FINAL DECISIONS & REASONS FOR DECISIONS BY DELEGATES OF THE SECRETARY TO THE DEPARTMENT OF HEALTH AND AGEING

28 NOVEMBER 2012

The following delegates' final decisions and reasons on scheduling matters relate to:

- applications initially referred to the October 2011 meeting of the Advisory Committee on Medicines Scheduling (ACMS) [**ACMS #4**];
- applications considered as delegate-only matters, i.e. not referred to an expert advisory committee.

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

A delegate of the Secretary to the Department of Health and Ageing hereby gives notice of 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 Regulations. This notice also provides the reasons for each decision and the date of effect of the decision.

Matters referred to ACMS #4

Delegates' interim decisions on recommendations by ACMS #4 were published on 21 December 2011, accessible at www.tga.gov.au/industry/scheduling-decisions-interim.htm. This public notice also invited further comment from the applicant and from those parties who made a valid submission in response to the original invitation for submissions.

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

Redacted versions of further public submissions on interim decisions for matters referred to ACMS #4 are also available at www.tga.gov.au/industry/scheduling-submissions.htm.

In accordance with subsection 42ZCZR of the Regulations, if a delegate makes an interim decision on an application, that delegate may make a final decision confirming, varying or setting aside the interim decision only after considering any further valid submissions.

Matters not referred to an advisory committee

A delegate may decide not to refer a scheduling matter to an expert advisory committee for advice and instead may make a delegate-only decision. When deciding not to refer a matter to an expert advisory committee for advice, the delegate considers the scheduling guidelines as set out in the Scheduling Policy Framework (SPF) accessible at

www.tga.gov.au/industry/scheduling-spf.htm

Implementation

The SUSMP and its Amendments are also available electronically at the ComLaw website, a link to which can be found at www.tga.gov.au/industry/scheduling-poisons-standard.htm.

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PART A - FINAL DECISIONS ON MATTERS REFERRED TO AN EXPERT ADVISORY COMMITTEE

1. MATTERS INITIALLY REFERRED TO ACMS #4 - OCTOBER 2011

1.1 ADRENALINE

SCHEDULING PROPOSAL

The medicines scheduling delegate (the delegate) considered an application for adrenaline auto-injectors containing between 0.02 and 1 per cent adrenaline to be included in Appendix H.

The delegate referred the proposal to the October 2011 meeting of the Advisory Committee on Medicines Scheduling (ACMS) for advice.

PRE-MEETING SUBMISSIONS

Five pre-meeting submissions were received. One in support and four opposing the proposal

The redacted public submissions are available at http://www.tga.gov.au/industry/scheduling-submissions.htm

ADVISORY COMMITTEE ON MEDICINES SCHEDULING (ACMS) ADVICE TO THE DELEGATE

The October 2011 meeting of the ACMS considered the referral from the delegate and recommended that it would not be appropriate to include adrenaline auto-injectors in Appendix H.

DELEGATE'S CONSIDERATION

The delegate considered the following in regards to this application.

The advice of the October 2011 meeting of the ACMS.

The evaluation report and the applicant's comments in response to that report.

The pre-meeting public submissions.

The February 2010 decision of the National Drugs and Poisons Schedule Committee to not include adrenaline auto-injectors in Appendix H.

Adrenaline auto-injectors for use in severe acute allergic reactions have been approved in Australia since August 1993 and are recommended as a part of the action plan for anaphylaxis. That adrenaline 0.15 mg (.05 per cent) and 0.3 mg (0.1 per cent) auto-injectors are also listed on the Pharmaceutical benefits Scheme (PBS) as an authority-required listing for the management of acute allergic reactions with anaphylaxis.

Concern that brand advertising could draw on community misperceptions of the risks of anaphylaxis v. less serious but more common food sensitivities, which could lead to an increase in inappropriate purchasing and possession of these devices.

Inclusion in Appendix H did not control the type of advertising a company could use to promote a substance, although the content of such advertising was subject to significant consideration against the requirements of the *Therapeutic Goods Act 1989* prior to approval.

The appropriateness of direct-to-consumer advertising on the use of this device by someone with a commercial interest.

Information training could be run by public health groups with input from sponsor companies.

The current efforts by the Australasian Society of Clinical Immunology and Allergy (ASCIA) and Anaphylaxis Australia in increasing community awareness of anaphylaxis and training in the use of auto-injectors.

Relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989*.

Scheduling factors for an Appendix H listing[1].

DELEGATE'S INTERIM DECISION

The delegate made an interim decision to not include adrenaline auto-injectors in Appendix H.

The delegate's interim decision inviting further comment was published on the TGA website on 21 December 2011.

SUBMISSIONS ON INTERIM DECISION

No public submissions were received.

DELEGATE'S FINAL DECISION

The delegate has made a final decision that the current scheduling of adrenaline remains appropriate, i.e. no listing in Appendix H.

The delegate decided that the relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989* include (b) the purposes and extent of use, and (f) any other matters that the delegate considers necessary to protect public health.

The reasons for the delegate's final decision comprised of the following.

Advertising is not required to address issues of access and extent of use.

There is no public health matter that requires adrenaline auto-injectors to be advertised.

[1] **Scheduling Policy Framework for Medicines and Chemicals //www.tga.gov.au/industry/scheduling-spf.htm**

1.2 FINGOLIMOD

SCHEDULING PROPOSAL

The medicines scheduling delegate (the delegate) considered a proposal to include fingolimod in Appendix L with warning statement 76 "*Do not become pregnant during use or within [2] months of stopping treatment*."

The delegate referred the proposal to the October 2011 meeting of the Advisory Committee on Medicines Scheduling (ACMS) for advice.

SCHEDULING STATUS

Fingolimod is currently included in Schedule 4.

PRE-MEETING SUBMISSIONS

No public submissions were received.

ADVISORY COMMITTEE OF MEDICINES SCHEDULING (ACMS) ADVICE TO THE DELEGATE

The October 2011 meeting of the ACMS considered the referral from the delegate and recommended that fingolimod be included in Appendix L.

DELEGATE'S CONSIDERATION

The delegate considered the following in regards to this proposal.

In December 2010, the Therapeutic Goods Administration's (TGA) Advisory Committee on Prescription Medicines (ACPM) considered an application to register fingolimod, a new chemical entity for a human therapeutic medicine.

In June 2011, a delegate-only decision was made to include fingolimod in Schedule 4, with the delegate noting that fingolimod was associated with teratogenicity affecting organogenesis and that TGA had classified it as a Pregnancy Category D medicine.

Medicines containing substances listed in Appendix L must not be dispensed unless labelled with a warning statement(s) specified in Appendix F of the SUSMP.

Advice from the October 2011 meeting of the ACMS.

Relevant matters under ubsection 52E(1) of the *Therapeutic Goods Act 1989.*

Scheduling factors for listing in Appendix L[2].

DELEGATE'S INTERIM DECISION

In December 2011, the delegate made an interim decision to include fingolimod in Appendix L. The interim decision was made following advice from the October 2011 meeting of the ACMS

[2] **Scheduling Policy Framework for Medicines and Chemicals** http://www.tga.gov.au/industry/scheduling-spf.htm

and in response to concerns regarding the use of fingolimod during pregnancy, with evidence showing that it is associated with teratogenicity affecting organogenesis.

The delegate's interim decision inviting further public comment was published on the TGA website on 21 December 2011.

SUBMISSIONS ON INTERIM DECISION

No public submissions were received.

DELEGATE'S FINAL DECISION

The delegate has made a final decision to include fingolimod in Appendix L with warning statement 76 "*Do not become pregnant during use or within [2] months of stopping treatment*."

The implementation date for this decision is 1 January 2013.

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

The reason for the delegate's final decision is the requirement to notify women of potential risk if used in pregnancy.

Appendix L – New entry

Column 1 **Substance**	**Column 2** **Warning Statement**
Fingolimod.	76

PART B - FINAL DECISIONS ON MATTERS NOT REFERRED TO AN EXPERT ADVISORY COMMITTEE

2. NEW CHEMICAL ENTITIES

2.1 ABIRATERONE ACETATE

SCHEDULING PROPOSAL

The delegate considered an application from the Therapeutic Goods Administration (TGA) to schedule abiraterone, a new chemical entity for a human therapeutic medicine.

The delegate has made a delegate-only decision to include abiraterone acetate in Schedule 4. The Advisory Committee on Medicines Scheduling was not consulted.

SCHEDULING STATUS

Abiraterone is not specifically scheduled in Australia.

DELEGATE'S CONSIDERATION

The delegate considered the following in regards to this application.

Abiraterone suppresses testosterone production by inhibiting CYP17A1, an enzyme which is expressed in testicular, adrenal and prostatic tumor tissues. CYP catalyzes two sequential reactions: (a) the conversion of pregnenolone and progesterone; and (b) the subsequent formation of dehydroepiandrosterone (DHEA) and androstenedione respectively. Inhibition of CYP17 activity by abiraterone decreases circulating levels of testosterone.

It is used in combination with prednisone to treat patients with metastatic castration-resistant prostate cancer (prostate cancer that has already spread to other parts of the body) and in patients who have received cancer treatments, such as docetaxel.

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

It is not classified in New Zealand. In the United States and the United Kingdom, it has been approved as a prescription medicine for the treatment of advanced prostate cancer.

Abiraterone has been classified as a Pregnancy Category X drug by the United States (US) Food and Drug Administration. The US warning statements in the Prescribing Information are "Women and children should not use this medicine. Pregnant women or women who may become pregnant should not handle or touch the tablets without protection (e.g., gloves). This medicine may also cause birth defects if the father is using it when his sexual partner becomes pregnant. You must use a condom and another effective method of birth control during and for 1 week after the last dose of abiraterone. If a pregnancy occurs while you are using this medicine, tell your doctor right away."

The TGA proposes to classify abiraterone as a Pregnancy Category D medicine. Women who may be pregnant should not handle it without protection. However, as it is indicated for the treatment of prostate cancer and will not be used in women, additional labelling controls and/or requirements for dispensing labels are considered not to be warranted.

Common adverse reactions (>5 per cent) include joint swelling or discomfort, hypokalemia, edema, muscle discomfort, hot flush, diarrhea, urinary tract infection, cough, hypertension, arrhythmia, urinary frequency, nocturia, dyspepsia and upper respiratory tract infection.

In a pivotal placebo controlled study, there was no notable increase in the incidence of fatigue/lethargy/somnolence compared to placebo.

There are no issues of concern that require additional control other than by inclusion in Schedule 4.

Relevant matters under subsection 52E(1) of the Therapeutic Goods Act 1989.

Scheduling factors for inclusion in Schedule 43.

DELEGATE'S FINAL DECISION

The delegate has made a final decision to include abiraterone acetate in Schedule 4.

The implementation date for this decision is 1 January 2013.

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

The reasons for the delegate's final decision comprised of the following.

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

The benefits are considered to outweigh the risks in the population where use is indicated.

It is to be used to treat patients with metastatic castration-resistant prostate cancer and in patients who have received prior chemotherapy containing a taxane, requiring diagnosis, management and monitoring by medical professionals.

Extent of use may increase if new indications are approved.

Women who may be pregnant should not handle abiraterone without protection.

[3] Scheduling Policy Policy Framework http://www.tga.gov.au/industry/scheduling-spf.htm

Schedule 4 – New entry

ABIRATERONE ACETATE.

2.2 BOCEPREVIR

SCHEDULING PROPOSAL

The delegate considered an application from TGA to schedule boceprevir, a new chemical entity for a human therapeutic medicine.

The delegate has made a delegate-only decision to include boceprevir in Schedule 4. The Advisory Committee on Medicines Scheduling was not consulted.

SCHEDULING STATUS

Boceprevir is not specifically scheduled in Australia.

DELEGATE'S CONSIDERATION

The delegate considered the following in regards to this application.

Boceprevir is an antiviral drug that inhibits replication of Hepatitis C Virus (HCV) in host cells by binding to the NS3 protease active site serine (Serl39) to inhibit viral replication in HCV-infected host cells.

It is indicated for the treatment of chronic hepatitis C (HCV) genotype 1 infection, in a combination regimen with peginterferon alpha and ribavirin, in adult patients (18 years and older) with compensated liver disease who are previously untreated or who have failed previous therapy.

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

It is the first HCV protease inhibitor to be registered in Australia.

It is classified as a prescription medicine in New Zealand and has received marketing approval in the United States, the European Union, Canada, Brazil and Switzerland.

It is contraindicated for use with medicines that are highly dependent on CYP3A4/5 for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events, such as orally administered midazolam, triazolamn, amiodarone, cisapride, alfuzosin, simvastatin, lovastatin, sildenafil or tadalafil when useded for the treatment of pulmonary arterial hypertension, and ergot derivativeses (dihydroergotamine, ergotamine).

Anaemia and neutropenia have been reported with peginterferon alpha/ribavirin therapy. Boceprevir must not be used alone due to the high probability of increased resistance without combination anti-HCV therapies. Co-administration of boceprevir with simvastatin may increase plasma levels of simvastatin, which could increase the risk of myopathy, including rhabdomylolysis.

The most frequently reported adverse reactions of fatigue, anaemia, nausea and headache related to the combination of boceprevir with peginterferon alfa-2b and ribavirin in adult subjects in clinical studies.

Although it must be administered in combination with ribavirin, which has teratogenic effects, TGA have classified it as a Pregnancy Category B2 medicine with additional controls and/or requirements for dispensing labels considered not to be warranted.

It is in capsule form, with a combination pack together with peginterferon alfa-2b injection and ribavirin capsules also proposed.

Relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989*.

Scheduling factors for inclusion in Schedule 4[4].

DELEGATE'S FINAL DECISION

The delegate has made a final decision to include boceprevir in Schedule 4.

The implementation date for this decision is 1 January 2013.

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

The reasons for the delegate's final decision comprised of the following.

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

It is to be used in combination with peginterferon alfa and ribavirin, which are prescription only medicines, for a condition that requires diagnosis, management and prescription by medical professionals.

It must not be used alone due to the high probability of increased resistance without combination anti-HCV therapies.

It must not be coadministered with medicines that are highly dependent on CYP3A4/5 for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events such as orally administered midazolam, triazolam, amiodarone, cisapride, alfuzosin, simvastatin, lovastatin, sildenafil or tadalafil when used for the treatment of pulmonary arterial hypertension and ergot derivates (dihydroergotamine, ergotamine).

[4] Scheduling Policy Framework for Medicines and Chemicals http://www.tga.gov.au/industry/scheduling-spf.htm

Schedule 4 – New Entry

BOCEPREVIR.

2.3 FIDAXOMICIN

SCHEDULING PROPOSAL

The delegate considered an application from the Therapeutic goods Administration (TGA) to schedule fidaxomicin, a new chemical entity for a human therapeutic medicine.

The delegate has made a delegate-only decision to include fidaxomicin in Schedule 4. The Advisory Committee on Medicines Scheduling (ACMS) was not consulted.

SCHEDULING STATUS

Fidaxomicin is not specifically scheduled in Australia.

SCHEDULING CONSIDERATION

The delegate considered the following in regards to this application.

Fidaxomicin is an antibacterial agent indicated for the treatment of *Clostridium difficile*-associated diarrhea in adults.

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

It is not classified in New Zealand. In May 2011, it was approved by the United States Food and Drug Administration for the treatment of *Clostridium difficile*-associated diarrhea. In December 2011, it was approved in Europe for the treatment of adults with *Clostridium difficile infections.*

It is to be used for a condition that requires diagnosis, management and prescription by medical professionals.

To reduce the development of drug resistant bacteria and maintain its effectiveness and that of other antibacterial drugs:

- It should not be used to treat systemic infections as there is minimal absorption of the drug.
- It should only be used be used to treat infections that are proven or strongly suspected to be caused by *Clostridium difficile.*

The most common adverse reactions are nausea, vomiting, abdominal pain, gastrointestinal hemorrhage, anemia and neutropenia.

Pregnancy Category B1 is proposed, with additional controls and/or requirements for dispensing labels not considered to be warranted.

Safety and effectiveness for paediatric use has not been established.

There are no issues of concern that require additional control other than by inclusion in Schedule 4.

Relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989.*

Scheduling factors for inclusion in Schedule 4[5].

DELEGATE'S FINAL DECISION

The delegate has made a final decision to include fidaxomicin in Schedule 4.

The implementation date for this decision is 1 January 2013.

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

The reasons for the delegate's final decision comprised of the following.

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

The balance of benefits and risks will only be positive if it is used appropriately.

It is used to treat a specific infection in a certain population.

There are adverse events associated with its use.

Schedule 4 – New entry

FIDAXOMICIN.

2.4 RIDAFOROLIMUS

SCHEDULING PROPOSAL

The delegate considered an application from the Therapeutic Goods Administration (TGA) to schedule ridaforolimus, a new chemical entity for a human therapeutic medicine.

The delegate has made a delegate-only decision to include ridaforolimus in Schedule 4. The Advisory Committee on Medicines Scheduling was not consulted.

SCHEDULING HISTORY

Ridaforolimus is not specifically scheduled in Australia.

[5] ***Scheduling Policy Framework for Medicines and Chemicals*** ***http://www.tga.gov.au/industry/scheduling-spf.htm***

DELEGATE'S CONSIDERATION

The delegate considered the following with regards to this application.

Ridaforolimus is a small molecule and non-prodrug analogue of rapamycin. It is an antineoplastic agent and inhibits the mammalian target of rapamycin (mTOR), interfering with the cell cycle.

It is indicated for the treatment of patients with metastatic soft tissue or bone sarcoma.

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

It is not classified in New Zealand. The European Medicines Agency accepted filing (orphan drug) in August 2011. In May 2012, the US Food and Drug administration rejected a New Drug Application for ridaforolimus for maintenance treatment for patients with metastic soft tissue or bone sarcoma. Ridaforolimus is an mTOR inhibitor. Activation of the mTOR pathway occurs in multiple sarcoma subtypes. It has shown anti-tumour activity in nonclinical and clinical studies of sarcoma.

Other mammalian target of rapamycin (mTOR) inhibitors everolimus, sirolimus and temsirolimus are all Schedule 4 substances.

Clinical trials have reported high incidence and severity of adverse reactions.

Non-Infectious pneumonitis, aphthous stomatitis, mouth ulceration, tongue ulceration, and mucosal inflammation, are common adverse reactions considered as a class effect of derivatives of rapamycin. These adverse reactions were seen in clinical studies with ridaforolimus, and may require dose modification. Decreased haemoglobin, lymphocytes, neutrophils and platelets have been reported in patients treated with ridaforolimus. Elevations in blood creatinine, renal function impairment, and renal failure have occurred.

TGA have classified ridaforolimus as a Pregnancy Category D medicine as it can cause fetal harm when administered to a pregnant woman based on its mechanism of action. However, additional controls and/or requirements for dispensing labels are considered not to be warranted.

Relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989.*

Scheduling factors for inclusion in Schedule 4[6].

DELEGATE'S FINAL DECISION

The delegate has made a final decision to include ridaforolimus in Schedule 4.

[6] ***Scheduling Policy Framework for Medicines and Chemicals (1 July 2010).***

The implementation date for this decision is 1 January 2013.

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

The reasons for the delegate's final decision comprised of the following.

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

The condition it is to be used for requires expert medical diagnosis and treatment.

There is a small margin between therapeutic and toxic dose.

It has shown high incidence and severity of adverse reactions.

Schedule 4 – New entry

RIDAFOROLIMUS.

2.5 TELAPREVIR

SCHEDULING PROPOSAL

The delegate considered an application from TGA to schedule telaprevir, a new chemical entity for a human therapeutic medicine.

The delegate has made a delegate-only decision to include telaprevir in Schedule 4. The Advisory Committee on Medicines Scheduling was not consulted.

SCHEDULING STATUS

Telaprevir is not specifically scheduled in Australia.

DELEGATE'S CONSIDERATION

The delegate considered the following in regards to this application:

Telaprevir is an antiviral drug that inhibits replication of Hepatitis C Virus (HCV) in host cells by binding to NS3/4A serine protease to inhibit viral replication in HCV-infested host cells.

In a combination regimen with peginteferon alfa and ribavirin, it is indicated for the treatment of genotype 1 chronic hepatitis C in adult patients with compensated liver disease (including cirrhosis) who are treatment-naïve and who have previously been treated with interferon alfa (pegylated or non-pegylated) alone or in combination with ribavirin, including relapsers, partial responders and null responders. These medicines include afuzosin,amiodarone, bepridil, quinidine,cisapride, ergot derivatives, simvastatin, lovastatin, atorvastatin, sildenafil or tadalafil (only when used for the treatment of pulmonary arterial hypertension) and orally administered triazolan.

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

It is classified as a prescription medicine in New Zealand and has received marketing approval in the United States and the European Union.

It is contraindicated for use with medicines that are highly dependent on CYP3A4 for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events.

Co-administration with atorvastatin markedly increases the plasma concentrations of atorvastatin. Concomitant administration of telaprevir and atorvastatin is to be avoided.

The most frequently reported adverse drug reactions were anaemia, rash, pruritus and nausea when used in combination with peginterferon and ribavirin.

Relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989.*

Scheduling factors for inclusion in Schedule 4[7].

DELEGATE'S FINAL DECISION

The delegate has made a final decision to include telaprevir in Schedule 4.

The implementation date for this decision is 1 January 2013.

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

The reasons for the delegate's final decision comprised of the following.

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

It is to be used in a condition that requires diagnosis, management and prescription by medical professionals.

It must be administered in combination with peginterferon alfa and ribavirin (both prescription only medicines) due to the high probability of increased resistance without combination anti-HCV therapies.

It is contraindicated for use with medicines that are highly dependent on CYP3A4 for clearance, and for which elevated plasma concentrations are associated with serious and/or life-threatening events such alfuzosin, amiodarone, bepridil, quinidine, cisapride, ergot derivatives (dihydroergotamine, ergotamine), simvastatin, lovastatin, atorvastatin, sildenafil or tadalafil (only when used for the treatment of pulmonary arterial hypertension) and orally administered triazolam.

[7] *Scheduling Policy Framework for Medicines and Chemicals (1 July 2010).*

Severe rashes have been reported with telaprevir combination treatment.

Schedule 4 – New Entry

TELAPREVIR.

3. EDITORIAL AMENDMENTS

3.1 CICLOPIROX

SCHEDULING PROPOSAL

The medicines scheduling delegate (the delegate) considered a proposal to editorially amend the Schedule 2 entry for ciclopirox to achieve consistency of wording with other Schedule entries.

The delegate has made a delegate-only decision to amend the Schedule 2 entry for ciclopirox. The Advisory Committee on Medicines Scheduling was not consulted.

SCHEDULING HISTORY

In February 2002, the National Drugs and Poisons Schedule Committee (NDPSC) amended the Schedule 3 to Schedule 2 cut-off for ciclopirox dermal preparations from 1 per cent to 2 per cent.

In June 2006, the NDPSC decided to:

- extend the Schedule 3 to Schedule 2 cut-off for ciclopirox dermal preparations to include application to the nail and
- harmonise with New Zealand to exempt from scheduling ciclopirox preparations for the treatment of tinea pedis.

In May 2012, the delegate decided to:

- reschedule from Schedule 3 to Schedule 2, ciclopirox in preparations for application to the nail containing 8 per cent or less of ciclopirox; and
- editorially amend the Schedule 4 entry to clarify that ciclopirox in preparations for the treatment of tinea pedis were exempt from scheduling. This amendment had been overlooked by the NDPSC in June 2006 when exempting ciclopirox preparations for the treatment of tinea pedis.

SCHEDULING CONSIDERATION

The delegate noted that the wording of the Schedule 2 entry was not consistent with the wording of other Schedule entries in that the exemption in paragraph (a) "**except** in preparations for tinea pedis" should read "**except** in preparations for the treatment of tinea pedis".

DELEGATE'S FINAL DECISION

The delegate has made a final decision to editorially amend the Schedule 2 entry for ciclopirox to include "the treatment of" in the exception in paragraph (a).

The implementation date for this decision is 1 January 2013.

The reason for the decision is to achieve consistency of wording with other Schedule entries.

Schedule 2 – Amendment

CICLOPIROX:

(a) in preparations for dermal use containing 2 per cent or less of ciclopirox **except** in preparations for the treatment of tinea pedis; or

(b) in preparations for application to the nails containing 8 per cent or less of ciclopirox

3.2 FEXOFENADINE

SCHEDULING PROPOSAL

The medicines scheduling delegate (the delegate) considered a proposal from the Therapeutic Goods Administration (TGA) to editorially amend the Schedule 2 and Schedule 4 entries for fexofenadine to correct the intent of the wording in the Schedule entries by including an exemption specifically for divided preparations.

The delegate has made a delegate-only decision to editorially amend the Schedule 2 and Schedule 4 entries for fexofenadine. The Advisory Committee on Medicines Scheduling (ACMS) was not consulted.

SCHEDULING HISTORY

In June 2011, the delegate decided to exempt from scheduling fexofenadine when for the short-term symptomatic relief of seasonal allergic rhinitis (SAR) in adults and children 12 years of age and over when sold in small packs of 10 dosage units or less (i.e. not more than 5 day's supply at the current maximum recommended dose) with a maximum daily dose of 120 mg. The implementation date for this decision was 1 September 2011.

In September 2011, the delegate decided to amend the Schedule 2 and Schedule 4 entries for fexofenadine to specifically stipulate a limit of 5 days' supply in the exemption, with a retrospective implementation date of 1 September 2011. The reason for this decision was to clarify the intent of the June 2011 decision.

SCHEDULING CONSIDERATION

The delegate considered the following in regards to this proposal.

Issues raised by TGA:

- The current Schedule 2 entry does not specify an exemption for 'divided preparations'. The entry reads, in part, "FEXOFENADINE in preparations for oral use except in preparations for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when …".
- Fexofenadine is currently included on the Australian Register of Therapeutic Goods as tablets and oral liquids. However, TGA may register capsule form or any other solid dose form if a sponsor submits an appropriate application. As such, tablets, capsules and other divided preparations of fexofenadine should be exempt from scheduling, including effervescent tablets which should be covered under the SUSMP definition "divided preparations" as they are only a liquid when added to water.
- However, liquid preparations of fexofenadine are primarily intended for use in children and should not be exempted from scheduling, noting that the scheduling exemption for fexofenadine only applies to products indicated for use in adults and children 12 years of age and over.
- The Schedule 2 entry for fexofenadine should state an exemption specifically for 'divided preparations'. The Schedule 4 entry should include consistent wording and also refer to 'divided preparations'.

The original application considered by the February 2011 ACMS meeting to exempt from scheduling, oral fexofenadine (maximum 10 dosage units) when used for the short-term symptomatic relief (maximum 5 days of therapy) of SAR in adults and children 12 years and over, with a maximum daily dose of 120 mg.

The advice of the February 2011 ACMS meeting.

DELEGATE'S FINAL DECISION

The delegate has made a final decision to editorially amend the Schedule 2 and Schedule 4 entries for fexofenadine to include an exemption specifically for divided preparations.

The implementation date for this decision is 1 May 2013.

The reason for the decision is to correct the intent of the wording in the Schedule entries.

Schedule 2 – Amendment

FEXOFENADINE 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 10 dosage units or less and not more than 5 days' supply; and

(b) labelled with a recommended daily dose not exceeding 120 mg of fexofenadine.

Schedule 4 – Amendment

FEXOFENADINE **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 10 dosage units or less and not more than 5 days' supply; and

(ii) labelled with a recommended daily dose not exceeding 120 mg of fexofenadine.

3.3 IBUPROFEN IN COMBINATION WITH PHENYLEPHRINE

SCHEDULING PROPOSAL

Following publication of the *Delegates' reasons for final decisions, October 2012*, an anomaly was identified in the delegate's interim and final decisions, in that "5 mg or less of phenylephrine" was included in the wording of the delegate's decision, but was not included in the Schedule 2 amended entry.

SCHEDULING CONSIDERATION

The delegate noted that the wording "5 mg or less of phenylephrine" had been inadvertently included in the interim and final decision.

In making the original decision, the delegate had considered that:

the exemption in the Schedule 2 entry for phenylephrine already includes an adequate restriction on the amount of phenylephrine per dosage unit before Schedule 2 comes into effect, i.e. up to 50 mg of phenylephrine per day in packs containing up to 250 mg;

the quantity of phenylephrine per dosage unit in unscheduled products should be consistent with the exemption requirements of the Schedule 2 entry for phenylephrine.

the Schedule 2 entry for ibuprofen should be consistent with the exception for unscheduled paracetamol/phenylephrine combination products in the Schedule 2 entry for paracetamol, i.e. there is no reference to a strength of phenylephrine.

DELEGATE'S FINAL DECISION

The delegate has decided to editorially amend the wording of the October 2012 final decision to correctly reflect the intent of the decision to reschedule ibuprofen from Schedule 2 to unscheduled when in divided preparations containing 200 mg or less of ibuprofen in fixed dose combinations with phenylephrine in packs containing not more than 25 tables. This included restricting the entry for the treatment of adults and children aged 12 years of age and over.

The delegate confirms that the implementation date of 1 January 2013 and the amendment to the Schedule 2 entry, as published in the *Delegates' reasons for final decisions, October 2012*, remain unchanged.

Schedule 2 – Amendment

IBUPROFEN in preparations for oral use when labelled with recommended daily dose of 1200 mg or less of ibuprofen:

(a) in liquid preparations when sold in the manufacturer's original pack containing 8 grams or less of ibuprofen; or

(b) in divided preparations, each containing 200 mg or less of ibuprofen, in packs of not more than 100 dosage units **except** when:

(i) as the only therapeutically active constituent (other than phenylephrine or when combined with an effervescent agent);

(ii) packed in blister or strip packaging or in a container with a child-resistant closure;

(iii) in a primary pack containing nor more than 25 dosage units;

(iv) compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(v) not labelled for the treatment of children 6 years of age or less; and

(vi) not labelled for the treatment of children under 12 years of age when combined with phenylephrine.