Australian Government
Department of Health
Therapeutic Goods Administration

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

19 May 2016

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

The delegate of the Secretary to the Department of Health hereby give notice of delegate's 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 delegate's 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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Schedule 4 – New Entries

LESINURAD

RANOLAZINE

Implementation date: **1 June 2016.**

1.1 Lesinurad

Scheduling proposal

The proposal is to include lesinurad, 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 lesinurad, a new chemical entity for a human therapeutic medicine. The Advisory Committee on Medicines Scheduling was not consulted.

Substance summary

Lesinurad is a selective uric acid reabsorption inhibitor that inhibits uric acid transporter URAT1. URAT1 is responsible for the majority of the reabsorption of filtered uric acid from the renal tubular lumen. By inhibiting URAT1, lesinurad increases uric acid excretion and thereby lowers serum uric acid (sUA). Lesinurad also inhibits OAT4, a uric acid transporter involved in diuretic-induced hyperuricaemia.

Lesinurad is indicated for the treatment of hyperuricaemia associated with gout in combination with a xanthine oxidase inhibitor.

Scheduling status

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

Lesinurad 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 advice of the Advisory Committee on Prescription Medicines
- 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 lesinurad 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.

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

- It is a new chemical entity with no [clinical/marketing] experience in Australia.
- It has a similar risk profile to probenecid, another medicine that acts on the same enzyme in the kidney.
- It is intended for use in the management of a medical condition that requires ongoing monitoring and medical assessment
- It appears to have a similar risk profile to probenecid, an S4 medicine with additional risks due to potential medicines interactions.

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

Schedule entry

Schedule 4 – New Entry

LESINURAD

Implementation date: **1 June 2016**.

1.2 Ranolazine

Scheduling proposal

The proposal is to include ranolazine, 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 ranolazine, a new chemical entity for a human therapeutic medicine. The Advisory Committee on Medicines Scheduling was not consulted.

Substance summary

Ranolazine is a novel drug and a member of a new pharmacological class. It is thought to exert its anti-ischaemic and anti-anginal effects by inhibition of the late sodium current in cardiac cells. This reduces intracellular sodium accumulation and consequently decreases intracellular calcium overload. Calcium overload during ischaemia is believed to be a major contributor to the impairment in left ventricular relaxation and diastolic compliance. This reduction in cellular calcium overload is expected to improve myocardial relaxation and thereby decrease left ventricular diastolic stiffness. Ranolazine's anti-anginal effects do not appear to be related to changes in heart rate, blood pressure or vasodilatation.

Ranolazine is indicated for use in adults as add-on therapy for the symptomatic treatment of patients with stable angina pectoris who are inadequately controlled or intolerant to first-line anti-anginal therapies (such as beta-blockers and/or calcium antagonists).

Scheduling status

Ranolazine 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 ranolazine 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.

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

- It is a new chemical entity with no clinical/marketing experience in Australia.
- It is intended for the treatment of a medical condition that requires medical management.
- Ranolazine is indicated in adults as add-on therapy for the symptomatic treatment of stable angina pectoris in patients taking maximum tolerated doses of a beta-blocker or a calcium channel blocker and have inadequate symptom control.
- This substance has multiple drug interactions and its use requires careful dose titration and assessment of response in order to avoid side effects.

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

Schedule entry

Schedule 4 – New Entry

RANOLAZINE