HERPC

*Hull & East Riding Prescribing Committee*

# Prescribing Framework for Isocarboxazid 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

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|---|---|
| **Written by:** | ***Jackie Stark, Principal Pharmacist HFT***<br>***Wendy Tucker, Pharmacist***<br>*Reviewed by Karen Thompson Specialist Pharmacist May 2017, reference to SmPC last revised February 2015*<br>*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*** **March 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, section 8.0) 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, Isocarboxazid 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. Isocarboxazid 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.

3. **Dose:** Initially 30mg daily in single or divided doses until improvement occurs (increased after 4 weeks if necessary to max 60mg daily for 4-6 weeks under close supervision) then reduced to usual maintenance dose 10-20mg daily (but up to 40mg daily may be required); Half the usual maintenance dose may be sufficient in the elderly; 5-10mg daily; Child not recommended

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**
   Cerebrovascular disease, severe cardiovascular disease, phaeochromocytoma, liver impairment, actual or suspected phaeochromocytoma not indicated in manic phase.

   Selective serotonin reuptake inhibitors (SSRIs): Cases of serious and sometimes fatal reactions (serotonin syndrome) have been reported in patients receiving monoamine oxidase inhibitors (MAOIs) in combination with SSRIs, and in patients who have recently discontinued an SSRI and have been started on a MAOI. Treatment with SSRIs should only be started 2 weeks after discontinuation of Isocarboxazid.
   Conversely, treatment with Isocarboxazid should not be started until at least a week after stopping a SSRI or related anti-depressant (at least 5 weeks for fluoxetine).

   Do not give Isocarboxazid until at least two weeks after stopping treatment with other MAOIs.

6. **Cautions**

The drug should be used cautiously in patients with impaired renal function, to prevent accumulation taking place, and also in the elderly or debilitated and those with cardiovascular disease, diabetes or blood dyscrasias. Caution should also be exercised in patients undergoing concurrent electroconvulsive therapy; monitor blood pressure (risk of postural hypotension and hypertensive responses—discontinue if palpitations or frequent headaches); if possible avoid abrupt withdrawal; severe hypertensive reactions to certain drugs and foods Avoid in acute porphyria

In restless or agitated patients, Isocarboxazid may precipitate states of excessive excitement. Isocarboxazid appears to have varying effects in epileptic patients; while some have a decrease in frequency of seizures, others have more seizures.

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.

Concurrent administration of Isocarboxazid with other central nervous system depressants (especially barbiturates and phenothiazines), stimulants, local anaesthetics, ganglion-blocking agents and other hypotensives (including methyl-dopa and reserpine), diuretics, vasopressors, anticholinergic drugs and hypoglycaemic agents may lead to potentiation of their effects. This should be borne in mind if dentistry, surgery or a change in treatment of a patient becomes necessary during treatment with Isocarboxazid.(**see BNF for interactions**)

All patients taking Isocarboxazid should be warned against self-medication with proprietary 'cold-cure' preparations and nasal decongestants and advised of the dietary restriction (see BNF for interactions) .

Avoid use in pregnancy, especially during the first and last trimesters, unless there are compelling reasons. Evidence for safety in human pregnancy is lacking, nor is there evidence from animal work that it is free from hazard As there is no information on the secretion of the drug into breast milk, Isocarboxazid is also contra-indicated during lactation.

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

7. **Adverse effects**

In general, Isocarboxazid is well tolerated by the majority of patients. Side-effects, if they occur, are those common to the group of monoamine oxidase inhibitors.

The most frequently reported have been orthostatic hypotension, associated in some patients with disturbances in cardiac rhythm, peripheral oedema, complaints of dizziness, dryness of the mouth, nausea and vomiting, constipation, blurred vision, insomnia, drowsiness, weakness and fatigue. These side-effects can usually be controlled by dosage reduction.

There have been infrequent reports of mild headaches, sweating, paraesthesia, peripheral neuritis, hyperreflexia, agitation, overactivity, muscle tremor, confusion and other behavioural changes, difficulty in micturition, impairment of erection and ejaculation, and skin rashes. Although rare, blood dyscrasias (purpura, granulocytopenia) have been reported. Response to Isocarboxazid may be accompanied by increased appetite and weight gain.

Cases of suicidal ideation and suicidal behaviours have been reported during Isocarboxazid therapy or early after treatment 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.

**For details of contraindications, cautions and drug interactions 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.
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.
The manufacturer recommends regular monitoring of liver function should be carried out during Isocarboxazid therapy. As no further advice on what would be considered regular, prescribers should consider yearly checks, in line with suggestions for other drugs. If there is any evidence of a hepatotoxic reaction, the drug should be withdrawn immediately.
The drug should be used cautiously in patients with impaired renal function, to prevent accumulation taking place, and also in the elderly or debilitated and those with cardiovascular disease, diabetes or blood dyscrasias.

**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.<br>• Discussion of risks and benefits with patients and carers in particular the dietary restrictions and interactions with medication, including those available over the counter | • Provide details of any concurrent medication, coexisting health problems and compliance issues to the specialist |

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| | • Provision of written information on the use, side effects and dietary restrictions | |
| Maintenance | • Provide details of concurrent medication prescribed via secondary psychiatric care to GP.<br>• Provide details of patient follow up including care plan.<br>• Inform GP of any identified problems e.g. compliance with treatment.<br>• Provide details of mental health key worker if appropriate. | • Continued discussion of risks and benefits of medication with patients and carers as required.<br>• Prescribing once maintenance doses established. Switching or discontinuation should only be done through the specialist<br>• 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<br>• Respond to adverse reactions and advise on concomitant medication.<br>• 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