HERPC

Hull & East Riding Prescribing Committee

Prescribing Framework for Phenelzine in the treatment of depressive illness

Patients Name:…….…. NHS Number: ……

Patients Address:……..……(Use addressograph sticker)

GP's Name:……..

Communication

We agree to treat this patient within this Prescribing Framework

Specialist Prescriber's Name…… Prof Reg. No. ……

Specialist Prescriber's Signature…… Date:…….

Where prescriber is not a consultant:
Consultant's Name: …… GMC No ……..

Consultant's Signature ……..... ……. Date:…….

GP's Signature:…… Date:……..

GP's Name (if different from listed above)……..

The front page of this form should be completed by the specialist and the form sent to the patient's general practitioner.
The patient's GP should sign and send back to specialist, to confirm agreement to enter into shared care arrangement. If the General Practitioner is unwilling to accept prescribing responsibility for the above patient the specialist should be informed within two weeks of receipt of this framework and specialist's letter.

Full copy of framework can also be found at : http://www.hey.nhs.uk/amber.htm

APPROVAL PROCESS

Written by:	***Jackie Stark, Principal Pharmacist HFT*** ***Wendy Tucker, Pharmacist*** ***Reviewed by Karen Thompson , Specialist Pharmacist May 2017*** ***Reviewed by Wendy Storey Feb 2021***
Consultation process:	***Include Specialist Team***
Approved by:	***Include MMIG, LMC, HFT DTC***
Ratified by:	***HERPC***
Review date:	***2 years*** **April 2024**

1. Background

Monoamine-oxidase inhibitors are used much less frequently than tricyclic and related antidepressants, or SSRIs and related antidepressants because of the dangers of dietary and drug interactions and the fact that it is easier to prescribe MAOIs when tricyclic antidepressants have been unsuccessful than vice versa.

MAOIs inhibit monoamine oxidase, thereby causing an accumulation of amine neurotransmitters. The metabolism of some amine drugs such as indirect-acting sympathomimetics (present in many cough and decongestant preparations) is also inhibited and their pressor action may be potentiated; the pressor effect of tyramine (in some foods, such as mature cheese, pickled herring, broad bean pods, and Bovril®, Oxo®, Marmite® or any similar meat or yeast extract or fermented soya bean extract) may also be dangerously potentiated. These interactions may in extreme cases cause a dangerous rise in blood pressure. An early warning symptom may be a throbbing headache. Phenelzine should therefore be discontinued immediately upon the occurrence of palpitations or frequent headaches. Patients should be advised to eat only fresh foods and avoid food that is suspected of being stale or 'going off'. This is especially important with meat, fish, poultry or offal; game should be avoided. The danger of interaction persists for up to 2 weeks after treatment with MAOIs is discontinued. Patients should also avoid alcoholic drinks or de-alcoholised (low alcohol) drinks.

NICE CG90 recommends that non-reversible monoamine oxidase inhibitors (MAOIs), should normally be prescribed only by specialist mental health professionals.

The guidelines should be read in conjunction with the general guidance on prescribing matters given in EL (91) 127 "Responsibility for prescribing between hospitals and GPs".

2. Indication

Depressive Illness. Phenelzine should be initiated in secondary care under specialist supervision. Once a patient's mental state and medication have been stabilised they may be considered suitable for shared care between the specialist and GP.

Phenelzine is licensed for the treatment of symptoms of depressive illness especially where phobic symptoms are present or where treatment with other types of anti-depressants has failed. It is not recommended for mild depressive states resulting from temporary situational difficulties

3. Dose

15 mg 3 times daily, increased if necessary to 4 times daily after 2 weeks (hospital patients, max. 30 mg 3 times daily), then reduced gradually to lowest possible maintenance dose (15 mg on alternate days may be adequate). The last dose of the day should be taken before 3pm. The effectiveness of the drug may not become apparent in less than 4 weeks therapy.

Child; not recommended.

Elderly; same as adult dose but side effects may be more common, risk of postural hypotension requires great caution in use.

4. Duration of treatment

NICE guidance states that people with depression who benefit from treatment with antidepressants are advised to continue with treatment for at least 6 months after remission, extending to at least 2 years for people at risk of relapse.

5. Contraindications

Phenelzine 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. Phenelzine sulphate 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 phenelzine therapy. It is recognised 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, Phenelzine should not be used in combination with these drugs and before initiating Phenelzine, 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 phenelzine. Phenelzine 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.

Phenelzine is not indicated in the manic phase

6. Cautions

Suicide/suicidal thoughts or clinical worsening

Depression is associated with an increased risk of suicidal thoughts, self harm and suicide (suicide-related events). This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery.

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. A meta-analysis of placebo-controlled clinical trials of antidepressant drugs in adult patients with psychiatric disorders showed an increased risk of suicidal behaviour with antidepressants compared to placebo in patients less than 25 years old. Close supervision of patients and in particular those at high risk should accompany drug therapy especially in early treatment and following dose changes. Patients (and caregivers of patients) should be alerted about the need to monitor for any clinical worsening, suicidal behaviour or thoughts and unusual changes in behaviour and to seek medical advice immediately if these symptoms present.

Phenelzine should be withdrawn two weeks before elective surgery/dentistry.

Phenelzine should not be given with cocaine or local anaesthesia containing sympathomimetic vasoconstrictors. The possible combined hypotensive effects of Phenelzine and spinal anaesthesia should be kept in mind.

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.

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.

Phenelzine may cause excessive stimulation in schizophrenic patients; in manic-depressive states it may result in a swing from a depressive to a manic phase.

Caution should be exercised if the patient undergoes concurrent electroconvulsive therapy (ECT).Acute porphyrias; avoid in agitated patients; blood disorders; cardiovascular disease; diabetes mellitus; elderly (great caution); epilepsy; severe hypertensive reactions to certain drugs and foods

Drowsiness:- may affect performance of skilled tasks (e.g. driving)

7. Adverse effects

Side-effects tend to be mild or moderate in severity, often subsiding as treatment continues, and can be minimised 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 (see section 6 suicidal thoughts)

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 reinstitution of low-dose Phenelzine therapy followed by cautious downward titration and discontinuation.

8. Interactions

Potentially life-threatening hypertensive crisis can develop in those taking MAOIs who eat tyramine-rich food (such as mature cheese, salami, pickled herring, Bovril®, Oxo®, Marmite® or any similar meat or yeast extract or fermented soya bean extract, and some beers, lagers or wines) or foods containing dopa (such as broad bean pods). Avoid tyramine-rich or dopa-rich food or drinks with, or for 2 to 3 weeks after stopping, the MAOI.

Details of contraindications, cautions, drug interactions and adverse effects listed above are not exhaustive. For further information always check with BNF www.bnf.org.uk or SPC (www.medicines.org.uk).

9. Monitoring

Regular blood pressure measurement is recommended during initiation and routine checks should be made during maintenance.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 Depression is associated with an increased risk of suicidal thoughts, self harm and suicide (suicide-related events). This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery.

10. Information to patient

Verbal information along with the patient information leaflet from the Choice & Medication website will be provided. It is essential that the patient has a good understanding of the food restrictions and is able to adhere to these. Information on these food risks will be given to the patient prior to starting treatment.

11. Responsibilities of clinicians involved

Stage of Treatment	Hospital Specialist	General Practitioner
Initiation	• Prescribing until maintenance regime established. • Discussion of risks and benefits with patients and carers in particular the dietary restrictions and interactions with medication, including those available over the counter • Provision of written information on the use, side effects and dietary restrictions	• Provide details of any concurrent medication, coexisting health problems and compliance issues to the specialist
Maintenance	• Provide details of concurrent medication prescribed via secondary psychiatric care to GP. • Provide details of patient follow up including care plan. • Inform GP of any identified problems e.g. compliance with treatment. • Provide details of mental health key worker if appropriate.	• Continued discussion of risks and benefits of medication with patients and carers as required. • Prescribing once maintenance doses established. Switching or discontinuation should only be done through the specialist • Continued monitoring (see Monitoring section above) as agreed with secondary care and referral back to secondary care if patient becomes non-compliant and/or if mental state deteriorates • Respond to adverse reactions and advise on concomitant medication. • Update specialist on any changes in medical condition or prescribed concomitant medication until discharged from specialist services
Switching	• Provide support to GP in response to queries about switching antidepressants	• Seek support from specialist when considering switching antidepressants

Contact Details:
During Office hours:
Mental Health Response Team 01482 301701
Pharmacy Department Humber Teaching NHS Foundation Trust 01482 389269
Out of hours: On Call Psychiatrist via Miranda House- Tel: 01482 216624