

## GP information sheet - Phenzelzine (Nardil®)

Phenzelzine is a non-reversible monoamine oxidase inhibitor (MAOI), a type of antidepressant that over the years has become less popular as newer and safer antidepressants have been developed. Though effective, it has a range of potential side-effects and interactions that mean patients need to be carefully selected to ensure they understand the risks and dietary restrictions, linked to the drug's use. Younger GPs may have never prescribed a non-reversible MAOI, so this information sheet has been produced to provide them with some background information when asked to take over prescribing once a patient has successfully responded to treatment and the dose has been stabilized. **It is only suitable for initiation by a specialist.**

### Indication

It has been found to be effective in depressed patients clinically characterized as 'atypical', 'non endogenous', 'neurotic' or where treatment with other antidepressants has failed. These patients often have mixed anxiety and depression and phobic or hypochondriacal features. There is less conclusive evidence of its usefulness with severely depressed patients with endogenous features.

### Dosage

One 15mg tablet three times a day. A response is usually seen within the first week. If no response is evident after two weeks, the dosage may be increased to a maximum of one 15mg tablet four times a day in the community. Doses of up to two 15mg tablets three times a day may be used during an inpatient stay, but needs to be reduced before discharge from the ward. The effectiveness of the drug may not become apparent in less than 4 weeks therapy. After a satisfactory response has been achieved, the dosage may be reduced very gradually to a suitable maintenance level. This may be as low as one 15mg tablet every other day. Postural hypotension may be an unwanted effect of phenzelzine in the elderly. Elderly patients as a group tend to receive multiple drug therapies and the possibility of increased risk of drug interactions should be borne in mind. Phenzelzine should only be used with great caution in elderly patients. Despite these problems, phenzelzine has been found to be useful in the treatment of depression in the elderly.

### Stopping and switching

Ideally phenzelzine should be withdrawn gradually over a period of four weeks. If another antidepressant is to be started, there should be a period of two weeks from discontinuation to initiation of the new antidepressant. The Sussex Partnership NHS Foundation Trust has antidepressant guidance on its website including advice on how to switch antidepressants (appendix 2) and what discontinuation symptoms may arise during withdrawal (appendix 3). This guidance is available at the link below: [www.sussexpartnership.nhs.uk/node/1451/attachment](http://www.sussexpartnership.nhs.uk/node/1451/attachment)

### Contraindications

- Phenzelzine should not be used in patients who are hypersensitive to any of the ingredients or with phaeochromocytoma, cerebrovascular disease, congestive heart failure, a history of liver disease or with abnormal liver function tests. Phenzelzine should not be administered at the same time as, or within 14 days of, treatment with other MAOIs, buspirone, or dibenzazepine derivative drugs (including tricyclic antidepressant agents, perphenazine or carbamazepine). In the cases of clomipramine and imipramine, 3 weeks should be left before starting phenzelzine therapy. It is recognized that there is some division of consultant opinion with respect to concomitant use of MAOIs and tricyclic antidepressants.
- There have been reports of serious reactions (including hyperthermia, rigidity, myoclonic movements and death) when serotonin reuptake inhibitors or serotonin/noradrenaline inhibitors (e.g. venlafaxine) have been combined with MAOIs. Therefore, phenzelzine should not be used in combination with these drugs and before initiating phenzelzine, a sufficient amount of time must be allowed for clearance of these drugs and their metabolites. For example, five weeks in the case of fluoxetine and two weeks with paroxetine. Conversely, these drugs should not be started within 14 days of discontinuing phenzelzine. Phenzelzine should not be used in combination with guanethidine, dextromethorphan, or with CNS depressants such as alcohol and narcotic analgesics. Death has been reported in patients receiving a single dose of pethidine.

## Cautions

- Patients with a history of suicide-related events, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment are known to be at greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment initiation and should remain under the care of a specialist until the dose is stable and benefits seen.
- **Ideally phenelzine should be withdrawn two weeks before elective surgery/dentistry**, i.e. ideally withdrawal should start six weeks before the procedure (see 'Stopping and switching'). Patients will be warned on initiation and at any review of the need to let healthcare staff planning dentistry or surgery that they are on phenelzine.
- Phenelzine should not be given with cocaine or local anaesthesia containing sympathomimetic vasoconstrictors.
- Phenelzine should be used only with great caution in agitated patients or those who have cardiovascular disease, epilepsy, blood dyscrasias, porphyria or diabetes; and in patients taking diuretics.
- Patients should be reminded that consuming certain foods and drinks may risk a hypertensive crisis and if any of the following symptoms occur: headache, light-headedness, dizziness, flushing of the face, pounding of the heart, stiff neck, or nausea and vomiting, they should not take any more doses and contact their doctor straight away. If not available, they should go to casualty at the nearest general hospital and explain they are taking phenelzine. These symptoms usually occur about two hours after eating or drinking something with tyramine in it. A leaflet explaining about food interactions is available on the Trust's website: [www.sussexpartnership.nhs.uk/node/1667/attachment](http://www.sussexpartnership.nhs.uk/node/1667/attachment)
- Blood pressure should be observed frequently to detect any pressor response and therapy discontinued if palpitations or frequent headaches occur.
- Patients should also be closely followed for symptoms of postural hypotension. Hypotensive side effects have occurred in hypertensive as well as normotensive and hypotensive patients.
- Due to the possibility of patients undergoing "Withdrawal Syndrome" abrupt withdrawal of phenelzine should be avoided where possible, see 'Stopping and switching' advice above.
- Phenelzine may cause excessive stimulation in patients with schizophrenia; in manic-depressive states it may result in a swing from a depressive to a manic phase.

## Interaction with other medicinal products and other forms of interaction

- Patients should be warned against self-medication, particularly cold cures, cough cures, hay fever medications, anti-appetite medicines, weight-reducing preparations and "pep" pills and about potential food interactions (see above for more information and a link to an appropriate leaflet).
- Patients under treatment with phenelzine should avoid high protein food that has undergone breakdown by ageing, fermentation, pickling, smoking or bacterial contamination. Patients should avoid cooked or plain cheese, Oxo, Bovril, Marmite, brewer's yeast, etc. during treatment and up to 14 days after ceasing treatment. Flavoured textured vegetable protein, hung game, pickled herrings, dry sausage (salami, pepperoni etc.), liver, yoghurt, broad bean pods, fermented soya bean extract, and excessive amounts of chocolate may also present a hazard. Patients should not consume alcoholic drink or non-alcoholic beers, lagers and wines and excessive amounts of tea and coffee should be avoided.
- Where a reaction between phenelzine and certain foodstuffs occurs, the intensity of the reaction is usually related to the tyramine content of the food. The reaction is now well recognized and serious hypertensive episodes are extremely rare. Should such a reaction occur, the patient should be sent to A & E and the hypertension should be controlled promptly by slow administration of phentolamine.
- Phenelzine may also potentiate the effects of alcohol.
- Phenelzine may potentiate the action of pethidine, morphine, adrenaline, amphetamines and other sympathomimetic amines such as fenfluramine, ephedrine, phenylpropanolamine, dopamine and levodopa (see also Contraindications). Phenelzine may also potentiate the effects of antihypertensives, hypoglycaemic agents, sympathomimetics, anti-Parkinson drugs, antimuscarinics, local anaesthetics and CNS depressants, including barbiturates.

- It is suggested that phenelzine is not administered at the same time as, or within 14 days of, treatment with bupropion or 5HT<sub>1</sub> agonists.
- It is suggested that phenelzine is not administered at the same time as anti-epileptics, altretamine, doxapram, tetrabenazine, oxypertine or clozapine.
- The combination of MAOIs and tryptophan has been reported to cause behavioural and neurological symptoms.

### **Use during pregnancy and lactation**

- Do not use during pregnancy, especially during the first and last trimesters, unless there are compelling reasons. There is no evidence as to drug safety in human pregnancy nor is there evidence from animal work that it is free from hazard.
- It is not known if phenelzine is excreted in breast milk. Because of the potential for serious adverse effects to the infant, a decision should be made whether to discontinue the drug or not to breast-feed.

### **Effects on ability to drive and use machines**

- Phenelzine produces adverse effects on driving ability.

### **Undesirable effects**

- Side-effects tend to be mild or moderate in severity, often subsiding as treatment continues, and can be minimized by adjusting dosage; rarely is it necessary to discontinue phenelzine.
- The most important reaction associated with phenelzine is the occurrence of hypertensive crises, which have been associated with intracranial bleeding and have sometimes been fatal.
- Cases of suicidal ideation and suicidal behaviours have been reported during phenelzine therapy or early after treatment discontinuation.
- Common side-effects include: dizziness, drowsiness, weakness and fatigue, oedema, gastro-intestinal disturbances (nausea, vomiting, dryness of the mouth, constipation), insomnia, blurred vision, adverse effects on driving ability, postural hypotension, twitching, myoclonic movements, hyperreflexia, elevated serum transaminases and anorgasmia.
- Uncommon side-effects are headache, nervousness, euphoria, paraesthesia, sweating, increased appetite and weight, rash, pruritus, difficulty in micturition, muscle tremor, peripheral neuritis, behavioural changes, arrhythmias, convulsions, impotence and delayed ejaculation, purpura, blood dyscrasias, jitteriness, palilalia, nystagmus, hypernatraemia, glaucoma, lupus-like illness, confusion, hallucinations and elevated liver enzymes.
- Other severe side-effects have been reported very rarely, including isolated reports in some cases. These include: ataxia, shock-like coma, toxic delirium, neuroleptic malignant syndrome (occasionally fatal), manic reaction, acute anxiety reaction, precipitation of schizophrenia, transient respiratory and cardiovascular depression following ECT, fatal progressive necrotising hepatocellular damage, reversible jaundice, hypermetabolic syndrome, oedema of the glottis and fever associated with increased muscle tone.
- Hyponatraemia (usually in the elderly and possibly due to inappropriate secretion of antidiuretic hormone) has been associated with all types of antidepressants and should be considered in all patients who develop drowsiness, confusion or convulsions while taking an antidepressant.
- Withdrawal may be associated with nausea, vomiting and malaise. An uncommon withdrawal syndrome following abrupt withdrawal of phenelzine has been infrequently reported. Signs and symptoms of this syndrome generally commence 24 to 72 hours after drug discontinuation and may vary from vivid nightmares and agitation to frank psychosis and convulsions. This syndrome generally responds to reinstatement of low-dose phenelzine therapy followed by cautious downward titration and discontinuation.

### **References**

1. Nardil 15mg tablets [phenelzine – Archimedes Pharma UK Ltd]. Electronic Medicines Compendium (8<sup>th</sup> December 2015). Available from <http://www.emc.medicines.org.uk> (29<sup>th</sup> December 2015).
2. Guidance on the use of Antidepressants for the Treatment of Unipolar Depression and Anxiety Spectrum Disorders in Adults – version 3. Sussex Partnership NHS Foundation Trust. October 2014