SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Isocarboxazid Tablets 10mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10mg Isocarboxazid.

Excipient(s) with known effect
Each tablet contains 100mg Lactose

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of the symptoms of depressive illness.

4.2 Posology and method of administration

Isocarboxazid Tablets are for oral administration.

Adults

A daily dose of 30mg, in single or divided doses, should be given until improvement is obtained. The maximal effect is only observed after a period varying from 1 - 4 weeks. If no improvement has been seen by 4 weeks, doses

up to 60mg may be tried, according to the patient's tolerance, for no longer than 4 - 6 weeks, provided the patient is closely monitored because of the increased risk of adverse reactions occurring.

Once the optimal effect is achieved, the dose should be reduced to the lowest possible amount sufficient to maintain the improvement. Clinical experience has shown this to be usually 10 - 20mg daily but up to 40mg daily may be required in some cases.

The elderly

The elderly are more likely to experience adverse reactions such as agitation, confusion and postural hypotension. Half the normal maintenance dose may be sufficient to produce a satisfactory clinical response.

Children

Isocarboxazid Tablets are not indicated for paediatric use.

4.3 Contraindications

Isocarboxazid is contra-indicated in patients with any impairment of hepatic function, cerebrovascular disorders or severe cardiovascular disease, and in those with actual or suspected phaeochromocytoma.

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).

Hypersensitivity to the active substance or any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Some monoamine oxidase inhibitors have occasionally caused hepatic complications and jaundice in patients, therefore regular monitoring of liver function should be carried out during Isocarboxazid therapy. 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.

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.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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.

4.5 Interaction with other medicinal products and other forms of interaction

Like other monoamine oxidase inhibitors, Isocarboxazid potentiates the action of a number of drugs and foods. Patients being treated with a monoamine oxidase inhibitor should not receive indirectly-acting sympathomimetic agents such as amphetamines, metaraminol, fenfluramine or similar anorectic agents, ephedrine or phenylpropanolamine (contained in many proprietary 'cold-cure' medications), dopamine or levodopa. Patients should also be warned to avoid foodstuffs and beverages with a high tyramine content: mature cheeses (including processed cheeses), hydrolysed yeast or meat extracts, alcoholic beverages, particularly heavy red wines such as Chianti, non-alcoholic beers, lagers and wines, and other foods which are not fresh and are fermented, pickled, 'hung', 'matured' or otherwise subject to protein degradation before consumption. Broad bean pods (which contain levodopa) and banana skins may also present a hazard. In extreme cases interactions may result in severe hypertensive episodes. Isocarboxazid should therefore be discontinued immediately upon the occurrence of palpitations or frequent headaches.

Pethidine should not be given to patients receiving monoamine oxidase inhibitors as serious, potentially fatal reactions, including central excitation, muscle rigidity, hyperpyrexia, circulatory collapse, respiratory depression and coma, can result. Such reactions are less likely with morphine, but experience of the interaction of Isocarboxazid with narcotic analgesics other than pethidine is limited and extreme caution is therefore necessary when administering morphine to patients undergoing therapy with Isocarboxazid.

Isocarboxazid should not be administered together with other monoamine oxidase inhibitors, selective serotonin reuptake inhibitors (SSRIs) or most tricyclic antidepressants (clomipramine, desipramine, imipramine, butriptyline, nortriptyline or protriptyline). Although there is no proof that combined therapy will be effective, refractory cases of depression may be treated with Isocarboxazid in combination with amitriptyline or trimipramine, provided appropriate care is taken. Hypotensive and other adverse reactions are likely to be increased.

An interval of 1 - 2 weeks should be allowed after treatment with Isocarboxazid before the administration of antidepressants with a different mode of action or any other drug which may interact. A similar interval is recommended before administration of Isocarboxazid when another antidepressant has been used; in the case of drugs with a very long half-life (such as fluoxetine), it may be advisable to extend this interval.

Isocarboxazid should be discontinued for at least 2 weeks prior to elective surgery requiring general anaesthesia. The anaesthetist should be warned that a patient is being treated with Isocarboxazid, in the event of emergency surgery being necessary. 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.

All patients taking Isocarboxazid should be warned against self-medication with proprietary 'cold-cure' preparations and nasal decongestants and advised of the dietary restrictions listed under 'warnings'.

With Isocarboxazid, as with other drugs acting on the central nervous system, patients should be instructed to avoid alcohol while under treatment, since the individual response cannot be foreseen.

4.6 Fertility, pregnancy and lactation

Do not use in 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. In addition, the effect of psychotropic drugs on the fine brain structure of the foetus is unknown. Since there is no information on the secretion of the drug into breast milk, Isocarboxazid is contra-indicated during lactation.

4.7 Effects on ability to drive and use machines

Like all medicaments of this type, Isocarboxazid may modify patients' reactions (driving ability, operation of machinery etc.) to a varying extent, depending on dosage and individual susceptibility.

4.8 Undesirable 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, paraesthesiae, 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 (see Section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card Scheme in the Google Play or Apple App Store.

4.9 Overdose

The primary symptoms of overdosage include dizziness, ataxia and irritability. In acute cases, hypotension or hypertension, tachycardia, pyrexia, psychotic manifestations, convulsions, respiratory depression and coma may occur and continue for 8 - 14 days before recovery.

Gastric lavage should be performed soon after ingestion and intensive supportive therapy carried out. Sympathomimetic agents should not be given to treat hypotension but plasma expanders may be used in severe cases.

Hypertensive crises may be treated by pentolinium or phentolamine, severe shock with hydrocortisone. Diazepam may be used to control convulsions or severe excitement. Dialysis is of value in eliminating the drug in severe cases.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Monoamine oxidase inhibitors, non-selective. ATC code: N06AF01

Isocarboxazid is a monoamine oxidase inhibitor, effective in small doses. Its antidepressant action is thought to be related to its effect on physiological amines such as serotonin and noradrenaline, and this effect is cumulative and persistent.

5.2 Pharmacokinetic properties

Isocarboxazid is readily absorbed after oral administration. Most of the drug-related material is excreted as metabolites in the urine.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Starch
Talc
Magnesium stearate
Gelatin
Iron oxide yellow El72
Iron oxide red E172

6.2 Incompatibilities

None known.

6.3 Shelf life

Three years.

6.4 Special precautions for storage

The recommended maximum storage temperature is 25^{o}C.
Isocarboxazid Tablets should be stored in well-closed containers.

6.5 Nature and contents of container

HDPE bottles with white child resistant caps, containing 56 tablets.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

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