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

May 2015

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 delegates' 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 delegates' final decisions and reasons relate to:

- scheduling proposals considered as delegate-only matters, i.e. not referred to an expert advisory committee.

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, 2015), available at https://www.tga.gov.au/publication/ahmac-scheduling-policy-framework-medicines-and-chemicalshttps://www.tga.gov.au/publication/ahmac-scheduling-policy-framework-medicines-and-chemicals.

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 https://www.tga.gov.au/publication/poisons-standard-susmp.

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

Abbreviation	Name
CAS	Chemical Abstract Service
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

Abbreviation	Name
IMAP	Inventory Multi-tiered Assessment Prioritisation
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

Abbreviation	Name
OCSEH	Office of Chemical Safety and Environmental Health (now Office of Chemical Safety [OCS])
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

Abbreviation	Name
SCCP	Scientific Committee on Consumer Products
STANZHA	States and Territories and New Zealand Health Authorities
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

Table of contents

Part A - Final decisions on matters not referred to an expert advisory committee 8

1. Delegate only decision – medicines for human therapeutic use _____ 8

1.1 ALLERGENS _____ 8

1.2 APREMILAST _____ 8

1.3 DASABUVIR _____ 10

1.4 OMBITASVIR _____ 11

1.5 PARITAPREVIR _____ 13

1.6 ULIPRISTAL _____ 14

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

1. Delegate only decision – medicines for human therapeutic use

1.1 ALLERGENS

Scheduling proposal

The delegate has initiated an amendment to the current allergens entry so that it will only capture allergens for therapeutic use. Currently, the Schedule 4 entry for allergens covers substances in products not intended for therapeutic use and as such there is potential for substances included in other Schedules, or not scheduled, to be inadvertently captured by the current allergens entry in Schedule 4.

Scheduling status

Schedule 4

ALLERGENS

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.

Delegate's final decision

The final decision is that the Schedule 4 entry for allergens is to be amended to include "for therapeutic use".

The reason for the decision is that it clarifies that the Schedule 4 entry only applies to allergens used in therapeutic circumstances.

Schedule entry

Schedule 4 – Amendment

ALLERGENS for therapeutic use.

The implementation date of this decision will be 1 June 2015.

1.2 APREMILAST

Scheduling proposal

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

Apremilast is a small molecule, acting to inhibit phosphodiesterase 4, which acts intracellularly to modulate various pro-inflammatory and anti-inflammatory mediators.

Apremilast is indicated for:

- The treatment of the signs and symptoms of active psoriatic arthritis in adult patients
- The treatment of adult patients with moderate to severe plaque psoriasis, who are candidates for phototherapy or systemic therapy.

The delegate decided to make a delegate-only decision to include this to Schedule 4. The Advisory Committee on Medicines Scheduling was not consulted.

Scheduling status

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

Apremilast 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.

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

Delegates' final decision

The delegate has made a final decision to amend the SUSMP to include apremilast in Schedule 4, with an implementation date of 1 June 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 the substance; (b) the purpose and the extent of use of the substance; (c) the toxicity of the substance; d) the dosage, formulation, labelling, packaging and presentation of the substance; and (e) the potential for abuse of the 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 treatment of signs and symptoms of active psoriatic arthritis in adult patients.
- The treatment of adult patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.
- The substance has specific toxicities related to the pharmacological mechanism of action. Diarrhoea, nausea and headache, occurred particularly during initial up-titration.
- There may be an increased background risk of depression/suicidal ideation in the indicated conditions, which may be worsened by apremilast therapy.
- A substantial proportion of patients experienced weight loss while taking apremilast.

- It has been placed in Pregnancy Category B3 (as recommended by the non-clinical evaluator) as preclinical studies demonstrated vasculitis-like changes. There is no experience of apremilast use in pregnancy; indeed, the FDA has mandated a pregnancy-exposure registry.
- A two-week titration pack (4 x 10 mg, 4 x 20 mg and 5 x 30 mg for the first week for dose titration and 14 x 30 mg tablets for the second week).
- A four-week pack (56 x 30 mg tablets)
- A 12 week pack (168 x 30 mg tablets)
- It does not appear to produce dependency and the abuse potential appears to be low.

Schedule entry

Schedule 4 – New Entry

APREMILAST

1.3 DASABUVIR

Scheduling proposal

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

Dasabuvir is a hepatitis C virus non-nucleoside NS5B palm polymerase inhibitor.

Dasabuvir is an active ingredient in the products VIEKIRA PAK-RBV and VIEKIRA PAK, both of which are indicated for the treatment of genotype 1 chronic hepatitis C infection, including patients with cirrhosis.

The delegate decided to make a delegate-only decision to include this to Schedule 4. The Advisory Committee on Medicines Scheduling was not consulted.

Scheduling status

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

Dasabuvir 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.

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

Delegates' final decision

The delegate has made a final decision to amend the SUSMP to include dasabuvir in Schedule 4, with an implementation date of 1 June 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 the substance; (b) the purpose and the extent of use of the substance; (c) the toxicity of the substance; and d) the dosage, formulation, labelling, packaging and presentation of the 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.
- Dasabuvir is to be given as part of the composite packs VIEKIRA PAK-RBV and VIEKIRA PAK.
- Dasabuvir is indicated for the treatment of genotype 1 chronic hepatitis C infection, including patients with compensated cirrhosis.
- Dasabuvir is to be used for a medical condition that requires careful diagnosis and management by medical professionals.
- There are many contraindications proposed due to possible drug interactions when co-administered with other medicines.
- Pregnancy category B1 is proposed. Please note that for the composite pack 'VIEKIRA PAK RBV', ribavirin is classified as pregnancy category X. Ritonavir as part of the composite packs VIEKIRA PAK and 'VIEKIRA PAK RBV' is currently classified as pregnancy category B3.
- There are side effects associated with the use of dasabuvir such as fatigue, nausea, pruritis.
- Dasabuvir should be prescribed by medical professionals who are familiar with the management of chronic liver diseases. The patients need to be instructed to follow the dosing regimens.

Schedule entry

Schedule 4 – New Entry

DASABUVIR.

1.4 OMBITASVIR

Scheduling proposal

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

Ombitasvir is a hepatitis C virus NS5A inhibitor.

Ombitasvir is an active ingredient in the products VIEKIRA PAK-RBV and VIEKIRA PAK, both of which are indicated for the treatment of genotype 1 chronic hepatitis C infection, including patients with cirrhosis.

The delegate decided to make a delegate-only decision to include this to Schedule 4. The Advisory Committee on Medicines Scheduling was not consulted.

Scheduling status

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

Ombitasvir 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.

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

Delegates' final decision

The delegate has made a final decision to amend the SUSMP to include ombitasvir in Schedule 4, with an implementation date of 1 June 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 the substance; (b) the purpose and the extent of use of the substance; (c) the toxicity of the substance and d) the dosage, formulation, labelling, packaging and presentation of the 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.
- Ombitasvir is to be given as part of the composite packs VIEKIRA PAK-RBV and VIEKIRA PAK.
- Ombitasvir is indicated for the treatment of genotype 1 chronic hepatitis C infection, including patients with compensated cirrhosis.
- Ombitasvir is to be used for a medical condition that requires careful diagnosis and management by medical professionals.
- Pregnancy category B1 is proposed. Please note that for the composite pack 'VIEKIRA PAK RBV', ribavirin is classified as pregnancy category X. Ritonavir as part of both VIEKIRA PAK and VIEKIRA PAK RBV is currently classified as pregnancy category B3.
- There are side effects associated with the use of ombitasvir including fatigue, nausea and pruritis.
- There are many contraindications proposed due to possible drug interactions when co-administered with other medicines.

- Ombitasvir should be prescribed by medical professionals who are familiar with the management of chronic liver diseases. The patients need to be instructed to follow the dosage regimens.

Schedule entry

Schedule 4 – New Entry

OMBITASVIR.

1.5 PARITAPREVIR

Scheduling proposal

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

Paritaprevir is a hepatitis C virus NS3/4A protease inhibitor.

Paritaprevir is an active ingredient in the products VIEKIRA PAK-RBV and VIEKIRA PAK, both of which are indicated forthe treatment of genotype 1 chronic hepatitis C infection, including patients with cirrhosis.

The delegate decided to make a delegate-only decision to include this to Schedule 4. The Advisory Committee on Medicines Scheduling was not consulted.

Scheduling status

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

Paritaprevir 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.

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

Delegates' final decision

The delegate has made a final decision to amend the SUSMP to include paritaprevir in Schedule 4, with an implementation date of 1 June 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 the substance; (b) the purpose and the extent of

use of the substance; (c) the toxicity of; and d) the dosage, formulation, labelling, packaging and presentation of the 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.
- Paritaprevir is to be given as part of the composite packs VIEKIRA PAK-RBV and VIEKIRA PAK.
- Paritaprevir is indicated for the treatment of genotype 1 chronic hepatitis C infection, including patients with compensated cirrhosis.
- Paritaprevir is to be used for a medical condition that requires careful diagnosis and management by medical professionals.
- Pregnancy category B1 is proposed. Please note that for the composite pack 'VIEKIRA PAK RBV', ribavirin is classified as pregnancy category X. Ritonavir as part of both VIEKIRA PAK and VIEKIRA PAK RBV is currently classified as pregnancy category B3.
- There are side effects associated with the use of paritaprevir including fatigue, nausea and pruritis.
- There are many contraindications proposed due to possible drug interactions when co-administered with other medicines.
- Paritaprevir should be prescribed by medical professionals who are familiar with the management of chronic liver diseases. The patients need to be instructed to follow the dosage regimens.

Schedule entry

Schedule 4 – New Entry

PARITAPREVIR

1.6 ULIPRISTAL

Scheduling proposal

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

Ulipristal is an orally-active synthetic selective progesterone receptor modulator that acts via high affinity binding to the human progesterone receptor. When used for emergency contraception the mechanism of action is inhibition or delay of ovulation via suppression of the lutenising hormone (LH) surge.

Ulipristal is indicated for emergency contraception within 120 hours (5 days) of unprotected sexual intercourse or contraceptive failure.

The delegate decided to make a delegate-only decision to include this to Schedule 4. The Advisory Committee on Medicines Scheduling was not consulted.

Scheduling status

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

Ulipristal 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.

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

Delegates' final decision

The delegate has made a final decision to amend the SUSMP to include ulipristal in Schedule 4, with an implementation date of 1 June 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 the substance.

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.

Schedule entry

Schedule 4 – New Entry

ULIPRISTAL.