Australian Government
Department of Health
Therapeutic Goods Administration

The Royal Australian & New Zealand College of Psychiatrists

Your Health in Mind

shpa

Medicine shortage alert

Discontinuation of Nardil (phenelzine sulfate)

Joint statement from the Therapeutic Goods Administration, the Royal Australian and New Zealand College of Psychiatrists, and the Society of Hospital Pharmacists of Australia

The sponsor of Nardil (phenelzine sulfate) tablets has notified the Therapeutic Goods Administration (TGA) that they can no longer supply this medication in Australia due to global issues with the manufacture of the active pharmaceutical ingredient.

There are no alternative brands of phenelzine on the Australian market. Supplies of phenelzine tablets are very limited.

This document contains:

- information about options for obtaining phenelzine through an alternative access pathway
- advice for prescribers about switching patients from phenelzine to another treatment.

Summary

- Supply of phenelzine sulfate has been discontinued in Australia.
- **Patients taking phenelzine sulfate** should see their doctor as soon as possible about their treatment.
- **General practitioners** should consult a psychiatrist with clinical experience with phenelzine for review of any of their patients taking phenelzine.
- **Psychiatrists** should review all of their patients being treated with phenelzine as soon as possible, and should not initiate any new patients on phenelzine. Clinical management advice is provided below.
- **Pharmacists** should advise patients taking phenelzine to see their doctor regarding their treatment as soon as possible.

Alternative access pathways for phenelzine

In Australia, unapproved phenelzine products may be accessed through alternative pathways, such as the Special Access Scheme (SAS) administered by the TGA. The SAS enables health practitioners to access medicines that are not included in the Australian Register of Therapeutic Goods (ARTG) for an individual patient on a case-by-case basis. **However, supply is not guaranteed and may be interrupted or cease in the future.**

Medicines obtained via the SAS pathway also cannot be subsidised by the Australian Government, and the cost may be prohibitive for some patients. There are physical and psychological risks associated with even brief cessation of phenelzine. This should be kept in mind when considering a SAS application.

Where an SAS application is considered appropriate, the prescriber needs to submit an SAS application to the TGA. The SAS Online Portal is available for electronic applications. The TGA is also available to assist with any application enquiries by phone on 1800 020 653 (free call) or email SAS@health.gov.au. A pharmacist will need to arrange the supply of the medicine with the pharmaceutical company that supplies the SAS medicine.

Under Section 19A of the Therapeutic Goods Act 1989, the TGA may grant approval to a pharmaceutical company to supply an overseas registered product to address a shortage. At the time of publication, phenelzine was not being supplied under Section 19A. However, this may change at any time. Any updates on Section 19A supply will be published on the TGA website.

Further information on accessing medicines during a shortage can be found on the TGA website (at: https://www.tga.gov.au/accessing-medicines-during-shortage).

Switching from phenelzine to another treatment

Key points for prescribers

- Identify patients taking phenelzine and contact them for review as soon as possible.
- Ensure that no new patients start treatment on phenelzine.
- Discuss alternative access pathways such as the Special Access Scheme (SAS), with the patient. Consider the patient's ability to sustain a supply of medicine via the SAS (e.g., cost, and supply uncertainty). There are physical and psychological risks associated with even brief cessation of phenelzine.
- If switching from phenelzine to another anti-depressant, see the below clinical management advice, under the close supervision of a psychiatrist.

  Patients with a higher risk of withdrawal symptoms or significant rebound depression should be treated as an in-patient in a hospital setting

Clinical management advice

Many patients will have used phenelzine for many years, often with a resolution of symptoms no other anti-depressant has achieved. There will be considerable anxiety and distress in this community about this discontinuation. This will be enhanced by a lack of experience in these medicines by GPs and psychiatrists. General practitioners should consult with a psychiatrist regarding treatment options and transition. Ideally, a patient on phenelzine should be reviewed by a psychiatrist. It will be appropriate for some patients to have a trial of being medicine free. Again, it is likely there will be considerable anxiety about this, and many patients will wish to switch to another antidepressant.

Phenelzine is a non-selective and irreversible monoamine oxidase inhibitor (MAOI) of the hydrazine class. The only remaining non-selective irreversible MAOI available in Australia is tranylcypromine. Tranylcypromine is a non-hydrazine MAOI and differs significantly from phenelzine in some aspects, as outlined below. Tranylcypromine may be an appropriate alternative antidepressant for some patients; however, it is important to consider an individual's physical health and psychiatric history, and whether a MAOI is still appropriate. The TGA is closely monitoring supply of tranylcypromine. Please refer to the TGA website for any supply update.

Reducing and stopping phenelzine

The dose of phenelzine should ideally be tapered down over a minimum of two weeks, starting immediately in light of very limited supplies. We acknowledge that a faster taper may be required in some cases due to rapidly declining stock. Irreversible MAOIs are associated with a high risk of discontinuation symptoms, such as nightmares, headache, irritability, feeling cold, disorientation, hypomania, nausea, sweating, palpitations, myoclonic jerks and, rarely, catatonia or psychosis. Significant discontinuation symptoms should be closely monitored and managed by the GP and psychiatrist.

It is important to maintain MAOI dietary and co-prescribed medication precautions for at least 10 days after stopping phenelzine.

Key points for reducing and stopping phenelzine

- Reduce dose of phenelzine by tapering over a minimum of two weeks.
- Monitor and manage discontinuation symptoms, under the close supervision of a psychiatrist.
- Maintain MAOI dietary and co-prescribed medicine precautions for at least 10 days after stopping phenelzine.
- Where transitioning to another anti-depressant, follow specific guidance on washout periods as detailed in this advice.

Switching from phenelzine to tranylcypromine (Parnate)

Taper and stop phenelzine as above. After a two-week washout period, tranylcypromine can be started at half the usual dose, i.e. 5 mg twice daily. After one week, cautiously increase the dose as needed. As a general guide, tranylcypromine 10 mg is approximately equivalent to phenelzine 15 mg. Careful observation of the patient is essential throughout, due to the risk of hypertensive crisis and serotonin toxicity.

Although phenelzine may have occasionally been used in combination with other antidepressants, this is not advised with tranylcypromine. There is a higher risk of hypertensive crisis with tranylcypromine than with other MAOIs, therefore MAOI dietary precautions should be observed closely. Tranylcypromine also has a higher incidence of severe drug interactions and care should be taken to review the patient's complete medication regime. Because tranylcypromine has additional amphetamine-like effects, it is more stimulating than phenelzine and should not be given any later than 3pm because of the risk of insomnia.

Switching from phenelzine to other antidepressants

Taper and stop phenelzine as above, allow a minimum ten-day washout period, and then start the new antidepressant cautiously. If switching to a strongly serotonergic antidepressant such as an SSRI or clomipramine, a longer washout period may be safer due to the risk of serotonin syndrome. If switching to any tricyclic antidepressant, low initial doses are recommended.

For most patients switching to an alternative antidepressant can be achieved as an outpatient with close monitoring for withdrawal symptoms and a return of symptoms of depression and anxiety (e.g. panic). If withdrawal symptoms become severe or if there is a significant rebound depression, particularly with the emergence of suicidal thoughts, hospital admission may be necessary.

Switching from phenelzine to other treatments

Many patients on phenelzine will have had remission of symptoms and will probably expect further treatment with medication. Psychotherapy, particularly Cognitive Behaviour Therapy, should be considered, either with a further anti-depressant, or on its own.

Acknowledgment: This advice for Australia draws on the Joint Guidance developed for the New Zealand context (May 2020).

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