-*N,N*-dimethyl-2-((5-(piperazin-1-yl)pyridin-2-yl)amino)-7*H*-pyrrolo[2,3-d]pyrimidine-6-carboxamide
Other names	Ribociclib (ANN and INN); CDK4/6 inhibitor LEE011

Scheduling status

Ribociclib is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

Ribociclib is not classified in New Zealand and Canada and is a prescription only medicine in the United States of America and the European Union.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors;
- The TGA evaluation report;
- The advice of the Advisory Committee on Prescription Medicines; and
- The new drug application.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include ribociclib in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

RIBOCICLIB.

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.

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

- Ribociclib is a new chemical entity with no marketing experience in Australia.

1.19. Tafenoquine succinate

Scheduling proposal

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

Substance summary

Tafenoquine succinate is an 8-aminoquinoline which eradicates *P. vivax* liver hypnozoites. The molecular target of tafenoquine is not known.

Tafenoquine succinate is indicated for radical cure (prevention of relapse) of Plasmodium vivax (*P. vivax*) malaria in patients aged 16 years and older.

Scheduling status

Tafenoquine succinate is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

Tafenoquine succinate is unclassified in New Zealand, Canada and the United States of America.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors; and
- The new drug application (pre-submission documents).

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include tafenoquine succinate in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

TAFENOQUINE SUCCINATE.

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; (c) the toxicity 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:

- Tafenoquine succinate is an NCE with no clinical or marketing experience in Australia.
- Requires specialised medical supervision for usage.
- Presentation will be in compliance with the prescription medicines labelling requirements.

1.20. Telotristat ethyl

Scheduling proposal

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

Substance summary

Telotristat ethyl, as telotristat etiprate, is a tryptophan hydroxylase inhibitor. Telotristat etiprate is the hippuric acid salt form of telotristat ethyl (the free base). Telotristat is the active metabolite of the prodrug, telotristat ethyl.

Both the prodrug (telotristat ethyl) and its active metabolite (telotristat) are inhibitors of L-tryptophan hydroxylases (TPH1 and TPH2, the rate limiting steps in serotonin biosynthesis). Serotonin plays a critical role in regulating several major physiological processes, including secretion, motility, inflammation, and sensation of the gastro-intestinal tract, and is over-secreted in patients with carcinoid syndrome. Through inhibition of peripheral TPH1, telotristat reduces the production of serotonin, thus alleviating symptoms associated with carcinoid syndrome.

Scheduling status

Telotristat ethyl is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

Telotristat ethyl is classified as a prescription medicine in the United States of America. It is unclassified in New Zealand and Canada.

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 (2015) scheduling factors; and
- The TGA evaluation report.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include telotristat ethyl in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

TELOTRISTAT ETHYL.

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.

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

- Telotristat ethyl is an NCE with no marketing experience in Australia.

1.21. Tipiracil

Scheduling proposal

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

Substance summary

Tipiracil (as tipiracil hydrochloride) is a thymidine phosphorylase inhibitor which increases the bioavailability of trifluridine when co-administered.

Tipiracil (as tipiracil hydrochloride), in combination with trifluridine, is indicated for the treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with, or are not considered candidates for fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-VEGF agents, and anti-EGFR agents.

Scheduling status

Tipiracil (as tipiracil hydrochloride) is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

Tipiracil (as tipiracil hydrochloride) is not classified in New Zealand and Canada. Tipiracil is listed as a prescription only medicine in the United States of America and the European Union.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors;
- The TGA evaluation report;
- The advice of the Advisory Committee on Prescription Medicines; and
- The new drug application.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include tipiracil (as tipiracil hydrochloride) in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

TIPIRACIL.

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; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse; and (f) any other matters that the Secretary considers necessary to protect public health.

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

- Tipiracil is an NCE with no marketing experience in Australia.
- The potential for abuse of tipiracil (as tipiracil hydrochloride) is unlikely.
- All matters under subsections 52E(1) have been considered as part of the evaluation and approval process.

1.22. Trifluridine

Scheduling proposal

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

Substance summary

Trifluridine is a thymidine-based nucleoside analogue.

Trifluridine, in combination with tipiracil hydrochloride, is indicated for the treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with, or are not considered candidates for fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-vascular endothelial growth factor (VEGF) agents, and anti-epidermal growth factor receptor (EGFR) agents.

Scheduling status

Trifluridine is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) – the Poisons Standard that was in effect at the time the decision was made (Poisons Standard October 2017 (SUSMP No. 18)).

International regulations

Trifluridine is not classified in New Zealand and is classified as a prescription only medicine in the United States of America and Canada.

Delegate's consideration

The delegate decided to make a delegate-only decision. The Advisory Committee on Medicines Scheduling was not consulted.

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 (2015) scheduling factors;
- The TGA evaluation report;
- The advice of the Advisory Committee on Prescription Medicines; and
- The new drug application.

The delegate noted that currently there are no issues of concern that require additional control other than by inclusion in Schedule 4.

Delegate's final decision

The delegate has made a final decision to amend the Poisons Standard to include trifluridine in Schedule 4, with an implementation date of **1 February 2018**.

The delegate has decided that the wording for the schedule entry will be as follows:

Schedule 4 – New Entry

TRIFLURIDINE.

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; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; (e) the potential for abuse; and (f) any other matters that the Secretary considers necessary to protect public health.

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

- Trifluridine is a new chemical entity with no marketing experience in Australia.
- The potential for abuse of trifluridine is unlikely.
- All matters under subsections 52E(1) have been considered as part of the evaluation and approval process.