Australian Government
Department of Health
Therapeutic Goods Administration

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

April 2016

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

The delegates of the Secretary to the Department of Health hereby give 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 the Therapeutic Goods Regulations 1990 (the Regulations). This notice also provides the reasons for each decision and the date of effect (implementation date) of the decision.

The delegates' final decisions and reasons relate to:

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

Matters not referred to an advisory committee

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

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 the Federal Register of Legislation 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 the Federal Register of Legislation, is available at SUSMP.

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Implementation date: 1 June 2016

1.1 Selexipag

Scheduling proposal

The proposal is to include selexipag, a new chemical entity for a human therapeutic medicine, in Schedule 4 of the SUSMP.

Scheduling application

The delegate considered an application from the Therapeutic Goods Administration (TGA) for the scheduling of selexipag. The Advisory Committee on Medicines Scheduling was not consulted.

Substance summary

Selexipag is a selective non-prostanoid prostacyclin IP receptor agonist.

Selexipag is indicated for the treatment of idiopathic pulmonary arterial hypertension, heritable pulmonary arterial hypertension, pulmonary arterial hypertension associated with connective tissue disease and pulmonary arterial hypertension associated with congenital heart disease with repaired shunts and pulmonary arterial hypertension associated with drugs and toxins in patients with WHO functional class II, III or IV symptoms.

Scheduling status

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

Selexipag is classified as a prescription medicine in New Zealand.

Scheduling history

Selexipag has not been previously considered for scheduling; therefore, scheduling history is not available.

Delegate's considerations

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[1]
- 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 selexipag in Schedule 4, with an implementation date of **1 June 2016**.

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

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

- It is a new chemical entity with no clinical experience in Australia.
- The risks and benefits of the medicine have been considered and are outlined in the Product Information, Delegate's Request for ACPM advice and the TGA evaluation reports.
- Selexipag is indicated for the treatment of idiopathic pulmonary arterial hypertension, heritable pulmonary arterial hypertension, pulmonary arterial hypertension associated with connective tissue disease and pulmonary arterial hypertension associated with congenital heart disease with repaired shunts and pulmonary arterial hypertension associated with drugs and toxins in patients with WHO functional class II, III or IV symptoms.
- It has no previous experience of use in Australia but has recently been approved for use overseas.
- It is proposed for use in the hospital and community.
- Treatment should only be initiated and monitored by a physician experienced in the treatment of Pulmonary arterial Hypertension (PAH).
- Selexipag is an oral, selective non-prostanoid prostacyclin receptor (IP receptor) agonist.
- The medicine has risks that require medical intervention, evaluation and monitoring by a medical practitioner.
- Labelling needs to comply with the requirements for a prescription only medicine.
- It does not appear to produce dependency and the abuse potential appears to be low.

[1] Schedulng Policy Framework for Medicines and Chemicals (SPF, 2015)

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

Schedule entry

Schedule 4—New Entry

SELEXIPAG

Implementation date: **1 June 2016**.

1.2 Vorapaxar

Scheduling proposal

The proposal is to include vorapaxar, a new chemical entity for a human therapeutic medicine, in Schedule 4 of the SUSMP.

Scheduling application

The delegate considered an application from the Therapeutic Goods Administration (TGA) for the scheduling of vorapaxar, a new chemical entity for a human therapeutic medicine. The Advisory Committee on Medicines Scheduling was not consulted.

Substance summary

Vorapaxar is an inhibitor of the PAR-1 receptors on platelets that are activated by thrombin.

Vorapaxar is indicated for the reduction of atherothrombotic events in patients with a history of myocardial infarction (MI) or with peripheral arterial disease (PAD).

Scheduling status

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

Vorapaxar 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 vorapaxar in Schedule 4, with an implementation date of **1 June 2016**.

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

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

- It is a new chemical entity with no clinical experience in Australia.
- The risks and benefits of the medicine have been considered and are outlined in the Product Information, Delegate's Request for ACPM advice and the TGA evaluation reports.
- Vorapaxar, an antagonist of the protease activated receptor-1 (PAR-1), is indicated for the reduction of atherothrombotic events in patients with a history of myocardial infarction (MI) or with peripheral arterial disease (PAD).
- It has no previous experience of use in Australia but has been approved for use overseas.
- It is proposed for use in the hospital and community.
- Vorapaxar is an inhibitor of the PAR-1 receptors on platelets that are activated by thrombin. It has risks mainly related to bleeding but there is also concern about retinal changes.
- The medicine has risks that require medical intervention, evaluation and monitoring by a medical practitioner.
- Labelling needs to comply with the requirements for a prescription only medicine.
- It does not appear to produce dependency and the abuse potential appears to be low.

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

Schedule entry

Schedule 4 – New Entry

VORAPAXAR

Implementation date: **1 June 2016**.

1.3 Alirocumab

Scheduling proposal

The proposal is to include alirocumab, a new chemical entity for a human therapeutic medicine, in Schedule 4 of the SUSMP.

Scheduling application

The delegate considered an application from the Therapeutic Goods Administration (TGA) for the scheduling of alirocumab, a new chemical entity for a human therapeutic medicine. The Advisory Committee on Medicines Scheduling was not consulted.

Substance summary

Alirocumab is a fully human monoclonal antibody (IgG1 isotype) that targets PCSK9. Alirocumab is produced by recombinant DNA technology in Chinese Hamster Ovary cell suspension culture.

Alirocumab is indicated as an adjunct therapy to diet, for long-term use in adult patients with primary hypercholesterolaemia (non-familial and heterozygous familial) to reduce low-density lipoprotein cholesterol (LDL-C). Alirocumab is indicated in combination with a statin (HMG-CoA reductase inhibitor), with or without other lipid-modifying therapy (LMT), in patients not appropriately controlled with a statin. Alirocumab (Praluent) is indicated as monotherapy, or as add-on to other non-statin LMT, in patients who cannot tolerate statins.

Scheduling status

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

Alirocumab 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 alirocumab in Schedule 4, with an implementation date of **1 June 2016**.

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

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

- It is a new chemical entity with no clinical experience in Australia apart from clinical trials.
- The risks and benefits of the medicine have been considered and are outlined in the Product Information, and the TGA evaluation reports.
- Alirocumab is indicated for the treatment of patients with primary hypercholesterolaemia to reduce LDL-C cholesterol.
- It has no previous experience of use in Australia outside the clinical trial setting but has recently been approved overseas.
- It is proposed for use in the hospital and community.
- Alirocumab is a fully human monoclonal antibody (IgG1) isotype that targets proprotein converase subtilisin kexin type 9 (PCSK9) and is given by subcutaneous injection.
- Labelling needs to comply with the requirements for an injectable prescription only medicine.
- It does not appear to produce dependency and the abuse potential appears low.

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

Schedule entry

Schedule 4 – New Entry

ALIROCUMAB

Implementation date: **1 June 2016**.

1.4 Elbasvir

Scheduling proposal

The proposal is to include elbasvir, a new chemical entity for a human therapeutic medicine, in Schedule 4 of the SUSMP.

Scheduling application

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

The Advisory Committee on Medicines Scheduling was not consulted.

Substance summary

Elbasvir is a second generation HCV NS5A inhibitor.

Elbasvir is indicated for the treatment of Chronic Hepatitis C infection in adults.

Scheduling status

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

Elbasvir is not classified in New Zealand 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.

Delegate's final decision

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

The delegate decided that the relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of a substance; (b) the purpose and the extent of use of a substance; 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.
- Treatment of a serious chronic infection.
- Limited toxicity/safety data available at present, so needs monitoring.

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

Schedule entry

Schedule 4 – New Entry

ELBASVIR

Implementation date: **1 June 2016**.

1.5 Grazoprevir

Scheduling proposal

The proposal is to include grazoprevir, a new chemical entity for a human therapeutic medicine, in Schedule 4 of the SUSMP.

Scheduling application

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

The Advisory Committee on Medicines Scheduling was not consulted.

Substance summary

Grazoprevir is a second generation HCV NS3/4A protease inhibitor (PI).

Grazoprevir is indicated for the treatment of Chronic Hepatitis C infection in adults.

Scheduling status

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

Grazoprevir 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 grazoprevir in Schedule 4, with an implementation date of **1 June 2016**.

The delegate decided that the relevant matters under subsection 52E(1) of the *Therapeutic Goods Act 1989* are (a) the risks and benefits of the use of a substance; (b) the purpose and the extent of use of a substance; 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.
- Treatment of serious chronic infection.
- Safety data still quite limited so monitoring is required.

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

Schedule entry

Schedule 4 – New Entry

GRAZOPREVIR

Implementation date: **1 June 2016**.

1.6 Idarucizumab

Scheduling proposal

The proposal is to include idarucizumab, a new chemical entity for a human therapeutic medicine, in Schedule 4 of the SUSMP.

Scheduling application

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

The Advisory Committee on Medicines Scheduling was not consulted.

Substance summary

Idarucizumab binds specifically to dabigatran and reverses its anticoagulant effect. It will not reverse the effects of other anticoagulants.

Idarucizumab is indicated for the patients treated with dabigatran etexilate when rapid reversal of the anticoagulant effects of dabigatran is required:

- For emergency surgery/urgent procedures
- In life-threatening or uncontrolled bleeding.

Scheduling status

Idarucizumab 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 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 idarucizumab in Schedule 4, with an implementation date of **1 June 2016**.

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

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

- It is a new chemical entity with no marketing experience in Australia. There have been patients enrolled in a clinical trial in Australia.
- The risks and benefits of the medicine have been considered and are outlined in the Product Information and the TGA Evaluation reports.
- Idarucizumab is indicated in patients treated with dabigatran etexilate when rapid reversal of the anticoagulant effects of dabigatran is required:
  - For emergency surgery/urgent procedures
  - In life-threatening or uncontrolled bleeding
- It has no previous us in Australia outside the clinical trial setting but has recently been approved overseas for the same indication.
- It is proposed for use in the hospital.
- Idarucizumab is a humanised antibody fragment (Fab) molecule derived from an IgG1 isotype molecule directed against the direct thrombin inhibitor dabigatran.
- The medicine has risks that require medical intervention, evaluation and monitoring by a medical practitioner.
- Labelling needs to comply with the requirements for an injectable prescription only medicine.
- It does not appear to produce dependency and the abuse potential is low.

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

Schedule entry

Schedule 4 – New Entry

IDARUCIZUMAB

Implementation date: **1 June 2016**.

1.7 Hexyl Aminolevulinate

Scheduling proposal

The proposal is to include hexaminolevulinate, a new chemical entity for a human therapeutic medicine, in Schedule 4 of the SUSMP.

Scheduling application

The delegate considered an application from the Therapeutic Goods Administration (TGA) for the scheduling of hexaminolevulinate.

The Advisory Committee on Medicines Scheduling was not consulted.

Substance summary

Hexyl aminolevulinate (as hydrochloride) is a hexyl ester of 5-aminolevulinic acid (5-ALA or ALA), which is the first specific intermediate of heme biosynthesis.

Hexyl aminolevulinate is indicated as adjunct to standard white light cystoscopy to contribute to the diagnosis and management of bladder cancer in patients with known or high suspicion of bladder cancer.

Scheduling status

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

Hexyl aminolevulinate 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.

Delegates' final decision

The delegate has made a final decision to amend the SUSMP to include hexyl aminolevulinate (as hydrochloride) in Schedule 4, with an implementation date of **1 June 2016**.

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

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

- It is a new chemical entity with no clinical/marketing experience in Australia.
- Hexyl aminolevulinate hydrochloride is a blue light cystoscopy imaging agent.
- Hexyl aminolevulinate is to be used for a medical condition that requires careful diagnosis and management by medical professionals.
- There are limited data on the use of hexyl aminolevulinate in pregnant women.
- There are adverse events, such as haematuria and urinary retention, reported with the use of cystoscopy.

- Cystoscopy should only be performed by health care professionals who are trained specifically in cystoscopy.

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

Schedule entry

Schedule 4 – New Entry

HEXYL AMINOLEVULINATE (AS HYDROCHLORIDE)

Implementation date: **1 June 2016**.