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

March 2015

(ACMS Meeting – 17 March 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 March 2015 meeting of the Advisory Committee on Medicines Scheduling (ACMS#14);
- 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 13 November 2014 at https://www.tga.gov.au/consultation-invitation/consultation-invitation-public-comment-acms-meeting-march-2015.

Interim decisions

The delegate's interim decisions on recommendations by the ACMS #14 were published on 4 June 2015 at https://www.tga.gov.au/scheduling-decision-interim/reasons-scheduling-delegates-interim-decision-and-invitation-further-comment-acms-june-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.

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

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

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

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

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

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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 #14)

1.1 CONTRACEPTIVE PILL

Scheduling proposal

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

- To down-schedule oral contraceptive pills from Schedule 4 to Schedule 3. The Schedule 3 entry would be on condition that the pharmacist conducts a questionnaire about family history of heart problems, hypertension and stroke and that either an in-house blood pressure test is conducted or results from a recent blood pressure test is provided to ensure suitability of the substances. Finally the proposal recommends that the supply of the substances be limited to 3 to 6 months.

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

Substance summary

The applicant provided the following information on the substance:

Oral contraceptives are divided into two main types, progestin only and combined. Progestin-only contain synthetic progestogens (progestin), including norethindrone, ethynodiol diacetate, levenorgestrol, desogestrol and lynestronol. Combined pills contain a mixture of synthetic oestrogens and progestins, including those listed above in addition to ethinyl oestradiol and mestranol. Combined pills work by suppressing the release of gonadotropins from the pituitary gland, including follicle stimulating hormone (FSH) and luteinizing hormone (LH).

The reduction in these hormones inhibits both follicular development and ovulation, which is the primary mechanism of action of the medication. This also sees a decrease in the water content of cervical mucus, increasing its viscosity and inhibiting sperm movement. Other impacts include a thinning of endometrial lining. Uses of the contraceptive pill, aside from the obvious contraceptive effects include clearer skin, reduced risk of ovarian cancer and reduced severity of periods. Toxicity is rare but side effects can be seen on those with underlying conditions, including heart conditions, high blood pressure and those with a history of stroke. Hormonal imbalances can also cause mood swings and depression.

Scheduling status

A number of contraceptive substances are listed in Schedule 4 with the exception of LEVONORGESTREL for emergency post-coital contraception, which is included in Schedule 3.

Cyproterone, gestodene, desogestrel, drospirenone, ethinyloestradiol, levonorgestrel, mestranol and mifepristone are all listed in Schedule 4.

Scheduling history

Oestradiol

National Health and Medical Research Council Poisons Schedule (Standing) Committee – August 1979

Elanco Product Company proposed the scheduling of its product Compudose – a silicone rubber implant containing the natural hormone oestradiol-17 beta designed to improve growth rate and feed efficiency in beef cattle by controlled release over 200 to 400 days. Outcome: New Entry: OESTRADIOL-17 beta in silicone rubber controlled release implants for use in cattle.

National Health and Medical Research Council Poisons Schedule (Standing) Committee – March 1980

Committee noted that the Standing Committee and Agriculture had established a working party to review the use of hormones in cattle production.

National Drugs and Poisons Schedule Committee – May 1996

The Committee considered correspondence from Elanco Animal Health in response to advice of the rescheduling of several oral veterinary products from Schedule 6 to Schedule 5. In view of the possibility that rescheduling may affect monitoring by other agencies it was agreed the proposal should be foreshadowed in the outcomes gazette from the meeting and comment sought on the implications of the proposal. The Committee further considered that Schedule 5 may be appropriate for some of these ear implant products. However, it was agreed that the issue required further attention in view of the current scheduling concerns in regard to testosterone, the toxicity of the products and the complexity of the drafting of appropriate schedule entries.

Desogestrel

National Health and Medical Research Council Poisons Schedule (Standing) Committee – February 1993

The Committee noted that ADEC had recommended approval for registration of desogestrel (Marvelon tablets-Organon) for use with ethinyloestradiol 30 mg, as a combined oral contraceptive preparation for the inhibition of ovulation. Decision: the Committee recommended Schedule 4. Recommendation: Schedule 4 – New Entry, DESOGESTREL.

Ethinyloestradiol – No scheduling history available.

Norethisterone – No scheduling history available.

Levonorgestrel

National Health and Medical Research Council Poisons Schedule (Standing) Committee – November 1998

The Committee noted that in some states weight lifters were abusing sex hormones and anabolic steroids used for humans and/or animals. It was recommended that all such products available on the Australian market, either for humans or animals, be placed in Schedule 4 with an individual entry. The Committee recommended that various hormones listed in the National Therapeutic Goods Register be given individual entries in Schedule 4 – including levonorgestrel.

National Drugs and Poisons Schedule Committee – March 2003

A proposal was put forward to the Committee to consider releasing NDPSC decisions and outcomes of considerations as ‘resolutions’ within a week of the meeting. The Committee agreed, given the considerable interest on the scheduling consideration of levonorgestrel at this meeting, to publicly

release a document immediately containing the details of the decision and a brief statement outlining the reasons. This document was to be provided to members for information.

National Drugs and Poisons Schedule Committee – October 2003

The Committee considered post-meeting submissions in relation to the June 2003 initial decision to reschedule levonorgestrel in a two-tablet pack, of 0.75 mg per tablet, for emergency post-coital contraception from Schedule 4 to Schedule 3 of the SUSDP. The Committee confirmed the view taken at the June 2003 Meeting that an Appendix H listing for levonorgestrel was not warranted due to insufficient information available to support an informed decision about advertising. Overall the Committee reiterated that levonorgestrel EC in a dose of 2 x 0.75 mg tablets clearly conforms to the criteria for a Schedule 3 medicine both in terms of the characteristics of the drug and the indications for use.

National Drugs and Poisons Schedule Committee – June 2004

The Committee considered the implementation of scheduling amendments subject to post-meeting submissions. It was proposed that S4 to S3 rescheduling be a two part decision-making process where confirmation is contingent on the Committee being satisfied with the pharmacy educational material. It was also proposed that the first decision be a qualified decision based upon the sponsor's pharmacists' educational/training plan and subject to seeing the final educational material.

National Drugs and Poisons Schedule Committee – October 2004

Prochlorperazine – supply with Levonorgestrel: The Committee considered the need to make provision for the availability of medicines for the treatment of nausea associated with emergency contraception (EC) and, in particular, in association with the supply of levonorgestrel EC. The Committee agreed that if professional bodies or pharmaceutical companies regarded nausea/vomiting associated with the use of levonorgestrel EC as a significant problem, then they could raise the associated scheduling issues with the Committee. To date, no concerns had been raised.

Levonorgestrel – request for advice: The Committee considered correspondence from the Minister for Health and Ageing, the Hon Tony Abbott MP, seeking advice on whether pharmacists are appropriately supplying Postinor-2 as a "Pharmacist Only Medicine". The Committee was of a view that Postinor-2 was generally being supplied in accordance with information and considerations set out in the PSA protocol.

National Drugs and Poisons Schedule Committee – February 2005

The Committee considered comments from Schering Pty Limited, the distributor of Postinor-2 (levonorgestrel), in response to the issues raised at the June 2004 NDPSC meeting relating to the website created by the distributor. The Committee reaffirmed its view that the distributor had met its obligation and commitments made in its scheduling application with regard to the appropriate supply of Postinor-2 as an S3 medicine. It was further noted that the distributor had satisfactorily addressed the issues raised by the jurisdictions in relation to the Pharmacist-Only section of the Postinor-2 website.

National Drugs and Poisons Schedule Committee – February 2006

The Committee considered a proposal to amend the Schedule 3 entry for levonorgestrel to accommodate a single 1.5 mg tablet. The Committee agreed to amend the Schedule 3 entry for levonorgestrel for emergency post-coital contraception without specifying a particular dose regime.

National Drugs and Poisons Schedule Committee – June 2006

Unharmonised Medicines in the AusNZ Scheduling Database: The Committee considered the recommendations of the June 2006 TTHWP meeting. The Committee endorsed the TTHWP recommendations and agreed that substances for consideration of the NDPSC should be included on the agenda and pre-meeting gazette notice of the October 2006 NDPSC meeting. Similarly, the Committee agreed that recommendations to New Zealand should be referred to the MCC consideration at its next meeting.

Cyproterone Acetate

National Health and Medical Research Council Poisons Schedule (Standing) Committee – May 1987

The Committee noted that general marketing approval had been granted for cyproterone acetate for treatment of moderate to severe androgenisation in females (including hirsutism), reduction of excessive sex drive in males with deviations and idiopathic precocious puberty. A Schedule 4 entry for cyproterone was recommended.

Gestodene

National Drugs and Poisons Schedule Committee – April 1994

The Committee noted that ADEC had recommended approval for the registration of gestodene for the prevention of pregnancy, subject to certain conditions being met. The Committee recommended a Schedule 4 entry.

Drospirenone

National Drugs and Poisons Schedule Committee – August 2001

The Australian Drug Evaluating Committee (ADEC) recommended that Yasmin tablets, containing drospirenone and ethinyloestradiol in a fixed combination, be approved for use as an oral contraceptive. The Committee agreed to include drospirenone in Schedule 4.Text

Pre-meeting public submissions

Twelve submissions were received.

Four submissions supported the proposal on the basis that the down scheduling would:

- Reduce the number of doctor visits and thereby help reduce the financial burden on the patients;
- Allow for repeat supply via pharmacy. However, the contributor considered that the initial take up of oral contraception should remain in the domain of general practice or other clinician;
- Allow pharmacists to provide these medications over the counter. However, the contributor considered that this should only be permitted for up to three to five years at a time, per client, before a prescription must be reissued by a GP or family planning clinician.
- The substances meet the scheduling factors for Schedule 3, however the substances should be prescribed by a GP in the first instance and legislation would need to be amended to allow trained pharmacists to authorise continuation of the substances under specified conditions.

Eight submissions opposed the proposal on the basis that:

- There is an increased risk of diabetes associated with the use of oral contraceptive pills;

- Doctor scripts last 12 months thereby minimising the number of doctor visits;
- No tests have been approved for oral contraceptive pills for use by women under 17.5 years;
- Currently, the systems and procedures for pharmacists to appropriately counsel, initiate and supply oral contraceptives to patients in community pharmacy settings are inadequate;
- The use of a checklist as proposed by the applicant is not considered an adequate alternative to comprehensive medical evaluations, factoring all aspects of a woman's medical history and current health status that should occur prior to initiation of a contraceptive and during continuing use;
- Oral contraceptives may be supplied by pharmacists for cycle control (of irregular periods), which poses a health risk to women;
- Cost to Australian women and the Australian Government would be higher; and
- Oral contraceptives are not a "one size fits all' medicine.

ACMS advice to the delegate

The ACMS recommended that the current scheduling of oestradiol, desogestrel, ethinyloestradiol, norethisterone, levonorgestrel, cyproterone, gestodene, drospirenone, mestranol, medroxyprogesterone, oestrogens and progestogens 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 f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the recommendation comprised the following:

- Risks included the potential increase in oral contraceptive pill use when alternative, safer, more effective and more appropriate contraceptive methods are available, potential exposure of females to oral contraceptives for up to 30 years, and that pharmacists are not currently trained to conduct physical examinations of patients. Risks to users depend on the stage of treatment – the first 3-12 months are highest risk, and may require titration and changes in treatment.
- Oral contraceptives have other uses (in addition to birth control). Concerns were expressed that women may falsely declare the indication for the purpose of supply, compromising monitoring.
- Use of oral contraceptives may potentially mask serious health issues. Chronic use is associated with adverse effects. The incidence and severity varies, and some may be detected by routine screening (e.g. cancer), while others require the patient to present for symptoms (migraine, thrombosis). There is a significant increase in the risk of stroke if the patient is a smoker.
- Inappropriate use of oral contraceptive pills, particularly to treat painful heavy bleeding, could increase future fertility problems and control symptoms for patients with undiagnosed endometrial hyperplasia, endometrial polyps or endometrial carcinoma.

Delegate's interim decision

The delegate's interim decision is that the current scheduling of oestradiol, desogestrel, ethinyloestradiol, norethisterone, levonorgestrel, cyproterone, gestodene, drospirenone, mestranol, medroxyprogesterone, oestrogens and progestogens 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; and f) any other matters that the Secretary considers necessary to protect public health.

The reasons for the recommendation comprised the following:

- Risks included the potential increase in oral contraceptive pill use when alternative, safer, more effective and more appropriate contraceptive methods are available, potential exposure of females to oral contraceptives for up to 30 years, and that pharmacists are not currently trained to conduct physical examinations of patients. Risks to users depend on the stage of treatment – the first 3-12 months are highest risk, and may require titration and changes in treatment.
- Oral contraceptives have other uses (in addition to birth control). Concerns were expressed that women may falsely declare the indication for the purpose of supply, compromising monitoring.
- Use of oral contraceptives may potentially mask serious health issues. Chronic use is associated with adverse effects. The incidence and severity varies, and some may be detected by routine screening (e.g. cancer), while others require the patient to present for symptoms (migraine, thrombosis). There is a significant increase in the risk of stroke if the patient is a smoker.
- Inappropriate use of oral contraceptive pills, particularly to treat painful heavy bleeding, could increase future fertility problems and control symptoms for patients with undiagnosed endometrial hyperplasia, endometrial polyps or endometrial carcinoma.
- The use of a checklist as proposed by the applicant is not considered an adequate alternative to comprehensive medical evaluations, factoring all aspects of a woman's medical history and current.

Delegate's considerations

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- Public submissions received;
- ACMS advice;
- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors[1];
- Other relevant information.

Public submissions on the interim decision

No public submissions were received.

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

Delegate's final decision

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

1.2 HYDROCOTISONE/ACICLOVIR

Scheduling proposal

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

- To amend the Schedule 3 entry for hydrocortisone 1 per cent (1%w/w) when compounded with aciclovir 5% w/w or less in primary packs of not more than 2 g for dermal use in adults and adolescents (12 years of age and older); and
- To include aciclovir in Appendix H.

Substance summary

The applicant has provided the following information regarding the substance:

- Aciclovir is a synthetic nucleoside analogue active, which is an antiviral agent highly active in vitro against HSV-1 and HSV-2.
- Hydrocortisone is the main glucocorticoid secreted by the adrenal cortex. Pharmacologically, it is a mild corticosteroid that exerts a range of immunomodulatory effects; when applied topically, it reduces skin inflammation.

Scheduling status

Hydrocortisone compounded with aciclovir is not specifically scheduled.

ACICLOVIR is currently listed in Schedule 4.

Schedule 4

ACICLOVIR **except** in preparations containing 5 per cent or less of aciclovir for the treatment of herpes labialis in packs containing 10 g or less.

HYDROCORTISONE and HYDROCORTISONE ACETATE is currently listed in Schedules 4, 3 and 2.

Schedule 4

HYDROCORTISONE:

(a) For human use except when included in Schedule 2 or 3; or

(b) For the treatment of animals.

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 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) (i) in undivided preparations, in packs of 35 g or less; or

ii) (ii) in packs containing 12 or less suppositories.

HYDROCORTISONE is also included under the entry Hydrocortisone in Appendix H and in Appendix F with the following statements.

APPENDIX F

Poisons	Warning statements	Safety direction
Hydrocortisone · For dermal use when included in Schedule 2 or 3	38	CAUTION – Do not use for children under 2 years old unless a doctor has told you to.
	72	Do not use in the eyes.
	73	Do not use for acne.
	74	Do not use under waterproof bandages unless a doctor has told you to.
	75	Do not use for more than 7 days unless a doctor has told you to.
· For topical rectal use when included in Schedule 2 or 3	38	CAUTION – Do not use for children under 2 years old unless a doctor has told you to.
	75	Do not use for more than 7 days unless a doctor has told you to.

Scheduling history

Hydrocortisone

National Health and Medical Research Poisons (Standing) Committee May 1981

The Committee confirmed that the scheduling of hydrocortisone remained appropriate, i.e. in Schedule 4. The PSC confirmed this position again in February 1982.

National Health and Medical Research Poisons (Standing) Committee: August 1985

The Committee decided to reschedule hydrocortisone to Schedule 3 for 0.5% or less of hydrocortisone when present as the only therapeutically active substance.

National Health and Medical Research Poisons (Standing) Committee: November 1988

The Committee decided not to reschedule 1% or less of hydrocortisone to Schedule 3 on the basis of advice from the then Australian Drug Evaluation Committee that the product in question was pharmacologically more active than other brands of 1% hydrocortisone cream in causing vasoconstriction.

National Drugs and Poisons Schedule Committee: May 1995

The Committee considered an application to reschedule rectal preparations containing hydrocortisone and cinchocaine from Schedule 4 to Schedule 3. In-principle support was given to the scheduling proposal, pending further advice. A decision was subsequently made out–of-session to reschedule hydrocortisone and cinchocaine topical preparations for rectal use, from Schedule 4 to Schedule 3.

National Drugs and Poisons Schedule Committee: February 1996

The Committee confirmed that the intent of the May 1995 decision was to allow preparations containing 0.5% or less of hydrocortisone (alone or in combination with cinchocaine) to be available for rectal use (internal and externally) in both the ointment and suppository form, as Schedule 3.

National Drugs and Poisons Schedule Committee: August 1998

The Committee decided not to list hydrocortisone and cinchocaine rectal preparations in Appendix H. This decision was primarily on the grounds that the incidence of misdiagnosis of fungal infections may be increased.

National Drugs and Poisons Schedule Committee: February 1999

The Committee decided to reschedule hydrocortisone and hydrocortisone acetate for dermal use containing 0.5% or less of hydrocortisone in packs containing 30 g or less of such preparation with no other therapeutically active substance or an antifungal as the only other therapeutically active substance, to Schedule 2. The Schedule 3 entry was also amended to include a specific reference to suppositories.

National Drugs and Poisons Schedule Committee: May 1999

The Committee decided to include hydrocortisone in preparations for rectal use in Appendix H.

National Drugs and Poisons Schedule Committee: November 2001

The Committee considered the scheduling of products containing hydrocortisone and hydrocortisone acetate, with astringents as active ingredients, for rectal use. The Committee decided to amend the scheduling of hydrocortisone and hydrocortisone acetate to exempt unscheduled astringents and restore the product to Schedule 3. The NDPSC considered that the presence of aluminium acetate and zinc oxide the product, whilst therapeutically active, were there primarily for their astringent effects rather than for systemic effects.

National Drugs and Poisons Schedule Committee: June 2002

The Committee decided not to include hydrocortisone for dermal use in Appendix H. However, in response to post-meeting comment, the October 2002 they reconsidered this scheduling proposal and decided to include hydrocortisone for dermal use in Appendix H.

National Drugs and Poisons Schedule Committee: October 2005

The Committee considered an application for the rescheduling of hydrocortisone acetate (in combination with an anaesthetic) for rectal use from Schedule 3 to Schedule 2. The NDPSC decided that the scheduling of hydrocortisone remained appropriate.

National Drugs and Poisons Schedule Committee: June 2006

The Committee reconsidered an application to reschedule hydrocortisone acetate (in combination with an anaesthetic) for rectal use. The Committee decided that the current scheduling of hydrocortisone and hydrocortisone acetate remained appropriate.

National Drugs and Poisons Schedule Committee: February 2007

The Committee decided to reschedule hydrocortisone 0.5% in combination with an anaesthetic for rectal use from Schedule 3 to Schedule 2 to harmonise with New Zealand.

National Drugs and Poisons Schedule Committee: June 2007

The Committee decided to amend the Schedule 2 and 3 entries to only capture human use. This was a result of a decision to vary the February 2007 decision to capture all veterinary use in Schedule 4.

National Drugs and Poisons Schedule Committee: October 2007

The Committee decided to correct the wording of the Schedule 2 entry for hydrocortisone to specify human rectal use, in line with the decision of the June 2007 meeting.

National Drugs and Poisons Schedule Committee: June 2008

The Committee decided to include hydrocortisone in Appendix F, Part 3, with warning statements 38, 72, 73, 74 and 75 (for dermal use when included in Schedule 2 or 3), and warning statements 38 & 75 (for topical rectal use when included in Schedule 2 or 3).

Advisory Committee on Medicines Scheduling: March 2014

The Committee considered a proposal to reschedule preparations containing 1 per cent or less of hydrocortisone and hydrocortisone acetate when combined with antifungal substances for dermal use from Schedule 3 to Schedule 2. The Committee decided that the current scheduling of hydrocortisone and hydrocortisone acetate remains appropriate.

Aciclovir

National Health and Medical Research Council Poisons Schedule (Standing) Committee: August 1984

The Committee agreed that cefoperazone, ciclacillin and acyclovir should be scheduled in Schedule4.

National Health and Medical Research Council Poisons Schedule (Standing) Committee: May 1993

The Committee considered a request from Wellcome Australia Limited to consider an application for a change of topical acyclovir scheduling from Schedule 4 to Schedule 3, for an OTC indication, without the product or indication having already been approved by the TGA. The Committee declined to consider the application for a drug product which it believed should be evaluated through the appropriate channels.

National Drugs and Poisons Schedule Committee: May 1996

The Committee considered a submission from GlaxoWellcome in support of a change from Schedule 4 to Schedule 2 for acyclovir cold sore cream (5% w/w, 2g). The Committee noted that when the sponsor had applied for ADEC approval for the indication for "the treatment of herpes simplex viral infection of the lips" that Committee had agreed to the indication. The Committee agreed to waive the “2 year rule” in view of the fact that acyclovir has been used for many years as an eye ointment in Australia and had been available overseas for many years as a cold sore non-prescription preparation, without giving rise to public health concerns.

National Drugs and Poisons Schedule Committee: August 1997

The Committee noted advice from the Proprietary Medicines Association of Australia that the TGA Approved Name for acyclovir had been changed to aciclovir.

Pre-meeting public submissions

Three submissions were received which supported the proposal on the basis that there is:

- no evidence that a departure from the existing scheduling policy is warranted for the combination of dermal hydrocortisone and aciclovir and that a Schedule 3 entry is appropriate; and
- sound justification for the combination of hydrocortisone plus aciclovir to be covered by the existing Appendix H entry for hydrocortisone.

ACMS advice to the delegate

The ACMS recommended that the Schedule 3 entry for hydrocortisone be amended to allow for 1 per cent or less of hydrocortisone when compounded with aciclovir 5% w/w or less in primary packs of not more than 2 g for dermal use in adults and adolescents (12 years of age and older).

The ACMS recommended an implementation date of 1 October 2015.

Regarding the proposal to include aciclovir in Appendix H, the ACMS recommended that it is not necessary to create a new Appendix H entry for aciclovir.

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

The reasons for the recommendation comprised the following:

- Both hydrocortisone and aciclovir at the proposed topical concentrations have been individually available at Schedule 3 or exempt from scheduling for many years without any significant public health concerns. Data indicate a risk:benefit ratio consistent with a Schedule 3 listing for combination preparations for topical treatment of herpes labialis.
- Early access for consumers to this combination product from a pharmacist for recurrent cold sores is likely to be beneficial in reducing progression of symptoms and safe. Inclusion in Schedule 3 will mean that the product is accessed in consultation with a pharmacist for advice, education and checking appropriate use.
- Herpes labialis can be identified by the consumer. Topical aciclovir has been exempt from scheduling for over a decade without signals indicating significant risk at this scheduling level. Mandatory pharmacist assessment at the time of sale will reduce risk where hydrocortisone is combined with aciclovir for the same indication and ensures the patient will have sufficient information about the recommended duration of use.
- Toxicity is minimal at the proposed strength and duration of use.
- Both ingredients have been available without prescription (at the same strengths) for more than 10 years as dermal preparations with good safety profiles and large consumer experience. It is likely that risks would be similarly low in the combination product.
- Risks are minimised by the small pack size (2 g tube) and dermal application.
- Combination aciclovir 5% and hydrocortisone 1% dermal cream in packs of 2 g will be used for same indication and same route of administration, dose and timing (frequency, duration) as aciclovir 5% cream.
- The applicant's proposed labelling and Consumer Medicine Information promote appropriate use and health education.
- Very limited abuse potential – there is the same potential for possible off-label misuse (genital herpes) as for aciclovir 5% available on general sale.
- The combination product may be more effective in early treatment of cold sores, reducing progression rates and lesion area. Improving access to early treatment via a pharmacist reduces consumer treatment burden, and has the potential to improve self-management health outcomes. Allowing advertising to consumers would improve consumer awareness of timely access to the combination.

Delegate's interim decision

The interim decision is that:

- the Schedule 3 entry for hydrocortisone be amended to additionally allow for 1 per cent or less of hydrocortisone when compounded with aciclovir 5% w/w or less in primary packs of not more than 2 g for dermal use in adults and adolescents (12 years of age and older).
- that it is not necessary to create a new Appendix H entry for aciclovir.

Reason for the Schedule 3 decision is:

- the reasons that ACMS have noted above and included below in the table.

Reasons for the Appendix H decision are:

- The proposed product contains 1% hydrocortisone and aciclovir at or below 5% in a pack of 2g or less for the treatment of herpes labialis. Therefore the aciclovir component of the new product continues to be within the existing limit (5% or less, 10g or less) for exemption from the requirements of the Poisons Standard. Products containing ingredients that are exempt from these requirements may be advertised to the public in accordance with the advertising requirements.
- Hydrocortisone is included in Appendix H without qualification and any product containing hydrocortisone when included in Schedule 3 (amended as proposed) may therefore be advertised to the public in accordance with the advertising requirements.
- Accordingly, no additional change to the Poisons Standard is required to permit the advertising of the combination hydrocortisone/aciclovir product to the public.

Delegate's considerations

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- Public submissions received;
- ACMS advice;
- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors[2];
- Other relevant information.

Public submissions on the interim decision

No public submissions were received.

Delegate's final decision

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

The implementation date is 1 October 2015.

Schedule entry

Schedule 3 – Amendment

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

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

(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 dermal use, in packs containing 2 g or less of such preparations, containing no other therapeutically active constituent other than aciclovir (5% w/w or less) in adults and adolescents (12 years of age and older); or

(c) 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.

1.3 DIPHENOXYLATE

Scheduling proposal

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

· To down schedule diphenoxylate 2.5mg or less in packs of 8 or less dosage units, when combined with a quantity of atropine sulphate equivalent to at least 1 per cent of the dose of diphenoxylate from Schedule 3 to Schedule2; and

· To remove diphenoxylate from Appendix H.

Substance summary

The applicant has provided the following information regarding the substance:

· Diphenoxylate is chemically related to pethidine and acts by slowing intestinal motility and peristalsis allowing consolidation of intestinal content and protraction of its transit time, and extraction of moisture.

· Diphenoxylate is essentially devoid of 'morphine type subjective effects' at therapeutic doses. The potential for abuse appears to be limited.

· Diphenoxylate hydrochloride is well absorbed from the gastrointestinal tract and extensively metabolised in the liver to diphenoxin.

· Atropine sulphate is included in the formulation as an anti-abusing agent contributing to the safe use of the product and is sub-therapeutic at 0.025 mg.

Atropine is an antimuscarinic agent which competitively antagonizes acetylcholine at postganglionic nerve endings, thus affecting receptors of the exocrine glands, smooth muscle, cardiac muscle and the central nervous system.

Scheduling status

DIPHENOXYLATE is currently listed in Schedules 8, 4 and 3.

Schedule 8

DIPHENOXYLATE except when included in Schedule 3 or 4.

Schedule 4

DIPHENOXYLATE in preparations containing, per dosage unit, 2.5 mg or less of diphenoxylate and a quantity of atropine sulfate equivalent to at least 1 per cent of the dose of diphenoxylate except when included in Schedule 3.

Schedule 3

DIPHENOXYLATE in packs of 8 or less dosage units, each dosage unit containing 2.5 mg or less of diphenoxylate and a quantity of atropine sulfate equivalent to at least 1 percent of the dose of diphenoxylate.

Diphenoxylate is also included under the entry Diphenoxylate in Appendix H and F with the following statements:

APPENDIX F

Poisons	Warning statements	Safety direction
Diphenoxylate when included in Schedule 3	39 or	This medication may cause drowsiness. If affected do not drive a vehicle or operate machinery. Avoid alcohol.
	40	This medication may cause drowsiness and may increase the effects of alcohol. If affected do not operate a motor vehicle or operate machinery.
	41	Do not give to children under 12 years of age. Do not use beyond 48 hours or in pregnancy or lactation except on doctor's advice.

Scheduling history

National Health and Medical Research Council Poisons Scheduling Sub-committee (the Committee): November 1963

The Committee recommended that diphenoxylate in preparations containing 2.5 mg or less of diphenoxylate and not less than 25 micrograms of atropine (sulphate) per dosage unit be placed in Schedule 2.

National Health and Medical Research Council Poisons Scheduling Sub-committee: July 1964

Lomotil – The Public Health Advisory Committee requested the Committee to give an opinion as to whether or not there should be an upper limit specified for the amount of atropine sulphate which is required to be present in combination with the diphenoxylate. Information was to be sort from W.H.O.

National Health and Medical Research Council Poisons Scheduling Sub-committee: September 1964

Information received from W.H.O.: In setting the lower limit on the atropine the Narcotics Control Authorities were only interested in preventing abuse, not poisoning. The Committee advised the Public Health Advisory Committee that the amount of atropine which may be present in any schedule 2 preparation must be not greater than 0.25%.

National Health and Medical Research Council Poisons Scheduling Sub-committee: January 1965

Victoria raised concerns around indiscriminate use of preparations containing diphenoxylate which may result in intensification of bowel blockage when partial blockage was present plus upset blood chemistry. The Committee recommended that diphenoxylate remain in Schedule 2.

National Health and Medical Research Council Poisons Scheduling Sub-committee: December 1965

At the request of GD Searle and Co Ltd, the scheduling of the preparation of diphenoxylate hydrochloride with atropine sulphate (Lomotil) was reviewed. GD Searle had advised that Victoria had placed the preparation in Schedule 4. The Committee recommended that the entry in Schedule 2 regarding diphenoxylate be deleted and a similar entry be made in Schedule 4 to read: "Diphenoxylate is preparations containing 2.5 mg or less of diphenoxylate and note less than 25 micrograms of atropine sulphate per dosage units".

National Drugs and Poisons Schedule Committee: February 1998

The Committee considered a submission to down-schedule from Schedule 4 to Schedule 2 of packs of eight Lomotil® tablets (containing 2.5 mg of diphenoxylate and atropine sulfate 25 µg). The Committee decide that there was to be no change to the Schedule 4 entry for diphenoxylate.

National Drugs and Poisons Schedule Committee: May 1998

The Committee considered a request from Searle for reconsideration of the decision made in February 1998 meeting. The Committee did not support the rescheduling of Lomotil in small pack sizes to Schedule 2, but agreed that Schedule 3 would be the more appropriate classification.

National Drugs and Poisons Schedule Committee: August 1998

The Committee considered correspondence from the Australian College of Paediatrics, and the Director of Paediatrics at Canberra Hospital requesting reconsideration of the May 1998 Meeting decision to include diphenoxylate and atropine tablets in Schedule 3. The Committee agreed that the decision of the May 1998 Meeting to include diphenoxylate and atropine tablets in Schedule 3 was appropriate.

National Drugs and Poisons Schedule Committee: November 1998

The Committee considered a submission from Searle requesting the inclusion of diphenoxylate (as Lomotil) in Appendix H. The Committee was not convinced by the arguments in support of Schedule 3 advertising and decided that it should not be included in Appendix H.

National Drugs and Poisons Schedule Committee: February 1999

The Committee considered a submission from Searle requesting a reconsideration of the decision of the November 1998 Meeting that Lomotil® tablets (diphenoxylate 2.5 mg and atropine 0.025 mg) when included in Schedule 3 should not be permitted to be advertised. The Committee reaffirmed its previous decision – diphenoxylate should not be included in Appendix H.

National Drugs and Poisons Schedule Committee: May 2000

The Committee considered submissions from Searle requesting that diphenoxylate in combination with atropine be rescheduled from Schedule 3 to Schedule 2, or if that was not supported, be included in Appendix H. The Committee did not support the rescheduling of diphenoxylate from

Schedule 3 to Schedule 2, however, the proposal to include diphenoxylate in Appendix H was supported.

Pre-meeting public submissions

Two submissions were received. Both did not support the proposal as there is a risk of consumers incorrectly selecting diphenoxylate, particularly to treat diarrhoea in children or in pregnancy, and thus its use requires pharmacy intervention. One submission suggested removing the substance from Appendix H, as it carries a higher risk profile compared to other substances with similar indications.

ACMS advice to the delegate

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

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

The reasons for the recommendation comprised the following:

- Diphenoxylate carries a higher risk profile than other medications with similar indications. It can produce euphoria and other psychoactive effects in very high doses. In deliberate overuse, it is potentially habit-forming and can lead to significant tolerance and physical dependence if taken continuously for a protracted period.
- Like all anti-peristaltic agents, diphenoxylate may prolong / worsen diarrhoea associated with organisms that penetrate the intestinal mucosa.
- Diphenoxylate presents risks to patients with ulcerative colitis, as agents that inhibit motility have been reported to induce toxic megacolon.
- Diphenoxylate may interact with monoamine oxidase (MAO) inhibitors, potentially causing hypertensive crisis.
- Caution is required in patients with advanced hepatorenal disease, abnormal liver function, children aged under 12 years, the elderly, patients with other medical conditions, eg. diabetes, impaired renal or hepatic function, pregnancy and lactation.
- Risks also include adverse effects, as noted in the TGA's Database of Adverse Event Notifications (DAEN), the New Zealand Centre for Adverse Reactions Monitoring (CARM) database and the Product information (PI). OTC products containing diphenoxylate require a number of label warnings – the Required Advisory Statements for Medicines Labels (RASML) requires label warnings re drowsiness (and avoid alcohol), advice that treatment should not be continued beyond 48 hours, or in pregnancy or lactation, except on the advice of a doctor, and the contraindication "Do not give to children under 12 years of age".

Delegate's interim decision

The interim decision is that the current scheduling of diphenoxylate, including its Appendix H entry, remains appropriate.

Reason for the decision is:

- As indicated by ACMS in its recommendation above.

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

1.4 RANITIDINE

Scheduling proposal

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

- To exempt ranitidine from Schedule 2 when in divided preparations for oral use containing 300 mg or less of ranitidine per dosage unit in the manufacturer's original pack containing not more than 7 dosage units.

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

Substance summary

Ranitidine is a member of the class of histamine H2-receptor antagonists with antacid activity. Ranitidine is a competitive and reversible inhibitor of the action of histamine, released by enterochromaffin-like (ECL) cells, at the histamine H2-receptors on parietal cells in the stomach, thereby inhibiting the normal and meal-stimulated secretion of stomach acids. It is used in the management of dyspepsia, gastric ulcer and reflux oesophagitis.

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

Scheduling status

RANITIDINE is currently listed in Schedules 4 and 2.

Schedule 4

RANITIDINE except:

(a) when included in Schedule 2; or

(b) in divided preparations for oral use containing 150 mg or less of ranitidine per dosage unit when supplied in the manufacturer‘s original pack containing not more than 14 dosage units.

Schedule 2

RANITIDINE in preparations supplied in the manufacturer‘s original pack containing not more than 14 days’ supply except in divided preparations for oral use containing 150 mg or less of ranitidine per dosage unit in the manufacturer‘s original pack containing not more than 14 dosage units.

Scheduling history

Drugs and Poisons Schedule Standing Committee – November 1993

The Committee considered applications for rescheduling of small packs of H2-receptor antagonists (cimetidine, famotidine and ranitidine) from S4 to S3. The Committee supported this proposal.

National Drugs and Poisons Schedule Committee – August 1994

The Committee considered a submission from Glaxo Australia Pty Ltd to reschedule ranitidine 150 mg from Schedule 4 to Schedule 3 when indicated for the short term relief of heartburn and other symptoms of reflux oesophagitis, and supplied in packs containing 15 doses or less. The Committee decided to request:

· The Secretary to advise applicants to approach TGA (if they have not already done so) to have any proposed minor indications for OTC preparations approved by TGA before further consideration by Committee; and

· The Secretary to advise sponsors also of the preferred set of warning statements.

The Committee noted that the approved product indications for the use of ranitidine included "short-term symptomatic treatment of reflux oesophagitis unresponsive to conservative anti-reflux measures and simple drug therapies such as antacids". The Committee reaffirmed its original recommendation for the inclusion of ranitidine in Schedule 3 when in a pack containing not more than 14 days’ supply and when labelled with certain warning statements.

National Drugs and Poisons Schedule Committee – February 1996

The Committee noted that Australian Drub Evaluation Committee had recommended that approval should be given to the registration of ranitidine in preparations containing 75 mg of ranitidine per tablet for the symptomatic relief of heartburn, dyspepsia and hyperacidity.

National Drugs and Poisons Schedule Committee – February 1997

The Committee considered comment received in the post-meeting consultation period concerning the decision made at the November 1996 meeting relating to the removal of the dosage size and

formulation type from the Schedule 3 entries for cimetidine, famotidine, nizatidine and ranitidine. The Committee reaffirmed its decision.

National Drugs and Poisons Schedule Committee – August 1998

The Committee supported the inclusion of ranitidine in Appendix H.

National Drugs and Poisons Schedule Committee – May 1999

The Committee noted the recommendation from the Trans-Tasman Harmonisation Working Party that the SUSDP Schedule 4 and the Part 1 entries for the following drugs are harmonised: CIMETIDINE; FAMOTIDINE; NIZATIDINE; RANITIDINE.

National Drugs and Poisons Schedule Committee – November 1999

The committee noted that: The August 1999 Committee endorsed a recommendation from the Working Party that it remove the words 'as the only therapeutically active substance in preparations for oral use' from the S3 entries. With adoption of recommendations by the NZ MOH the S3 entries for these substances would be harmonised. The NDPSC supported the Working Party view that similar products should be available in both countries.

With regard to cimetidine, famotidine, nizatidine and ranitidine, the Committee accepted the findings of the AHMAC Committee in relation to matters mentioned in subsection 52E (1) of the Act, and decided that there should be no variation to the scheduling decision taken by AHMAC Committee.

National Drugs and Poisons Schedule Committee – February 2000

The Committee considered a request for advice from the OTC Medicines Evaluation Section in regard to the application of the NZ MOH Guidelines for OTC packs of the histamine-2 antagonists.

National Drugs and Poisons Schedule Committee – November 2000

The Committee supported a proposal to rescheduling of ranitidine from Schedule 3 to Schedule 2 with retention of the Appendix F warning statements, and consequential amendments to Schedule 3 and Appendix H.

National Drugs and Poisons Schedule Committee – February 2001

The Committee considered a proposal to include a Schedule 5 entry for ranitidine in the SUSDP, to accommodate the product. The Committee decided that as ranitidine was already included in Schedule 4 of the SUSDP, no further action was required.

National Drugs and Poisons Schedule Committee – June 2002

The Committee considered the proposal to exempt ranitidine from Warning Statements (WS) 68, 69 and 70. The Committee agreed to finalise the following foreshadowed amendments at the October 2002 meeting to: delete WS 35, 68 and 69 in Appendix F, Part 3 for cimetidine, famotidine, nizatidine and ranitidine and delete WS 70 in Appendix F, Part 3 for famotidine, nizatidine and ranitidine, but retain WS 70 for cimetidine. The Committee also decided to include a requirement for WS 96 in Appendix F, Part 3 for cimetidine, famotidine, nizatidine and ranitidine.

National Drugs and Poisons Schedule Committee – June 2002

The Committee considered the foreshadowed amendments to the Appendix F, Part 3 entries of the SUSDP for ranitidine, cimetidine, famotidine and nizatidine. The Committee agreed to amend the new WS 96 as proposed by MEC.

National Drugs and Poisons Schedule Committee – February 2005

The Committee noted advice from the Trans-Tasman Harmonisation Working Party that the scheduling for cimetidine, famotidine, nizatidine and ranitidine was almost "essentially harmonised". The Committee's foreshadowed decision was to be considered at the June 2005 meeting.

National Drugs and Poisons Schedule Committee – June 2005

The Committee considered amendments to the scheduling of cimetidine, ethyl chloride, famotidine, nizatidine, prilocaine, ranitidine and silver sulfadiazine to achieve harmonisation with New Zealand. The Committee agreed to the foreshadowed amendments to the scheduling of the H2 antagonists, (cimetidine, famotidine, nizatidine and ranitidine) and also the scheduling for prilocaine and ethyl chloride to harmonise with New Zealand.

National Drugs and Poisons Schedule Committee – February 2007

The Committee considered a proposal to reschedule ranitidine from Schedule 2 to exempt from scheduling for ranitidine 150 mg, with a maximum dose of 300 mg/day, for the effective long lasting relief of heartburn and acid indigestion in packs containing no more than 7 days' supply. The Committee agreed to amend the scheduling of ranitidine when sold in solid dosage forms in manufacturer's original pack containing not more than 7 day's supply with a maximum dose of 300 mg per day from Schedule 2 to exempt from scheduling. The Committee agreed to refer the matter to the Drafting Advisory Panel to fine tune the wording of the schedule entries.

National Drugs and Poisons Schedule Committee – June 2007

The Committee considered post-Meeting comment received in response to the February 2007 NDPSC Meeting decision on the scheduling of ranitidine. The Committee agreed to vary the February 2007 NDPSC decision to exempt from scheduling ranitidine when supplied as divided preparations for oral use containing 150 mg or less of ranitidine per dosage unit in the manufacturer's original pack, by removing the reference to 'days' supply' from the exemption and including reference to not more than 14 dosage units.

Pre-meeting public submissions

Three submissions were received. All opposed the proposal on the basis that there was a risk of inappropriate treatment masking underlying disease.

ACMS advice to the delegate

The ACMS recommended that ranitidine be exempted from Schedule 2 when in divided preparations for oral use containing 300 mg or less of ranitidine per dosage unit in the manufacturer's original pack containing not more than seven dosage units.

The ACMS recommended an implementation date of 1 October 2015.

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:

- Both the 300 mg and 150 mg ranitidine products are indicated for relief of symptoms of gastro-oesophageal reflux. The 7 x 300 mg tablet packs and 14 x 150 mg tablet packs each contain the same total quantity of ranitidine – both packs would provide seven days' supply at the maximum daily dose. Once daily dosing (with 300 mg tablets) could be seen as a benefit over the twice daily dosing which may be required for efficacy with the 150 mg tablets.
- Consumers are more likely to seek medical aid due to perceived inefficacy of a product marketed as being stronger.
- The 300 mg dosage unit provides an easier to access dosage form of a dose that is also possible with the currently unscheduled medication, albeit one that is not recommended (for all users) by the pack instructions.

Delegate's interim decision

The delegate's interim decision is that ranitidine be exempted from Schedule 2 when in divided preparations for oral use containing 300 mg or less of ranitidine per dosage unit in the manufacturer's original pack containing not more than seven dosage units.

The proposed implementation date is 1 October 2015.

The reasons for the recommendation comprised the following:

- Both the 300 mg and 150 mg ranitidine products are indicated for relief of symptoms of gastro-oesophageal reflux. The 7 x 300 product has the same quantity of Ranitidine as the currently exempted 14 x 150mg packs– both packs would still only provide seven days' supply at the maximum daily dose. Once daily dosing (with 300 mg tablets) could be seen as a benefit over the twice daily dosing which may be required for efficacy with the 150 mg tablets.
- Consumers are more likely to seek medical aid due to perceived inefficacy of a product marketed as being stronger.
- The 300 mg dosage unit provides an easier to access dosage form of a dose that is also possible with the currently unscheduled medication, albeit one that is not recommended (for all users) by the pack instructions.

Delegate's considerations

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- Public submissions received;
- ACMS advice;
- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors[4];

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

· Other relevant information.

Public submissions on the interim decision

No public submissions were received.

Delegate's final decision

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

The implementation date is 1 October 2015.

Schedule entry

Schedule 4 – Amendment

RANITIDINE except:

(a) when included in Schedule 2; or

(b) in divided preparations for oral use containing 150 mg or less of ranitidine per dosage unit in the manufacturer's original pack containing not more than 14 dosage units; or

(c) in divided preparations for oral use containing 300 mg or less of ranitidine per dosage unit in the manufacturer's original pack containing not more than 7 dosage units.

Schedule 2 – Amendment

RANITIDINE in preparations supplied in the manufacturer's original pack containing not more than 14 days' supply except:

(a) in divided preparations for oral use containing 150 mg or less of ranitidine per dosage unit in the manufacturer's original pack containing not more than 14 dosage units; or

(b) in divided preparations for oral use containing 300 mg or less of ranitidine per dosage unit in the manufacturer's original pack containing not more than 7 dosage units.

1.5 ESOMEPRAZOLE

Scheduling proposal

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

· To create a new entry in Appendix H for 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 (GORD), in packs containing not more than 14 days' supply.

Substance summary

Esomeprazole magnesium trihydrate is a proton pump inhibitor used for the relief of heartburn and other symptom of gastro-oesophageal reflux disease.

Scheduling status

ESOMEPRAZOLE is currently listed in Schedules 4 and 3

Schedule 4

ESOMEPRAZOLE except when included in Schedule 3

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.

Scheduling history

National Drugs and Poisons Schedule Committee: November 2000

New Zealand Ministry of Health requested the Committee to 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 Committee supported harmonisation and included esomeprazole in Schedule 4.

Omeprazole

National Drugs and Poisons Schedule Committee: May 1989

Omeprazole was considered by the Committee as the first in a new class of drug that was useful for the treatment of duodenal ulcers, reflux and Zollinger-Ellison syndrome. The committee recommended it be entered under Schedule 4. It was then reconsidered in November 2001 for veterinary use, which was captured by its Schedule 4 entry.

National Drugs and Poisons Schedule Committee: February 2010

Omeprazole and other Proton Pump Inhibitors (PPIs) (pantoprazole and lansoprazole) were considered by the Committee for a Schedule 3 entry. The committee decided to create a new Schedule 3 entry for omeprazole in oral preparations containing 20 mg or less per dosage unit of omeprazole for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 14 days of supply.

Pre-meeting public submissions

Five public submissions were received.

All the submissions supported the proposal and two were of the opinion that, if this proposal was supported, then all commercially available PPIs available should be considered for Appendix H given that they have similar safety and efficacy profiles.

One submission, an independent report on the proposal (paid for by the applicant), supported the proposal on the basis that there is a public health and cost benefit, and that there is currently a low level of consumer awareness of the availability of non-prescription PPIs that offer safe and effective therapies.

ACMS advice to the delegate

The ACMS recommended that a new entry be created in Appendix H for 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 (GORD), in packs containing not more than 14 days' supply.

The ACMS recommended an implementation date of 1 October 2015.

The matters under subsection 52E (1) of the Therapeutic Goods Act 1989 considered relevant by the Committee included: a) the risks and benefits of the use of the substance; b) the purposes for which a substance is to be used and the extent of use of the substance; d) the dosage, formulation, labelling, packaging and presentation of the 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.
- Gastro-oesophageal reflux disease is a common condition. Increasing public awareness of the availability of a Schedule 3 Proton Pump Inhibitor in Pharmacy may have public health benefits through making consumers aware of more effective treatment options. Consumers may be more likely to seek advice from a pharmacist about the most appropriate treatment option.
- The Schedule 3 pack size, 14 days' supply, minimises the risk of inappropriate use. The RASML (Required Advisory Statements for Medicine Labels) warning statements help ensure appropriate use of the product.
- Other less effective treatments for the symptoms of gastro oesophageal reflux disease are advertised to consumers.

The ACMS also recommended:

(a) consideration of other PPIs being listed in Appendix H, based on the quality of evidence included in this proposal; and

(b) review of the scheduling of PPIs.

Delegate's interim decision

The delegate's interim decision is that a new entry be created in Appendix H for esomeprazole.

Reasons for the decision are:

- Esomeprazole is a safe and effective first line treatment for consumers with frequent symptoms of gastro-oesophageal reflux disease.
- Gastro-oesophageal reflux disease is a common condition. Increasing public awareness of the availability of a Schedule 3 Proton Pump Inhibitor in Pharmacy may have public health benefits through making consumers aware of more effective treatment options. Consumers may be more likely to seek advice from a pharmacist about the most appropriate treatment option.
- The Schedule 3 pack size, 14 days' supply, minimises the risk of inappropriate use. The RASML (Required Advisory Statements for Medicine Labels) warning statements help ensure appropriate use of the product.
- Other less effective treatments for the symptoms of gastro oesophageal reflux disease are advertised to consumers.
- The quality of evidence provided by the applicant in support of the proposal.

Delegate's considerations

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- Public submissions received;
- ACMS advice;
- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors[5];
- Other relevant information.

Public submissions on the interim decision

One public submission was received, supporting the decision to include esomeprazole in Appendix H.

Delegate's final decision

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

The implementation date is 1 October 2015.

Schedule entry

Appendix H – New Entry

ESOMEPRAZOLE

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

2. New chemical entities – medicines for human therapeutic use

2.1 NETUPITANT

Scheduling proposal

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

Netupitant is a neurokinin-1 receptor antagonist.

Netupitant is indicated in adult patients, in combination with palonosetron (as part of a fixed dose combination product), for the:

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

- Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy; and
- Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy.

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

Scheduling status

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

Netupitant is not classified in New Zealand.

Delegate's consideration

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

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

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 netupitant in Schedule 4, with an implementation date of 1 October 2015.

The delegate decided that the relevant matters under subsection 52E(1) of the Therapeutic Goods Act 1989 are (a) the risks and benefits of the use of a substance; (b) the purpose and the extent of use of a substance; (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 marketing experience in Australia.
- The benefits are considered to outweigh the risks at a population level.
- It is also noted that netupitant is currently proposed for use in a fixed dose combination with palonosetron, and benefit / risk has been assessed in this context.
- The purpose and extent of use is reflected in the indication, i.e. use in adults for:
  - Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy; and

- Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy.

· The potential for abuse of netupitant is unlikely.

Schedule entry

Schedule 4 – New Entry

NETUPITANT

2.2 IBRUTINIB

Scheduling proposal

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

Ibrutinib is a first-in-class, orally-administered, potent, covalently-binding inhibitor of Bruton's tyrosine kinase (BTK). Ibrutinib inhibits B-cell antigen receptor and chemokine-receptor signalling pathways in malignant B cells, disrupts integrin-dependent B-cell migration and adhesion in vitro and promotes egress of malignant cells from tissues and prevents homing of these cells to tissues in patients without clinically adverse effects on levels of normal B cells.

Ibrutinib is indicated for the treatment of patients with:

· Mantle Cell Lymphoma (MCL) who have received at least one prior therapy; and

· Chronic Lymphocytic Leukaemia/Small Lymphocytic Lymphoma (CLL/SLL) who have received at least one prior therapy, or as first line in patients with CLL with 17p deletion.

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

Scheduling status

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

Ibrutinib is not classified in New Zealand.

Delegate's consideration

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

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

· Subsection 52E(1) of the Therapeutic Goods Act 1989.

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 ibrutinib in Schedule 4, with an implementation date of 1 October 2015.

The delegate decided that the reason for the final decision comprised the following:

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

Schedule entry

Schedule 4 – New Entry

IBRUTINIB

2.3 CHOLIC ACID

Scheduling proposal

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

Cholic acid is a bile acid and used in patients with bile acid synthesis disorders due to single enzyme defects, and for patients with peroxisomal disorders.

Cholic acid is indicated for the treatment of inborn errors of bile acid synthesis responsive to treatment with cholic acid.

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

Scheduling status

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

Delegate's consideration

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

· Subsection 52E(1) of the Therapeutic Goods Act 1989

· The Scheduling Policy Framework scheduling factors

· The TGA evaluation report

· The new drug application.

Delegate's final decision

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

The delegate decided that the relevant matters under subsection 52E(1) of the Therapeutic Goods Act 1989 are (a) the risks and benefits of the use of a substance; and (b) the purpose and the extent of use of a substance.

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

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

· This cholic acid is a synthetic version of a naturally occurring bile acid. It has a relatively good safety profile.

- Cholic acid is intended to be used in the management of certain inborn errors of bile acid synthesis that, if untreated, result in liver failure. It's use will be in the context of long-term management of patients with a serious medical condition that requires ongoing assessment.

Schedule entry

Schedule 4 – New Entry

CHOLIC ACID

2.4 LEVOMILNACIPRAN

Scheduling proposal

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

Levomilnacipran is a selective serotonin and noradrenaline reuptake inhibitor (SNRI). It is reported to inhibit both the norepinephrine (NE) and 5-hydroxytryptamine (5-HT, serotonin) reuptake with an approximate two fold more potent inhibition of NE reuptake than 5-HT reuptake transporters. It is the more active enantiomer of the racemate milnacipran.

Levomilnacipran is indicated for the treatment of Major Depressive Disorder (MDD) in adults.

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

Scheduling status

Levomilnacipran is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons.

Levomilnacipran is not classified in New Zealand.

Delegate's consideration

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

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

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

Delegate's final decision

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

The delegate decided that the relevant matters under subsection 52E(1) of the Therapeutic Goods Act 1989 are (a) the risks and benefits of the use of a substance; (b) the purpose and the extent of use of a substance; and (c) the toxicity of a substance.

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

- It is a new chemical entity with no clinical/marketing experience in Australia.
- This active may cause increases in heart rate and blood pressure as well as nausea, vomiting and dizziness. Less frequent adverse effects may also occur that may require assessment and management by a medical doctor.
- It is intended for the treatment of depression, a medical condition that requires management by a healthcare professional.
- It has side effects that may require management by a doctor.

2.5 NALOXEGOL

Scheduling proposal

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

Naloxegol is a PEGylated derivative of the mu-opioid receptor antagonist naloxone.

Naloxegol is indicated for the treatment of opioid-induced constipation (OIC).

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

Scheduling status

Naloxegol is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons No.8.

Naloxegol is not classified as a prescription medicine in New Zealand.

Delegate's consideration

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

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

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

Delegates' final decision

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

The delegate decided that the relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of a substance; (b) the purpose and the extent of use of a substance; and (c) the toxicity of a substance.

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

- It is a new chemical entity with no clinical/marketing experience in Australia.
- This active can cross the blood brain barrier in certain medical conditions and interacts with many other medications via CYP metabolism pathways
- Naloxegol is intended for the treatment of opioid induced constipation.It is a new chemical entity.
- While naloxegol when used as intended has a good safety profile it can interfere with the action of other medicines and must not be given where there is a possibility of bowel obstruction. A medical assessment should be performed prior to its initial use and where there is significant abdominal pain.

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

Schedule entry

Schedule 4 – New Entry

NALOXEGOL

2.6 MILNACIPRAN

Scheduling proposal

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

Milnacipran is a balanced, specific, dual reuptake inhibitor of noradrenaline (NA) and serotonin (5-hydroxytryptamine [5 HT]), inhibiting noradrenaline uptake with greater potency than serotonin.

Milnacipran is indicated for the treatment of fibromyalgia.

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

Scheduling status

Milnacipran is not specifically scheduled and is not captured by any entry in the Standard for the Uniform Scheduling of Medicines and Poisons No.8.

Milnacipran is not classified as a prescription medicine in New Zealand.

Delegate's consideration

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

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

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

Delegates' final decision

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

The delegate decided that the relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of a substance; (b) the purpose and the extent of use of a substance; and (c) the toxicity of a substance.

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

- It is a new chemical entity.
- This active may cause increases in heart rate and blood pressure as well as nausea, vomiting and dizziness. Less frequent adverse effects may also occur that may require assessment and management by a medical doctor. It is intended for the treatment of depression, a medical condition that requires management by a healthcare professional.
- It is intended for the treatment of a chronic pain condition that requires management by a healthcare professional.
- It has side effects that may require management by a doctor

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

Schedule entry

Schedule 4 – New Entry

MILNACIPRAN