

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

November 2015

(ACMS Meeting – 4 August 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 initially referred to the August 2015 meeting of the Advisory Committee on Medicines Scheduling (ACMS#15);
- scheduling proposals considered as delegate-only matters, i.e. not referred to an expert advisory committee.

Scheduling proposals referred to the expert advisory committees

Pre-meeting public notice

A 'pre-meeting' public notice inviting submissions on the scheduling proposals referred to the expert advisory committees was published on 2 April 2015 and the second public notice was published on 11 June 2015 at <https://www.tga.gov.au/consultation-invitation/consultation-invitation-public-comment-acms-meeting-july-2015> and <https://www.tga.gov.au/consultation-invitation/consultation-invitation-public-comment-acms-meeting-july-2015-0>, respectively.

Edited versions of these public submissions received in response to this invitation were published on 6 October 2015 at <https://www.tga.gov.au/scheduling-submission/public-submissions-scheduling-matters-referred-acms-15-august-2015>.

Interim decisions

The delegate's/delegates' interim decisions on recommendations by the ACMS#15 were published on 1 October 2015 at <https://www.tga.gov.au/scheduling-decision-interim/reasons-scheduling-delegates-interim-decision-and-invitation-further-comment-acms-october-2015>. This public notice also invited further comment from the applicant

and from those parties who made a valid submission in response to the original invitation for submissions.

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

Edited versions of valid public submissions received in response to the interim decisions will be published on or after 19 November 2015 and are available at <https://www.tga.gov.au/public-submissions-scheduling-matters>.

Final decisions

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

Matters not referred to an advisory committee

A delegate may decide not to refer a scheduling proposal to an expert advisory committee for advice and instead may make a delegate-only decision. When deciding not to refer a matter to a committee, the delegate considers the scheduling guidelines as set out in the *Scheduling Policy Framework for Chemicals and Medicines* (SPF, 2015), available at <https://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
CAS	Chemical Abstract Service

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

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

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

Abbreviation	Name
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

Contents

FINAL DECISIONS AND REASONS FOR DECISIONS BY DELEGATES OF THE SECRETARY TO THE DEPARTMENT OF HEALTH..... 1

Part A - Final decisions on matters referred to an expert advisory committee..... 9

1. Scheduling proposals referred to the month year meeting of the Advisory Committee on Medicines Scheduling (ACMS#15).....	9
1.1 Codeine.....	9
1.2 Naloxone.....	11
1.3 Orlistat.....	14
1.4 Hydrocortisone.....	17
1.5 2-Hydroxyethyl methacrylate.....	21
1.6 Esomeprazole.....	25
1.7 Proton pump inhibitors.....	29
1.8 Levocetirizine.....	33

Part B - Final decisions on matters not referred to an expert advisory committee 38

2. New Chemical Entities – medicines for human therapeutic use.....	38
2.1 Armodafinil.....	38
2.2 Asfotase alfa.....	39
2.3 Nintedanib.....	40
2.4 Sacubitril.....	42
3. Editorial amendments.....	43
3.1 Di-iodohydroxyquinoline.....	43

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

1. Scheduling proposals referred to the month year meeting of the Advisory Committee on Medicines Scheduling (ACMS#15)

1.1 Codeine

Scheduling proposal

The medicines scheduling delegate (the delegate) has referred the following scheduling proposal for consideration by and advice from the Advisory Committee on Medicines Scheduling (ACMS):

- Proposal to delete the Schedule 3 entry for codeine, and reschedule all current Schedule 3 codeine to Schedule 4 due to issues including morbidity, toxicity and dependence.
- Consideration could include whether all current Schedule 3 preparations should be rescheduled to Schedule 4, or whether any rescheduling to Schedule 4 should only apply to combination analgesic products containing codeine.

Consideration could include whether the Schedule 2 entry for codeine should also be amended.

Delegate's interim decision

The delegate's interim decision is available at <https://www.tga.gov.au/scheduling-decision-interim/reasons-scheduling-delegates-interim-decision-and-invitation-further-comment-acms-october-2015>.

Delegate's considerations

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- Public submissions received;
- ACMS advice;
- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors¹;
- Other relevant information.

Public submissions on the interim decision

127 submissions were received.

113 did not support the proposal.

¹ Scheduling Policy Framework for Chemicals and Medicines (SPF, 2015)
[<https://www.tga.gov.au/publication/ahmac-scheduling-policy-framework-medicines-and-chemicals>]

Main points:

- Consumers are able to self-manage pain responsibly
- Upscheduling seen as prevention of accessing pain relief
- Issues with access to/Cost associated seeing GPs
- Alternative medications not seen as effective
- Cost to Medicare
- Benefits of codeine outweigh 'morbidity, toxicity and dependence'
- The issue of abuse of prescription codeine verses OTC codeine is not addressed by this scheduling change
- Not able to take Non-Steroidal Anti-Inflammatory Drugs
- The issue of abuse of prescription codeine verses OTC codeine is not addressed by this scheduling change
- There has been no increased demand or change in patterns of use of codeine containing cold and flu products since the up-scheduling of codeine containing analgesics in 2010
- There is no evidence of harm, abuse or dependency associated with codeine containing cold and flu preparations
- Pharmacists are accessible and suitably qualified to implement an effective risk mitigation strategy to address concerns of misuse or abuse
- Introduce system similar to pseudoephedrine
- Introduce real time monitoring/reporting system
- Suggest reducing pack size
- 1 June 2016 implementation is not adequate time and a longer transition period would be required

14 submissions supported the proposal.

Main points:

- Seen too many addicts and health problems associated with OTC codeine
- Ease of access to OTC codeine
- Other effective alternative medication available
- Arguments regarding increased cost to public purse are disingenuous as there are alternative analgesics on the market
- Good evidence now demonstrates that under current arrangements (Schedule 3 Pharmacist Medicine) there is a substantial level of harm from the easy and widespread availability of these opioid medicines
- Personal accounts of family members addicted to codeine, abusing OTC analgesics and cough syrup

Edited versions of these submissions are available at [Public submissions on scheduling matters](#).

Delegate's decision

The delegate has deferred making a final decision at this time regarding the possible rescheduling of codeine. This is due to the large number of submissions received during the most recent consultation period, and the deferral of a decision will allow the submissions and the subsequent information provided to be thoroughly considered. This will also allow the delegate the option available under the legislation to seek further advice, including from the ACMS at its March 2016 meeting, prior to making a final decision, which will not be before 23 June 2016 (the publication date of final decision outcomes of March 2016 meeting). Should the final decision require an implementation date, it will be announced at the time of publication and will not be before 2017.

1.2 Naloxone

Scheduling proposal

The medicines scheduling delegate (the delegate) has referred the following scheduling proposal for consideration by and advice from the Advisory Committee on Medicines Scheduling (ACMS):

- To create a new Schedule 3 entry for naloxone when in single use prefilled syringe preparations for injection containing 400 µg/mL of naloxone or less.

Substance summary

Naloxone is a specific opioid antagonist that acts competitively at opioid receptors. It is an antagonist of opioids that possesses agonist or mixed agonist-antagonist activity, although larger doses may be needed for compounds with the latter activity. Naloxone is used to reverse opioid central depression, including respiratory depression, induced by natural or synthetic opioids, in the management of known or suspected opioid overdose, postoperatively after the use of opioids during surgery, and in neonates when opioid analgesics have been given to the mother during labour.

Naloxone hydrochloride is usually given intravenously for the most rapid action, with onset within two minutes. The onset of action is only slightly less rapid when it is given intramuscularly or subcutaneously. Other routes of administration, including endotracheal, have also been used. The duration of action of naloxone is dependent on the dose and route, but is generally in the range of 1 to 4 hours. An intravenous infusion may be used for a sustained response; commonly, 2 mg of naloxone hydrochloride is added to 500 mL of sodium chloride 0.9% or glucose 5% to obtain a concentration of 4 micrograms/mL.

In the management of known or suspected opioid overdose, the initial dose of naloxone hydrochloride is 0.4 to 2 mg given intravenously and repeated if necessary at intervals of 2 to 3 minutes. If no response has been seen after a total dose of 10 mg then the diagnosis of overdose with drugs other than opioids should be considered. If the intravenous route is not feasible the intramuscular or subcutaneous route can be used. When sustained opioid antagonism is needed, an intravenous infusion may be used. Dosage regimens have not been well established, and the rate of infusion must be titrated according to the patient's response.

Some have recommended an infusion of 60% of the initial dose per hour given via an infusion pump, either undiluted, or diluted to a concentration of 200 micrograms/mL in glucose. Others have suggested an initial intravenous loading dose of 400 micrograms, followed by a continuous infusion at an initial rate of 400 micrograms/hour. Alternatively, an intravenous loading dose of 5 micrograms/kg has been suggested, followed by a continuous infusion of 2.5 micrograms/kg per hour.

Scheduling status

Naloxone is currently listed in Schedule 4.

Scheduling history

National Health and Medical Research Council – Poisons Scheduling Sub-committee: March 1973

The committee recommended that the Schedule 4 entry for Morphine antagonists should be amended to include naloxone, and that the Schedule 8 entry for Oxymorphone should be amended to specify “Oxymorphone except when included in Schedule 4” (as naloxone and some other morphine antagonists were derivatives of oxymorphone).

National Health and Medical Research Council – Poisons Scheduling Sub-committee: August 1985

The committee decided to delete the general Schedule 4 entry for Morphine antagonists, and create a new Schedule 4 entry for Naloxone.

Pre-meeting public submissions

96 submissions were received. (57 as a part of a campaign).

All submissions supported the proposal to down-schedule naloxone in single use pre-filled syringes for injections to Schedule 3. Main points:

- Schedule 3 entry will remove barriers to access;
- Naloxone is safe and has no effect on anyone without opioids in their system;
- Low to no abuse potential.

One submission, while supporting down-scheduling of naloxone, did not support the wording of the proposal. This submission suggested new wording to restrict Schedule 3 listing to a single dose form:

- To amend the scheduling of naloxone to include single doses containing 2 mg or less and a recommended total dose of 10 mg or less.

Edited versions of these submissions are available at [Public submissions on scheduling matters](#).

ACMS advice to the delegate

The ACMS recommended a new Schedule 3 entry for naloxone when packaged and labelled for the treatment of opioid overdose.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate included: a) the risks and benefits of the use of the substance; b) the purposes for which a substance is to be used and the extent of use of a substance; d) the dosage, formulation labelling, packaging and presentation of a substance; and f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the recommendation comprised the following:

- Naloxone is a well-tolerated life-saving medicine with minimal side effects.
- The benefits of increasing availability of naloxone outweigh the risks.
- Naloxone is used as an antidote to opioid overdose.

- The dose form, labelling and packaging of Schedule 3 naloxone must be made suitable for consumer use.
- Naloxone does not replace other resuscitation treatments and procedures.

ACMS recommended an implementation date of 1 February 2016.

Delegate's interim decision

The delegate's interim decision is that a new Schedule 3 entry for naloxone when used for the treatment of opioid overdose be created.

The proposed implementation date for the new Schedule 3 entry is 1 February 2016.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate included: a) the risks and benefits of the use of the substance; b) the purposes for which a substance is to be used and the extent of use of a substance; c) the toxicity of the substance; d) the dosage, formulation, labelling, packaging and presentation of a substance; and f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the decision comprise the following:

- Naloxone is a well-tolerated life-saving medicine with minimal side effects. The benefits outweigh the risks.
- Naloxone is used as an antidote to opioid overdose. The dose form, labelling and packaging of Schedule 3 naloxone must be made suitable for consumer use. Naloxone does not replace other resuscitation treatments and procedures.
- International experience and the outcomes of a trial conducted in the Australian Capital Territory support the view that easier availability of naloxone is likely to decrease the proportion of opioid overdoses which result in death.
- Benefits of rescheduling naloxone for reversal of opioid overdose to Schedule 3 include that products would be supplied labelled with full and clear instructions for use, understandable by consumers. People who need naloxone would be able to obtain it more easily, which is likely to decrease the proportion of (deliberate or accidental, usually illicitly obtained) opioid overdoses that result in death. Increased accessibility would also potentially reduce morbidity due to opioid overdose, such as hypoxic brain damage.
- Risks of rescheduling include an incentive for supply when not necessary, that opioid users may use opioids in a riskier manner knowing that an antidote is available (although there is no evidence that this is the case), that bystanders may be less likely to call an ambulance, and risks of unsafe administration.
- However, there are few inherent risks with use of naloxone. There is no risk of abuse of naloxone itself. Adverse events are rare, there are no major adverse effects if naloxone is given wrongly or not absorbed, and naloxone has no effect in the absence of an opioid.

Delegate's considerations

The delegate considered the following in regards to this proposal:

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

- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors²;
- Other relevant information.

Public submissions on the interim decision

13 submissions were received. 13 submissions supported the delegate's interim decision.

Edited versions of these submissions are available at [Public submissions on scheduling matters](#).

Delegate's final decision

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

The implementation date is 1 February 2016.

Schedule entry

Schedule 3 – New Entry

NALOXONE when used for the treatment of opioid overdose.

Schedule 4 – Amendment

NALOXONE except when in Schedule 3.

1.3 Orlistat

Scheduling proposal

The medicines scheduling delegate (the delegate) has referred the following scheduling proposal for consideration by and advice from the Advisory Committee on Medicines Scheduling (ACMS):

- To amend the scheduling of orlistat to down-schedule oral preparations for weight control purposes containing 120 mg or less of orlistat per dosage unit from Schedule 3 to Schedule 2.

Substance summary

Orlistat is a gastric and pancreatic lipase inhibitor that limits the absorption of dietary fat. It is used together with dietary modification in the management of obesity, i.e. in patients with a BMI of 30 kg/m² or greater. It may also be used in overweight patients with a BMI of 27 kg/m² or more, if there are associated risk factors. Orlistat is given orally in a usual dose of 120 mg three times daily, immediately before, during, or up to 1 hour after meals. The patient's diet should be reduced in calories and nutritionally balanced with 30% of calories obtained from fat, and the daily intake of the major nutrients spread over the three main meals. If a meal is missed or contains no fat, the dose should be omitted. Orlistat may also be used at a lower dose of 60 mg three times daily by the same patient group.

² Scheduling Policy Framework for Chemicals and Medicines (SPF, 2015)
[<https://www.tga.gov.au/publication/ahmac-scheduling-policy-framework-medicines-and-chemicals>]

Scheduling status

Orlistat is currently listed in Schedules 3 and 4.

Schedule 3

ORLISTAT in oral preparations for weight control purposes containing 120 mg or less of orlistat per dosage unit.

Schedule 4

ORLISTAT except when included in Schedule 3.

Scheduling history

National Drugs and Poisons Schedule Committee: August 1999

The NDPSC recommended that orlistat should be included in Schedule 4.

National Drugs and Poisons Schedule Committee: June 2002

The NDPSC considered an application to reschedule orlistat for the treatment of obesity from Schedule 4 to Schedule 3. At that time, the NDPSC decided that the existing scheduling of orlistat (Schedule 4) remained appropriate.

National Drugs and Poisons Schedule Committee: February 2003

The NDPSC considered a further application to reschedule orlistat for the treatment of obesity from Schedule 4 to Schedule 3. The NDPSC decided that the application did not resolve the concerns raised at the June 2002 meeting, and reconfirmed the inclusion of orlistat in Schedule 4.

National Drugs and Poisons Schedule Committee: October 2003

The NDPSC recommended inclusion in Schedule 3 of orlistat in oral preparations for weight control purposes containing 120 mg or less of orlistat. The NDPSC's decision was made on the following grounds: Safety profile of orlistat based on the low incidence of adverse effects; Orlistat was reasonably efficacious for gradual and long term weight loss when used in conjunction with exercise and dietary restriction; Obesity is a disease which can be easily recognised by consumers; Pharmacists in Australia have good training and experience in providing advice and consultation in relation to management of weight loss and treatment of obesity; and Orlistat for use in weight loss has low potential for abuse or overdose.

Pre-meeting public submissions

5 submissions were received.

Two submissions supported the proposal to down-schedule orlistat in oral preparations for weight control purposes containing 120 mg or less of orlistat per dosage unit from Schedule 3 to Schedule 2.

Main points:

- Ease supply restriction; and
- Safe medicine to use.

Three submissions opposed the rescheduling of orlistat.

Main point:

- Potential for abuse.

Edited versions of these submissions are available at [Public submissions on scheduling matters](#).

ACMS advice to the delegate

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

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate included: a) the risks and benefits of the use of the substance; b) the purposes for which a substance is to be used and the extent of use of a substance; c) the toxicity of the substance; and e) the potential for abuse of a substance.

The reasons for the recommendation comprised the following:

- Risks include decreased absorption of fat-soluble vitamins; some drug interactions; renal failure.
- Orlistat is used for the management of obesity.
- Orlistat has minimal toxicity, due to minimal absorption from oral administration.
- However, risks of rescheduling include the potential for misuse, decreased absorption of fat-soluble vitamins, some drug interactions and renal failure.

Delegate's interim decision

The delegate's interim decision is that the current scheduling of orlistat remains appropriate.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate included: a) the risks and benefits of the use of the substance; b) the purposes for which a substance is to be used and the extent of use of a substance; c) the toxicity of the substance; and e) the potential for abuse of a substance.

The reasons for the decision comprised the following:

- Rescheduling orlistat to Schedule 2 is inconsistent with the SPF criterion for Schedule 2 that use is substantially safe for short-term treatment.
- Orlistat has minimal toxicity, due to minimal absorption from oral administration.
- However, there is a risk of misuse if orlistat is down-scheduled to Schedule 2 as professional advice is required to ensure appropriate use of over-the-counter (OTC) orlistat. Inclusion in Schedule 2 could increase the potential for inappropriate use or misuse of orlistat by people with anorexia, bulimia or other mental health issues.
- There are also concerns that advertising of orlistat (if included in Schedule 2) may encourage misuse or inappropriate use.
- There are risks of decreased absorption of fat-soluble vitamins, some drug interactions and renal failure.

Delegate's considerations

The delegate considered the following in regards to this proposal:

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

- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors³;
- Other relevant information.

Public submissions on the interim decision

No public submissions were received.

Delegate's final decision

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

1.4 Hydrocortisone

Scheduling proposal

The medicines scheduling delegate (the delegate) has referred the following scheduling proposal for consideration by and advice from the Advisory Committee on Medicines Scheduling (ACMS):

- To amend the scheduling of hydrocortisone and hydrocortisone acetate to include preparations for dermal human therapeutic use containing 1% or less of hydrocortisone when combined with an antifungal substance (and no other therapeutically active substance) in Schedule 2 under the following conditions:
 - in packs containing 15 g or less; and
 - for the treatment of tinea (tinea pedis, tinea cruris, tinea corporis) and other fungal skin infections; and
 - not labelled for the treatment of children under 12 years.

Substance summary

Hydrocortisone is a corticosteroid with both glucocorticoid and to a lesser extent mineralocorticoid activity. Hydrocortisone is used, usually with a more potent mineralocorticoid, for replacement therapy in adrenocortical insufficiency. It may also be used for its glucocorticoid properties in other conditions for which corticosteroid therapy is indicated but drugs with fewer mineralocorticoid effects tend to be preferred for the long-term systemic therapy of auto-immune and inflammatory disease. Hydrocortisone and its esters (including hydrocortisone acetate) may be used in creams, ointments or lotions, at concentrations ranging from 0.1 to 2.5%, for topical application in the treatment of skin disorders.

A number of antifungal agents are scheduled as OTC medicines for the topical treatment of fungal skin diseases (e.g. bifonazole, clotrimazole, econazole, ketoconazole, miconazole, terbinafine).

Scheduling status

Hydrocortisone is currently listed in Schedules 2, 3 and 4, and Appendix F.

³ Scheduling Policy Framework for Chemicals and Medicines (SPF, 2015)
[<https://www.tga.gov.au/publication/ahmac-scheduling-policy-framework-medicines-and-chemicals>]

Hydrocortisone acetate is currently listed in Schedules 2 and 3.

Schedule 2

HYDROCORTISONE and HYDROCORTISONE ACETATE, but excluding other salts and derivatives, in preparations for human therapeutic use containing 0.5 per cent or less of hydrocortisone:

- (a) for dermal use, in packs containing 30 g or less of such preparations, containing no other therapeutically active constituent other than an antifungal substance; or
- (b) for rectal use when combined with a local anaesthetic substance but no other therapeutically active constituent except unscheduled astringents:
 - (i) in undivided preparations in packs of 35 g or less; or
 - (ii) in packs containing 12 or less suppositories.

Schedule 3

HYDROCORTISONE and HYDROCORTISONE ACETATE, but excluding other salts and derivatives, in preparations for human therapeutic use containing 1 per cent or less of hydrocortisone:

- (a) for dermal use, in packs containing 30 g or less of such preparations, containing no other therapeutically active constituent other than an antifungal substance; or
- (b) for rectal use when combined with a local anaesthetic substance but no other therapeutically active constituent except unscheduled astringents:
 - (i) in undivided preparations in packs of 35 g or less; or
 - (ii) in packs containing 12 or less suppositories,

except when included in Schedule 2.

Schedule 4

HYDROCORTISONE:

- (a) for human use except when included in Schedule 2 or 3; or
- (b) for the treatment of animals.

Scheduling history

National Drugs and Poisons Scheduling Committee: February 1999

The NDPSC agreed to include hydrocortisone in Schedule 2 in dermal preparations containing 0.5% or less of hydrocortisone in packs containing 30 g or less, and containing no other active ingredient or an antifungal as the only other active constituent. The NDPSC also amended the Schedule 3 entry to include dermal preparations containing 1% or less of hydrocortisone in packs containing 30 g or less, and containing no other active ingredient or an antifungal as the only other active constituent (except when included in Schedule 2).

National Drugs and Poisons Scheduling Committee: February 2007

The NDPSC agreed to amend the scheduling of preparations containing 0.5% of hydrocortisone in combination with an anaesthetic for rectal use from Schedule 3 to Schedule 2. The NDPSC noted that this would also harmonise scheduling of the substances with New Zealand. Editorial amendments were made in June and October 2007, to limit the Schedule 2 and 3 entries to human use only.

Advisory Committee on Medicines Scheduling: March 2013

The ACMS considered an application to down-schedule hydrocortisone and hydrocortisone in preparations containing 1% or less of hydrocortisone when combined with antifungal substances for dermal use from Schedule 3 to Schedule 2. The ACMS advised the delegate that the current scheduling remained appropriate.

Pre-meeting public submissions

5 submissions were received.

3 submissions supported the rescheduling proposal.

Main point:

- Ease restrictions.

2 submissions opposed the rescheduling proposal.

Main points:

- Current scheduling is appropriate
- Potential for inappropriate consumer self-treatment of skin conditions caused by an underlying contraindicated condition.

Edited versions of these submissions are available at [Public submissions on scheduling matters](#).

ACMS advice to the delegate

The ACMS recommended that hydrocortisone 1% when combined with antifungal substances for dermal use in packs containing 15 g or less be down scheduled from Schedule 3 to Schedule 2 – specifically, hydrocortisone and hydrocortisone acetate should be included in Schedule 2 in preparations for dermal use containing 1% or less of hydrocortisone when combined with an antifungal substance (and no other therapeutically active substance), under the following conditions:

- in packs containing 15 g or less; and
- for the treatment of tinea (tinea pedis, tinea cruris, tinea corporis) and fungal skin infections; and
- not labelled for the treatment of children under 12 years.

The ACMS recommended an implementation date of 1 February 2016.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate included: a) the risks and benefits of the use of the substance; b) the purposes for which a substance is to be used and the extent of use of a substance; c) the toxicity of the substance; d) the dosage, formulation, labelling, packaging and presentation of a substance; and f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the recommendation comprised the following:

- Hydrocortisone 1% is more effective than 0.5% and the overall adverse reports are similar. The 1% strength does not produce more severe adverse reactions.
- Tinea and fungal infections are common. Itching and inflammation may occur with these infections.

- The overall risk of adverse events from topical hydrocortisone use is very small and the relative risk between the 0.5% and 1% strengths are hardly distinguishable. It has a good safety profile in short term dermal use.
- The proposed 15 g pack size minimises duration of use and the proposed labelling reduces the risk of inappropriate use.
- Providing easier access to a more effective product may be beneficial for consumers.

Delegate's interim decision

The delegate's interim decision is that hydrocortisone 1% when combined with antifungal substances for dermal use in packs containing 15 g or less be down scheduled from Schedule 3 to Schedule 2 – specifically, hydrocortisone and hydrocortisone acetate should be included in Schedule 2 in preparations for dermal use containing 1% or less of hydrocortisone when combined with an antifungal substance (and no other therapeutically active substance), under the following conditions:

- in packs containing 15 g or less; and
- for the treatment of tinea (tinea pedis, tinea cruris, tinea corporis) and other fungal skin infections; and
- not labelled for the treatment of children under 12 years.

The delegate recommended an implementation date for the Schedule 2 amendment of 1 February 2016.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate included: a) the risks and benefits of the use of the substance; b) the purposes for which a substance is to be used and the extent of use of a substance; c) the toxicity of the substance; d) the dosage, formulation, labelling, packaging and presentation of a substance; and f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the decision comprised the following:

- Hydrocortisone 1% is more effective than 0.5% and the overall adverse reports are similar. The 1% strength does not produce more severe adverse reactions.
- Tinea and fungal infections are common. Itching and inflammation may occur with these infections.
- The overall risk of adverse events from topical hydrocortisone use is very small and the relative risk between the 0.5% and 1% strengths are hardly distinguishable. It has a good safety profile in short term dermal use.
- The proposed 15 g pack size minimises duration of use and the proposed labelling reduces the risk of inappropriate use.
- Providing easier access to a more effective product may be beneficial for consumers.

Delegate's considerations

The delegate considered the following in regards to this proposal:

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

- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors⁴;
- Other relevant information.

Public submissions on the interim decision

1 submission was received which did not support the delegate's interim decision.

Edited versions of these submissions are available at [Public submissions on scheduling matters](#).

Delegate's final decision

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

The implementation date will be 1 February 2016.

Schedule entry

Schedule 2 – Amendment

HYDROCORTISONE and HYDROCORTISONE ACETATE, but excluding other salts and derivatives, in preparations for human therapeutic use:

- (a) for dermal use in preparations containing 0.5 per cent or less of hydrocortisone, in packs containing 30 g or less of such preparations, containing no other therapeutically active constituent other than an antifungal substance; or
- (b) for dermal use in preparations containing 1 per cent or less of hydrocortisone, in packs containing 15 g or less of such preparations, containing an antifungal substance and no other therapeutically active constituent:
 - (i) for the treatment of tinea (tinea pedis, tinea cruris, tinea corporis) and other fungal skin infections; and
 - (ii) not labelled for the treatment of children under 12 years of age; or
- (c) for rectal use in preparations containing 0.5 per cent or less of hydrocortisone, when combined with a local anaesthetic substance but no other therapeutically active constituent except unscheduled astringents:
 - (i) in undivided preparations in packs of 35 g or less; or
 - (ii) in packs containing 12 or less suppositories.

1.5 2-Hydroxyethyl methacrylate

Scheduling proposal

The medicines scheduling delegate (the delegate) has referred the following scheduling proposal for consideration by and advice from the Advisory Committee on Medicines Scheduling (ACMS):

⁴ Scheduling Policy Framework for Chemicals and Medicines (SPF, 2015)
 [https://www.tga.gov.au/publication/ahmac-scheduling-policy-framework-medicines-and-chemicals]

- Noting the Chemical Delegate's interim decision to create a new Schedule 5 entry, 2-hydroxyethyl methacrylate except when in nail preparations labelled "Avoid contact with skin", should therapeutic and/or dental use of this substance be exempt from scheduling or have a cut-off of strength? If a cut-off of strength is to be applied, is the previously proposed implementation date of 1 February 2016 appropriate for therapeutic and/or dental use?

Substance summary

2-Hydroxyethyl methacrylate is a methacrylate ester. It is used in cosmetic products (including in artificial nail builders, in finger paints and as a film-forming agent) and in domestic products (e.g. adhesives and sealants; paint, thinners and paint removers; washing and cleaning products; anti-freeze products). Uses at concentrations up to 10% in cosmetic products and up to 80% in domestic products have been identified in Australia. The substance also has commercial, site-limited and non-industrial uses. The main toxicity concerns relate to skin sensitisation potential, eye irritation and skin irritation. Please refer to the NICNAS IMAP human health Tier II assessment report for 2-propenoic acid, 2-methyl-, 2-hydroxyethyl ester – this report is publicly available on the NICNAS website: [NICNAS IMAP-assessment ID 1187](#).

2-Hydroxyethyl methacrylate is also used in dental restorative products in Australia.

Scheduling status

2-Hydroxyethyl methacrylate is not currently scheduled. Following the March 2015 meeting of the Advisory Committee on Chemicals Scheduling, a new Schedule 5 entry was proposed for 2-hydroxyethyl methacrylate except when in nail preparations labelled "Avoid contact with skin". New Appendix E and Appendix F entries were also proposed for 2-hydroxyethyl methacrylate when in Schedule 5. The proposed implementation date was 1 February 2016.

The scheduling delegate subsequently became aware that 2-hydroxyethyl methacrylate is also used in dental restorative products for human use.

Scheduling history

2-Hydroxyethyl methacrylate

Advisory Committee on Chemicals Scheduling: March 2015

The ACCS considered a proposal to create a new Schedule 5 entry for 2-hydroxyethyl methacrylate (primarily for use in cosmetics or domestic products). Concerns regarding skin sensitisation potential and evidence of eye irritation with 2-hydroxyethyl methacrylate were noted. The ACCS recommended inclusion of 2-hydroxyethyl methacrylate in Schedule 5, except when in nail preparations labelled "Avoid contact with skin". Appendix E and Appendix F statements were also proposed.

Other methacrylate esters

2-Hydroxyethyl methacrylate belongs to a group of chemicals known as methacrylate esters, and other chemicals in this group have been considered by National Drugs and Poisons Scheduling Committee (NDPSC) and Advisory Committee on Chemicals Scheduling (ACCS), for the same use and due to the same hazardous property of skin sensitisation. Two other chemicals belonging to this group of chemicals, namely ethyl methacrylate and methyl methacrylate are listed in the Poisons Standard.

National Drugs and Poisons Scheduling Committee: 2006-2008

The NDPSC considered ethyl methacrylate and methyl methacrylate several times over the period 2006-2008. The NDPSC decided to include ethyl methacrylate in Schedule 5 at

concentrations above 1% as the low irritancy and skin sensitisation risks of ethyl methacrylate could be appropriately reduced through including a new Schedule 5 entry for cosmetic use, and to create an Appendix F entry providing appropriate warning statements and safety directions and that these risks are sufficiently reduced when there is $\leq 1\%$ monomer present as a residue in a polymer as to warrant exclusion from the requirements of scheduling.

The NDPSC decided to include methyl methacrylate (MMA) in Schedule 6 for non-cosmetic uses at concentrations above 1% and Appendix C for all cosmetic uses. The NDPSC noted that the severe dermal irritancy, moderate respiratory irritancy and evidence of moderate sensitising potential of methyl methacrylate constituted a moderate potential for causing harm (when for non-cosmetic uses), the extent of which could be reduced through the use of appropriate packaging and labelling and that these risks are sufficiently reduced when there is $\leq 1\%$ monomer present as a residue in a polymer as to warrant exclusion from the requirements of scheduling. However, the cosmetic use of MMA posed sufficient danger as to warrant prohibition of sale, supply and use through inclusion in Appendix C.

Advisory Committee on Chemicals Scheduling: July 2014

Another methacrylate ester, 2-hydroxypropyl methacrylate, was considered by the ACCS. The chemicals delegate's decision was to add the substance to schedule 5 in nail preparations except when labelled 'avoid contact with skin'. The chemicals delegate noted the toxicity of 2-hydroxypropyl methacrylate appears to be less severe than the methyl- and ethylmethacrylates currently listed in Schedule 5, 6 and Appendix C, although there is some potential for cross sensitisation to occur between these methacrylate derivatives when used in nail preparations. The implementation date for this decision is 1 January 2016. The final decision of 2-hydroxypropyl methacrylate is available at <https://www.tga.gov.au/book/final-decisions-matters-referred-expert-advisory-committee-11-14#hydroxypropyl-methacrylate>.

Pre-meeting public submissions

No public submissions were received.

ACMS advice to the delegate

The ACMS recommended that 2-hydroxyethyl methacrylate be included in Schedule 5 except when included in dental restorative preparations for therapeutic use when labelled "Avoid contact with skin" (this is in addition to the previously agreed exemption for nail preparations labelled "Avoid contact with skin").

The ACMS recommended an implementation date for the new Schedule 5 entry of 1 February 2016.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate included: a) the risks and benefits of the use of the substance; b) the purposes for which a substance is to be used and the extent of use of a substance; c) the toxicity of the substance; d) the dosage, formulation, labelling, packaging and presentation of a substance; and f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the recommendation comprised the following:

- Risks: irritation and skin sensitisation; and lower risk due to inhalation of the chemical.
- 2-Hydroxyethyl methacrylate is used in therapeutic goods for dental use that are regulated by the TGA.
- There were some concerns regarding the potential for occupational exposure of dental technicians.

- Labels of products containing 2-hydroxyethyl methacrylate should be required to include a warning statement regarding skin sensitisation.

Delegate's interim decision

The delegate's interim decision is that 2-hydroxyethyl methacrylate be included in Schedule 5 except when included in dental restorative preparations for therapeutic use when labelled "Avoid contact with skin" (this is in addition to the previously agreed exemption for nail preparations labelled "Avoid contact with skin").

The proposed implementation date is 1 February 2016.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate included: a) the risks and benefits of the use of the substance; b) the purposes for which a substance is to be used and the extent of use of a substance; c) the toxicity of the substance; d) the dosage, formulation, labelling, packaging and presentation of a substance; and f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the decision comprised the following:

- The main risks with 2-hydroxyethyl methacrylate are irritation and skin sensitisation. There were some concerns regarding the potential for occupational exposure of dental technicians.
- 2-Hydroxyethyl methacrylate is used in therapeutic goods for dental use that are regulated by the TGA.
- The SUSMP Appendix A general exemption does not apply to dental restorative compounds, as they are not Class III medical devices.
- Exemption of 2-hydroxyethyl methacrylate from scheduling in products for therapeutic or dental use is appropriate. Dental restorative compounds are used by highly trained people and the 2-hydroxyethyl methacrylate is converted to the polymer form (cured by UV light). There is a low risk of deliberate or accidental misuse.
- There were some concerns regarding the potential for occupational exposure of dental technicians.
- The only effect of exempting dental restoratives from Schedule 5 (with products required to be labelled "Avoid contact with the skin") is that product labels would not require a "CAUTION" heading.
- Insufficient information is available to support any specific concentration cut-off for a scheduling exemption for 2-hydroxyethyl methacrylate in dental preparations. Therefore, dental products should be scheduled in the same way as nail preparations.
- Labels of products containing 2-hydroxyethyl methacrylate should be required to include a warning statement regarding skin sensitisation.

Delegate's considerations

The delegate considered the following in regards to this proposal:

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

- Scheduling factors⁵;
- Other relevant information.

Public submissions on the interim decision

No public submissions were received.

Delegate's final decision

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

The implementation date will be 1 February 2016.

Schedule entry

Schedule 5 – New entry

2-HYDROXYETHYL METHACRYLATE except when included in dental restorative preparations for therapeutic use or in nail preparations when labelled “Avoid contact with skin”.

Appendix E, Part 2 – New entry

Poison	Standard statements
2-hydroxyethyl methacrylate	<p>A – For advice, contact a Poisons Information Centre (e.g. phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor (at once).</p> <p>E1 – If in eyes wash out immediately with water.</p> <p>S1 – If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water.</p>

Appendix F, Part 3 – New entry

Poison	Warning statements	Safety direction
2-hydroxyethyl methacrylate	28. (Over) (Repeated) exposure may cause sensitisation.	4. Avoid contact with skin

1.6 Esomeprazole

Scheduling proposal

The medicines scheduling delegate (the delegate) has referred the following scheduling proposal for consideration by and advice from the Advisory Committee on Medicines Scheduling (ACMS):

⁵ Scheduling Policy Framework for Chemicals and Medicines (SPF, 2015) [<https://www.tga.gov.au/publication/ahmac-scheduling-policy-framework-medicines-and-chemicals>]

- To amend the scheduling of esomeprazole to include oral preparations containing 20 mg or less of esomeprazole per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than seven days' supply from Schedule 3 to Schedule 2.

Substance summary

Esomeprazole is the S-isomer of the proton pump inhibitor (PPI), omeprazole, and is used similarly in the treatment of peptic ulcer disease and NSAID-associated ulceration, in gastro-oesophageal reflux disease, and in Zollinger-Ellison syndrome. Esomeprazole is given as the magnesium, sodium, or strontium salts but doses are calculated in terms of esomeprazole. Esomeprazole magnesium 22.2 mg, esomeprazole sodium 21.3 mg, and esomeprazole strontium 24.7 mg are each equivalent to about 20 mg of esomeprazole.

Scheduling status

Esomeprazole is currently listed in Schedules 3 and 4.

Schedule 3

ESOMEPRAZOLE in oral preparations containing 20 mg or less per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 14 days' supply.

Schedule 4

ESOMEPRAZOLE except when included in Schedule 3.

Scheduling history

National Drugs and Poisons Schedule Committee: November 2000

The New Zealand Ministry of Health requested that the NDPSC consider scheduling esomeprazole to harmonise with New Zealand's inclusion of the substance in Schedule 1, Part 1 (equivalent to Schedule 4 in the SUSMP). The NDPSC supported harmonisation and included esomeprazole in Schedule 4.

Advisory Committee on Medicines Scheduling: November 2013

The ACMS considered an application to down-schedule from Schedule 4 to Schedule 3 esomeprazole in oral preparations containing 20 mg or less per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 14 days' supply. The ACMS advised the delegate to down-schedule esomeprazole to Schedule 3, as requested.

Pre-meeting public submissions

7 submissions were received.

3 submissions supported the applicant's proposal to reschedule esomeprazole from Schedule 3 to Schedule 2 when in packs containing not more than seven days' supply.

Main points:

- Esomeprazole is available OTC in the USA.
- Recommend appropriate warning statements.

3 submissions opposed the rescheduling proposal. Main points:

- No monitoring of ongoing/long-term use of PPIs which may lead to adverse reactions.
- Need to ensure appropriate consultation and review by pharmacists.

1 submission did not state a position. Main points:

- If esomeprazole down-scheduled then recommend all PPIs have new Schedule 2 entry.

Edited versions of these submissions are available at [Public submissions on scheduling matters](#).

ACMS advice to the delegate

The ACMS recommended that esomeprazole in oral preparations containing 20 mg or less per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than seven days' supply, be down-scheduled from Schedule 3 to Schedule 2.

The committee also recommended to the delegate that consideration be given to down-scheduling the other OTC PPIs (i.e. lansoprazole, omeprazole and rabeprazole) from Schedule 3 to Schedule 2 in packs containing not more than seven days' supply.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate included: a) the risks and benefits of the use of the substance; b) the purposes for which a substance is to be used and the extent of use of a substance; c) the toxicity of the substance; d) the dosage, formulation, labelling, packaging and presentation of a substance; and f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the recommendation comprised the following:

- Esomeprazole is a safe and effective first line treatment for consumers with frequent symptoms of gastro-oesophageal reflux disease.
- Heartburn and other symptoms of gastro-oesophageal reflux disease are common.
- Esomeprazole has very low toxicity with short-term use.
- The proposed Schedule 2 pack size (seven days' supply), labelling (including Required Advisory Statements for Medicine Labels (RASML) warning statements) and provision of Consumer medicine information will help ensure appropriate use of esomeprazole as a Schedule 2 medicine.
- The current RASML label warnings for all OTC PPIs would apply to esomeprazole in Schedule 2 or Schedule 3.
- Esomeprazole may be more effective in the treatment of gastro oesophageal reflux disease than ranitidine which is currently available as an unscheduled medicine (seven days' supply) and as a Schedule 2 medicine (14 days' supply).

Delegate's interim decision

The delegate's interim decision is that esomeprazole, in oral preparations containing 20 mg or less per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than seven days' supply, be down-scheduled from Schedule 3 to Schedule 2.

The proposed implementation date is 1 February 2016.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate included: a) the risks and benefits of the use of the substance; b) the purposes for which a substance is to be used and the extent of use of a substance; c) the toxicity of the substance; d) the dosage, formulation, labelling, packaging and presentation of a substance; and f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the decision comprised the following:

- Esomeprazole is a safe and effective first line treatment for consumers with frequent symptoms of gastro-oesophageal reflux disease.
- Heartburn and other symptoms of gastro-oesophageal reflux disease are common.
- Esomeprazole has very low toxicity with short-term use.
- The proposed Schedule 2 pack size (seven days' supply), labelling (including RASML warning statements) and provision of Consumer medicine information will help ensure appropriate use of esomeprazole as a Schedule 2 medicine.
- The current RASML label warnings for all OTC PPIs would apply to esomeprazole in Schedule 2 or Schedule 3.
- Esomeprazole may be more effective in the treatment of gastro oesophageal reflux disease than ranitidine which is currently available as an unscheduled medicine (seven days' supply) and as a Schedule 2 medicine (14 days' supply).

Delegate's considerations

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- Public submissions received;
- ACMS advice;
- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors⁶;
- Other relevant information.

Public submissions on the interim decision

2 submissions were received. 1 submission in support; the other not supporting the decision.

Edited versions of these submissions are available at [Public submissions on scheduling matters](#).

Delegate's final decision

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

The implementation date will be 1 February 2016.

⁶ Scheduling Policy Framework for Chemicals and Medicines (SPF, 2015)
[<https://www.tga.gov.au/publication/ahmac-scheduling-policy-framework-medicines-and-chemicals>]

Schedule entry

Schedule 2 – New entry

ESOMEPRAZOLE in oral preparations containing 20 mg or less of esomeprazole per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 7 days' supply.

Schedule 3 – Amendment

ESOMEPRAZOLE in oral preparations containing 20 mg or less of esomeprazole per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 14 days' supply **except** when included in Schedule 2.

Schedule 4 – Amendment

ESOMEPRAZOLE **except** when included in Schedule 2 or 3.

1.7 Proton pump inhibitors

Scheduling proposal

The medicines scheduling delegate (the delegate) has referred the following scheduling proposal for consideration by and advice from the Advisory Committee on Medicines Scheduling (ACMS):

- To create new Appendix H entries for the following Schedule 3 proton pump inhibitors (PPIs):
 - lansoprazole;
 - omeprazole;
 - pantoprazole; and
 - rabeprazole.

Substance summary

Lansoprazole, omeprazole, pantoprazole and rabeprazole are PPIs. PPIs are used in the treatment of peptic ulcer disease and NSAID-associated ulceration, in gastro-oesophageal reflux disease, and in Zollinger-Ellison syndrome.

Scheduling status

Lansoprazole, omeprazole and rabeprazole are currently listed in Schedules 3 and 4.

Pantoprazole is currently listed in Schedules 2, 3 and 4.

Lansoprazole

Schedule 3

LANSOPRAZOLE in oral preparations containing 15 mg or less of lansoprazole per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 14 days' supply.

Schedule 4

LANSOPRAZOLE **except** when included in Schedule 3.

Omeprazole

Schedule 3

OMEPRAZOLE in oral preparations containing 20 mg or less of omeprazole per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 14 days' supply.

Schedule 4

OMEPRAZOLE except when included in Schedule 3.

Rabeprazole

Schedule 3

RABEPRAZOLE in oral preparations containing 10 mg or less of rabeprazole per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 14 days' supply.

Schedule 4

RABEPRAZOLE except when included in Schedule 3.

Pantoprazole

Schedule 2

PANTOPRAZOLE in oral preparations containing 20 mg or less of pantoprazole per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 7 days' supply.

Schedule 3

PANTOPRAZOLE in oral preparations containing 20 mg or less of pantoprazole per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 14 days' supply except when included in Schedule 2.

Schedule 4

PANTOPRAZOLE except when included in Schedule 2 or 3.

Scheduling history

National Drugs and Poisons Schedule Committee: June 2005

The NDPSC included pantoprazole in Schedule 3, in oral preparations containing 20 mg or less of pantoprazole for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 14 days' supply (the NDPSC subsequently amended the implementation date until 1 May 2008). The NDPSC did not consider Appendix H listing at that time.

National Drugs and Poisons Schedule Committee: June 2009

The NDPSC agreed to down-schedule rabeprazole to Schedule 3 (with pack size and indication restrictions similar to those for pantoprazole). A request for Appendix H listing was rejected.

National Drugs and Poisons Schedule Committee: February 2010

The NDPSC decided that inclusion of pantoprazole in Appendix H listing was not appropriate.

Lansoprazole and omeprazole were scheduled similarly to pantoprazole and rabeprazole, to harmonise with New Zealand. In both cases, the NDPSC agreed that a consistent approach for all PPIs should be undertaken in relation to Appendix H listing, i.e. lansoprazole and omeprazole were not included in Appendix H.

National Drugs and Poisons Schedule Committee: June 2010

The NDPSC again rejected a proposal to include rabeprazole in Appendix H. The NDPSC generally agreed that an Appendix H listing was not appropriate at this time and that it would be beneficial for pharmacists to first become accustomed to having rabeprazole available as a Schedule 3 medicine.

Advisory Committee on Medicines Scheduling: November 2014

The ACMS recommended a new entry in Schedule 2 for pantoprazole when supplied in oral preparations containing 20 mg or less of pantoprazole per dosage unit for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 7 days of supply.

Advisory Committee on Medicines Scheduling: March 2015

The ACMS recommended inclusion of esomeprazole in Appendix H. The ACMS also proposed that the medicines delegate consider initiating a proposal to list all Schedule 3 proton pump inhibitors (PPIs) in Appendix H.

Pre-meeting public submissions

3 submissions were received

All three submissions supported the scheduling proposal with one on the condition that all advertisements for these products highlight the mandatory role of the pharmacist in determining the suitability of the product for consumers.

Edited versions of these submissions are available at [Public submissions on scheduling matters](#).

ACMS advice to the delegate

The ACMS recommended that new Appendix H entries be created for the following Schedule 3 proton pump inhibitors: Lansoprazole, Omeprazole, Pantoprazole and Rabeprazole.

The ACMS recommended an implementation date of 1 February 2016.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate included: a) the risks and benefits of the use of the substance; b) the purposes for which a substance is to be used and the extent of use of a substance; and f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the recommendation comprised the following:

- The ACMS, at its March 2015 meeting, had recommended inclusion of esomeprazole in Appendix H.
- The delegate decided that esomeprazole would be included in Appendix H as of 1 October 2015.
- There are no relevant clinical differences between esomeprazole and the other over-the-counter (OTC) PPI medications that would affect their listing in Appendix H.
- All the OTC PPIs have similar mechanisms of action and similar efficacy and safety profiles.

- The same indications and Required Advisory Statements for Medicine Labels (RASML) label statement requirements apply to all OTC PPIs.

Delegate's interim decision

The delegate's interim decision is that new Appendix H entries be created for the following Schedule 3 proton pump inhibitors: Lansoprazole, Omeprazole, Pantoprazole and Rabeprazole.

The proposed implementation date is 1 February 2016.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate included: a) the risks and benefits of the use of the substance; b) the purposes for which a substance is to be used and the extent of use of a substance; and f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the decision comprised the following:

- The ACMS, at its March 2015 meeting, had recommended inclusion of esomeprazole in Appendix H.
- The delegate decided that esomeprazole would be included in Appendix H as of 1 October 2015.
- There are no relevant clinical differences between esomeprazole and the other over-the-counter (OTC) PPI medications that would affect their listing in Appendix H.
- All the OTC PPIs have similar mechanisms of action and similar efficacy and safety profiles.
- The same indications and Required Advisory Statements for Medicine Labels (RASML) label statement requirements apply to all OTC PPIs.

Delegate's considerations

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- Public submissions received;
- ACMS advice;
- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors⁷;
- Other relevant information.

Public submissions on the interim decision

No public submissions were received.

Delegate's final decision

The delegate notes the submissions received in response to publication of the interim decision and confirms the interim decision as no evidence has been received to alter the

⁷ Scheduling Policy Framework for Chemicals and Medicines (SPF, 2015)
[<https://www.tga.gov.au/publication/ahmac-scheduling-policy-framework-medicines-and-chemicals>]

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

The implementation date will be 1 February 2016.

Schedule entry

Schedule H – New entry

Lansoprazole.

Omeprazole.

Pantoprazole.

Rabeprazole.

1.8 Levocetirizine

Scheduling proposal

The medicines scheduling delegate (the delegate) has referred the following scheduling proposal for consideration by and advice from the Advisory Committee on Medicines Scheduling (ACMS):

- Although levocetirizine is covered by the schedule entries for cetirizine, it is proposed to include specific entries for levocetirizine in Schedule 2, Schedule 4 and Appendix K in the SUSMP.

Consideration should include:

- whether all levocetirizine preparations for oral use should be in Schedule 2; or
- whether levocetirizine should be exempt from scheduling in divided preparations for oral use for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when: (a) in a primary pack containing not more than five days' supply; and (b) labelled with a recommended daily dose not exceeding 5 mg of levocetirizine (ie. consistent with the scheduling exemption for cetirizine).

Substance summary

Levocetirizine is the active enantiomer of cetirizine (5 mg of levocetirizine is equivalent to 10 mg of cetirizine).

Levocetirizine is an antihistamine, and is used for relief of symptoms of allergic conditions such as allergic rhinitis and chronic idiopathic urticaria. In Australia, levocetirizine is approved for use in adults and children aged 2 years and over. In some other countries, levocetirizine is approved for use in children from 6 months of age (e.g. in the US, levocetirizine is approved for relief of symptoms of seasonal allergic rhinitis in adults and children aged from 2 years, and for relief of symptoms of perennial allergic rhinitis and chronic idiopathic urticaria in adults and children aged from 6 months).

Cetirizine is a piperazine derivative and metabolite of hydroxyzine. It is a long-acting, low-sedating antihistamine with some mast-cell stabilising activity.

Scheduling status

Levocetirizine is not currently listed in the SUSMP, but would be covered by the Schedule 2 and 4 entries for cetirizine.

The SUSMP Part 1, Interpretation, point 1(2) states: "Unless the contrary intention appears a reference to a substance in a Schedule or an Appendix to this Standard includes:

... (c) every salt, active principle or derivative of the substance, including esters and ethers, and every salt of such an active principle or derivative; ... (e) every stereoisomer of the substance and every salt of such a stereoisomer; ...”.

Cetirizine is currently listed in Schedules 2 and 4.

Schedule 2

CETIRIZINE in preparations for oral use except in divided preparations for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:

- (a) in a primary pack containing not more than 5 days' supply; and
- (b) labelled with a recommended daily dose not exceeding 10 mg of cetirizine.

Schedule 4

CETIRIZINE except:

- (a) when included in Schedule 2; or
- (b) in divided preparations for oral use for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:
 - (i) in a primary pack containing not more than 5 days' supply; and
 - (ii) labelled with a recommended daily dose not exceeding 10 mg of cetirizine.

Cetirizine is also listed in Appendix K.

Scheduling history

Levocetirizine

No previous scheduling considerations. Drugs and Poisons Schedule Standing Committee (DPSSC), NDPSC and ACMS considerations of cetirizine make no mention of levocetirizine.

Cetirizine

Drugs and Poisons Schedule Standing Committee: May 1993

The DPSSC decided to include cetirizine in Schedule 4 and in Appendix K (Drugs required to be labelled with a sedation warning).

National Drugs and Poisons Scheduling Committee: May 1997

The NDPSC decided to include cetirizine in Schedule 3 as the only therapeutically active substance in divided preparations for oral use containing 10 mg or less of cetirizine. A limit on pack size was not considered necessary. Cetirizine remained in Schedule 4 except when included in Schedule 3.

National Drugs and Poisons Scheduling Committee: February 1998

The NDPSC decided to amend the Schedule 3 entry for cetirizine to include all oral formulations of cetirizine, when it was the only active substance in the preparation (the Schedule 3 entry was no longer to be restricted to divided preparations and the maximum dosage unit size was deleted).

National Drugs and Poisons Scheduling Committee: November 1999

The NDPSC decided to reschedule cetirizine in all preparations for oral use to Schedule 2. The Appendix H entry for cetirizine was deleted.

Advisory Committee on Medicines Scheduling: June 2012

The ACMS recommended that cetirizine should be exempt from scheduling, when in divided forms for oral use containing 10 mg or less of cetirizine hydrochloride per dose, in packs containing not more than 5 days' supply for the treatment of seasonal allergic rhinitis.

Pre-meeting public submissions

2 submissions were received.

1 submission supported the proposal to include separate schedule entries for levocetirizine, but did not support a scheduling exemption of levocetirizine.

Main points:

- Risk of sedation and its potential impact on driving capacity.
- Levocetirizine is six times more likely to result in sedation than other non-sedating antihistamines.
- Combination with other impairing drugs (including alcohol) increases the opportunity for impairment.
- Inclusion of warnings on medicine packs is insufficient.

1 submission supported the proposal to schedule levocetirizine as for cetirizine.

Edited versions of these submissions are available at [Public submissions on scheduling matters](#).

ACMS advice to the delegate

The ACMS recommended that a separate schedule entry in the Poisons Standard for levocetirizine be included in Schedule 2 and Appendix K, and that levocetirizine should be scheduled as for cetirizine.

The ACMS recommended an implementation date of 1 February 2016.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate included: a) the risks and benefits of the use of the substance; b) the purposes for which a substance is to be used and the extent of use of a substance; c) the toxicity of the substance; and d) the dosage, formulation, labelling, packaging and presentation of a substance.

The reasons for the recommendation comprised the following:

- Levocetirizine is the active isomer of cetirizine. The risks and benefits of levocetirizine and cetirizine will be the same, so the scheduling outcomes for the two substances should also be the same, taking the 1:2 dose ratio into account. Scheduling exemption would be similar to other less-sedating antihistamines.
- The indications for levocetirizine are as for cetirizine.
- Levocetirizine has the same efficacy and safety profiles as cetirizine.
- Schedule entries for levocetirizine and cetirizine should therefore have the same outcome.

Delegate's interim decision

The delegate's interim decision is that separate schedule entries be included in the Poisons Standard for levocetirizine in Schedule 2, Schedule 4 and Appendix K, and that levocetirizine should be scheduled as for cetirizine.

The proposed implementation date is 1 February 2016.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate included: a) the risks and benefits of the use of the substance; b) the purposes for which a substance is to be used and the extent of use of a substance; c) the toxicity of the substance; and d) the dosage, formulation, labelling, packaging and presentation of a substance.

The reasons for the decision comprised the following:

- Levocetirizine is the active isomer of cetirizine. The risks and benefits of levocetirizine and cetirizine will be the same, so the scheduling outcomes for the two substances should also be the same, taking the 1:2 dose ratio into account. Scheduling exemption would be similar to other less-sedating antihistamines.
- The indications for levocetirizine are as for cetirizine.
- Levocetirizine has the same efficacy and safety profiles as cetirizine.
- Schedule entries for levocetirizine and cetirizine should therefore have the same outcome.

Delegate's considerations

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- Public submissions received;
- ACMS advice;
- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors⁸;
- Other relevant information.

Public submissions on the interim decision

No public submissions were received.

Delegate's final decision

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

The implementation date will be 1 February 2016.

⁸ Scheduling Policy Framework for Chemicals and Medicines (SPF, 2015)
[<https://www.tga.gov.au/publication/ahmac-scheduling-policy-framework-medicines-and-chemicals>]

Schedule entry

Schedule 2 – New entry

LEVOCETIRIZINE in preparations for oral use except in divided preparations for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:

- (a) in a primary pack containing not more than 5 days' supply; and
- (b) labelled with a recommended daily dose not exceeding 5 mg of levocetirizine.

Schedule 4 – Amendment

LEVOCETIRIZINE except:

- (a) when included in Schedule 2; or
- (b) in divided preparations for oral use for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when:
 - (i) in a primary pack containing not more than 5 days' supply; and
 - (ii) labelled with a recommended daily dose not exceeding 5 mg of levocetirizine.

Appendix K – New entry

Levocetirizine

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

2. New Chemical Entities – medicines for human therapeutic use

2.1 Armodafinil

Scheduling proposal

The delegate considered an application from the TGA for the scheduling of armodafinil, a new chemical entity for a human therapeutic medicine.

Armodafinil - Modafinil is a racemic mixture of the enantiomers R-modafinil and S-modafinil with the stereogenic centre at the sulphur atom. Armodafinil is R-modafinil only.

Modafinil/armodafinil are oral wakefulness promoting agents, but pharmacologically different from other stimulants (including sympathomimetic amines). The exact mechanism of action is unknown.

Armodafinil is indicated:

- to improve wakefulness in patients with excessive daytime sleepiness associated with narcolepsy
- to treat excessive sleepiness associated with moderate to severe chronic shift work sleep disorder where nonpharmacological interventions are unsuccessful or inappropriate
- as an adjunct to continuous positive airways pressure (CPAP) in obstructive sleep apnoea/hypopnoea syndrome in order to improve wakefulness.

The delegate decided to make a delegate-only decision to include this to Schedule 4. The ACMS was not consulted.

Scheduling status

Armodafinil is not specifically scheduled and is not captured by any entry in the SUSMP No. 9.

Armodafinil 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.
- 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.

Delegate's final decision

The delegate has made a final decision to amend the SUSMP to include armodafinil in Schedule 4, with an implementation date of 1 February 2016.

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:

- It is a new chemical entity with no [clinical/marketing] experience in Australia.
- It has been proposed for the treatment of conditions that require the medical supervision.
- It is anticipated to have a toxicity/ risk profile similar to the racemic mixture of which this active is a component. The racemic mixture is currently on the SUSMP.
- This substance has a moderate likelihood of abuse but not of dependency.

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

Schedule entry

Schedule 4 – New entry

ARMODAFINIL

2.2 Asfotase alfa

Scheduling proposal

The delegate considered an application from the TGA for the scheduling of asfotase alfa, a new chemical entity for a human therapeutic medicine.

Asfotase alfa is a human recombinant tissue-nonspecific alkaline phosphatase (TNSALP)-Fc-deca-aspartate fusion protein with enzymatic activity, produced by recombinant DNA technology using mammalian Chinese Hamster Ovary (CHO) cell culture.

Asfotase alfa is indicated for long-term enzyme replacement therapy in patients with paediatric-onset hypophosphatasia.

The delegate decided to make a delegate-only decision to include this to Schedule 4. The ACMS was not consulted.

Scheduling status

Asfotase alfa is not specifically scheduled and is not captured by any entry in the SUSMP No. 9.

Asfotase alfa 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.
- 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.

Delegate's final decision

The delegate has made a final decision to amend the SUSMP to include asfotase alfa in Schedule 4, with an implementation date of 1 February 2016.

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:

- It is a new chemical entity with no clinical experience in Australia.
- The risks and benefits of the medicine have been considered and are outlined in the Product Information, Delegate's Request for ACPM advice and the TGA evaluation reports.
- Asfotase alfa is indicated for long-term enzyme replacement therapy in patients with paediatric-onset hypophosphatasia.
- It has no previous experience of use in Australia but has recently been approved for use overseas.
- It is proposed for use in the hospital and community.
- Treatment should be initiated by a physician experienced in the management of patients with metabolic or bone disorders.
- Asfotase alfa is a first in class human recombinant tissue-nonspecific alkaline phosphatase (TNSALP)-Fc-deca-aspartate fusion protein.
- The medicine has risks that require medical intervention, evaluation and monitoring by a medical practitioner.
- Labelling needs to comply with the requirements for a prescription only medicine.
- It does not appear to produce dependency and the abuse potential appears to be low.

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

Schedule entry

Schedule 4 – New entry

ASFOTASE ALFA

2.3 Nintedanib

Scheduling proposal

The delegate considered an application from the TGA for the scheduling of nintedanib, a new chemical entity for a human therapeutic medicine.

Nintedanib esilate is a triple angiokinase inhibitor blocking vascular endothelial growth factor receptors (VEGFR 1-3), platelet-derived growth factor receptors (PDGFR α and β) and fibroblast growth factor receptors (FGFR 1-3) kinase activity.

Nintedanib esilate is indicated, in combination with docetaxel, for the treatment of patients with locally advanced, metastatic or recurrent non-small cell lung cancer (NSCLC) of adenocarcinoma tumour histology after failure of first line chemotherapy. OFEV is also indicated for the treatment of Idiopathic Pulmonary Fibrosis (IPF).

The delegate decided to make a delegate-only decision to include this to Schedule 4. The ACMS was not consulted.

Scheduling status

Nintedanib is not specifically scheduled and is not captured by any entry in the SUSMP No. 9.

Nintedanib 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.
- 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.

Delegate's final decision

The delegate has made a final decision to amend the SUSMP to include nintedanib in Schedule 4, with an implementation date of 1 February 2016.

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:

- Nintedanib is a new chemical entity with no marketing experience in Australia.
- The benefits and risks of nintedanib have been considered in the TGA evaluation process.
- Toxicity of the substance has been taken into account in the TGA evaluation process.
- The dosage, formulation, labelling, packaging and presentation of the substance has been taken into account in the TGA evaluation process.

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

Schedule entry

Schedule 4 – New entry

NINTEDANIB

2.4 Sacubitril

Scheduling proposal

The delegate considered an application from the TGA for the scheduling of sacubitril, a new chemical entity for a human therapeutic medicine.

Sacubitril in combination with valsartan, is a first-in-class angiotensin receptor neprilysin (neutral endopeptidase 24.11; NEP) inhibitor (ARNI).

Sacubitril, in combination with valsartan, is indicated for the treatment of adults with chronic heart failure (NYHA class II-IV) in patients with reduced ejection fraction.

The delegate decided to make a delegate-only decision to include this to Schedule 4. The ACMS was not consulted.

Scheduling status

Sacubitril is not specifically scheduled and is not captured by any entry in the SUSMP No. 9.

Sacubitril 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.
- 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.

Delegate's final decision

The delegate has made a final decision to amend the SUSMP to include sacubitril in Schedule 4, with an implementation date of 1 February 2016.

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:

- It is a new chemical entity with no clinical experience in Australia.
- The risks and benefits of the medicine have been considered and are outlined in the Product Information, Delegate's Request for ACPM advice and the TGA evaluation reports.
- Sacubitril, in combination with valsartan, is indicated for the treatment of adults with chronic heart failure (NYHA class II-IV) in patients with reduced ejection fraction.
- It has no previous experience of use in Australia but has recently been approved for use overseas.

- It is proposed for use in the hospital and community.
- Sacubitril, in combination with valsartan, is a first-in-class angiotensin receptor neprilysin inhibitor. Sacubitril is a neprilysin (neutral endopeptidase) inhibitor.
- The medicine has risks that require medical intervention, evaluation and monitoring by a medical practitioner.
- It is contraindicated in pregnancy.
- Labelling needs to comply with the requirements for a prescription only medicine.
- It does not appear to produce dependency and the abuse potential appears to be low.

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

Schedule entry

Schedule 4 – New entry

SACUBITRIL

3. Editorial amendments

3.1 Di-iodohydroxyquinoline

Scheduling proposal

The medicines scheduling delegate has initiated an editorial amendment to clarify the scheduling of di-iodohydroxyquinoline by reinstating the Schedule 10/Appendix C entry for di-iodohydroxyquinoline for human internal use, which was removed from the SUSMP in 2009.

Schedule 10 – Editorial amendment

DI-IODOHYDROXYQUINOLINE (iodoquinol) for human internal use.

Scheduling status

Di-iodohydroxyquinoline (iodoquinol) is currently listed in Schedules 3 and 4.

Schedule 4

DI-IODOHYDROXYQUINOLONE (iodoquinol) except:

- (a) when included in Schedule 3; or
- (b) for human internal use.

Schedule 3

DI-IODOHYDROXYQUINOLONE (iodoquinol) for vaginal use.

Clioquinol is currently listed in Schedule 4 and 10/Appendix C.

Schedule 10/Appendix C

CLIOQUINOL and other halogenated derivatives of 8-hydroxyquinoline for human internal use except when in Schedule 4 or when being used solely for experimental purposes in humans and where such use:

- (a) is in accordance with:

- (i) an approval granted under paragraph 19(1)(b) of the *Therapeutic Goods Act 1989*, including any conditions specified in the notice of approval; and
 - (ii) any conditions specified in the *Therapeutic Goods Regulations 1990* for the purposes of subsection 19(1A) of the *Therapeutic Goods Act 1989*; and
 - iii) any conditions specified in the *Therapeutic Goods Regulations 1990* for the purposes of subsection 19(4A) of the *Therapeutic Goods Act 1989*; or
- (b) is in accordance with the requirements of item 3 of Schedule 5A to the *Therapeutic Goods Regulations 1990*.

Schedule 4

CLIOQUINOL and other halogenated derivatives of 8-hydroxyquinoline for human topical use except when separately specified in this Schedule.

Scheduling history

National Drugs and Poisons Scheduling Committee - February 1999

Recommendation No. 82 of the Trans-Tasman Harmonisation Working Party was that the Schedule 4 entry for di-iodohydroxyquinoline be amended to exclude for oral use and create an Appendix C entry.

National Drugs and Poisons Scheduling Committee – June 2009

The Committee decided that the entry for di-iodohydroxyquinoline (iodoquinol) for human internal use be removed from Appendix C as it was appropriately captured by the Appendix C entry for clioquinol and other halogenated derivatives of 8-hydroxyquinoline. Further, the Committee agreed to cross-reference diiodohydroxyquinoline with the clioquinol Appendix C entry in the SUSDP index.

Delegate's consideration

The delegate considered the following in regards to this editorial amendment:

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

Delegate's final decision

The delegate's final decision is that di-iodohydroxyquinoline for human internal use is reinstated in Schedule 10/Appendix C.

The implementation date is 1 February 2016.

Reasons for the decision are:

- Although di-iodohydroxyquinoline is covered by the Schedule 10 /Appendix C entry for Clioquinol there is potential confusion as di-iodohydroxyquinoline is specifically listed in Schedules 3 and 4.
- This decision clarifies the status of di-iodohydroxyquinoline as also being covered by Schedule 10/Appendix C.

Schedule entry

Schedule 10 – Editorial amendment

DI-IODOHYDROXYQUINOLINE (iodoquinol) for human internal use.