

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Parnate 10mg Coated tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each coated tablet contains 10mg tranylcypromine as tranylcypromine sulphate.
Excipients: contains 3.2mg of Carmoisine (E122) & Ponceau 4R (E124) and 55.64mg of sucrose per tablet.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Coated tablet.

Geranium-red coloured, biconvex, sugar-coated tablets marked FW251 on one side only.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Parnate is indicated for use in the management of depression but excluding mild depressive states resulting from temporary situational difficulties.

4.2 Posology and method of administration

Route of administration: Oral

Adults only: The usual daily dosage is 20mg in divided doses (morning and afternoon) with a subsequent to 30mg if necessary (additional tablet at mid-day). After optimal control, the maintenance dose is reached by gradual decrements, usually to a level of 10mg daily. When used during electroconvulsive therapy the usual dose is 10mg twice daily during the course and 10mg daily thereafter.

Elderly: Use with great caution and at lower dosage.

4.3. Contraindications

Do not give Parnate less than a week after stopping treatment with any other antidepressant drug including other MAO Inhibitors, because of persisting effects, then give half the usual dosage for the first week. Similarly, after stopping Parnate allow at least two weeks to elapse before starting treatment with any drug or

ingesting any food that may interact.

Do not use in conjunction with food containing significant amounts of tyramine (See section 4.5).

Do not give Parnate with indirectly acting sympathomimetic amines such as Amphetamine, Fenfluramine or similar anti-obesity agents, Ephedrine or Phenylpropranolamine (certain cold cures may contain such agents) or with Levodopa or Dopamine, as severe hypertensive reactions may result; with pethidine and closely related narcotic analgesics, and nefopam, as potentiation may occur; with dextromethorphan as a similar reaction has been reported; with other MAO Inhibitors, as symptoms of overdose are possible; or with Buspirone, since increased blood pressure may occur.

Reports of hyperactivity, hypertonicity, hyperpyrexia, coma and death have been associated with the use of Parnate in combination with tricyclic antidepressants; Tetracyclic antidepressants should also be avoided. Use of MAO inhibitors with or after fluvoxamine has been reported to produce a serotonin syndrome, sometimes fatal.

Do not use Parnate in patients with actual or suspected cerebrovascular disease or severe cardiovascular disease; in those with actual or suspected pheochromocytoma, or with hyperthyroidism; or in those with known liver damage or blood dyscrasias

4.4. Special Warnings and Precautions for use

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.

Use Parnate with great caution in patients who are elderly or who have cardiovascular disease, epilepsy (as tranylcypromine as a variable effect on the convulsive threshold), liver dysfunction, or those with a previous history of dependence on drugs and alcohol.

Patients should be specifically asked if they are taking any other medication because of the possibility of drug interactions. Parnate should be discontinued at least two weeks before elective surgery because of the potential for interaction. Severe hypertensive reactions should be treated at once by reducing the blood pressure. Slow intravenous injection of 5mg phentolamine mesylate should be effective. Injectable or oral chlorpromazine is suitable for milder reactions. Acute symptoms generally subside within 24 hours.

This product contains the following excipients which may cause reactions. Sucrose, patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine. Carmosine and Ponceau 4R may cause allergic reaction.

4.5. Interaction with other medicinal products and other forms of interaction

Caution should be exercised when giving parnate with the following: certain antihypertensives such as Guanethidine, as its action may be antagonised; Reserpine, as hyperactivity may occur; Methyldopa, as central excitation may result; other hypotensive agents because of possible additive effects; oral hypoglycaemic agents or insulin, as their action may be potentiated; anticholinergic antiparkinsonism drugs, as potentiation has been reported, narcotic analgesics (except pethidine which is contraindicated (see section 4.3), because of possible potentiation; and carbamazepine, which has similarities with tricyclic antidepressants. The effects of central nervous system depressants such as barbiturates may be enhanced. Metrizamide should be avoided in patients on MAO Inhibitors since they may lower the seizure threshold. Although MAO Inhibitors have been used therapeutically with L-Tryptophan, a neuromotor syndrome has been reported with this combination.

Dietary Precautions: High levels of tyramine in certain foods have been the cause of severe hypertensive reactions in patients on MAO inhibitor therapy (See section 4.8).

Accordingly, patients must be warned to avoid the following: Matured cheeses, hydrolysed protein extracts such as Marmite or Bovril, alcoholic drinks, particularly red wines such as chianti, non-alcoholic beer and lager, and protein foods that are not fresh or whose preparation involved hydrolysis, fermentation, pickling or hanging, also broad bean pods which contain levopoda and banana skins.

4.6 Pregnancy and lactation

This drug should not be used in pregnancy unless considered essential by the

physician. There is no evidence in relation to safety of use in human beings. The drug passes into the milk in lactating dogs.

4.7 Effects on ability to drive and use machines

Parnate may affect the ability to drive and operate machinery. Patients should not undertake such activities unless it has been shown not to affect mental or physical capacity.

4.8 Undesirable effects

Insomnia is the most frequent side effect; it may usually be overcome by giving the last dose of the day not later than 3 p.m., by reducing dosage, or by prescribing a mild hypnotic.

Other undesirable effects include postural hypertension (which is usually temporary, but if it persists the drug should be stopped), dizziness, drowsiness, fatigue, dry mouth, blurred vision, headache, diarrhoea, nausea and vomiting, sleep disturbances, rash and rarely hepatocellular damage, jaundice, hallucinations and blood dyscrasias.

Overstimulation including anxiety and agitation, developing rarely into hypomanias has also been observed.

Severe hypertensive reactions may occur, notably in association with foods containing tyramine (see section 4.5). On occasions these have been fatal.

Symptoms may be pain and stiffness in the neck, multiple extrasystoles, often with substernal pain, sweating, pallor, sometimes followed by flushing, mydriasis and photophobia.

4.9 Overdose

Signs and symptoms are usually of the type already described as adverse reactions, but may be more intense, may include hyperpyrexia, tremor, and convulsions, and may follow a latent period. Treatment consists of the induction of vomiting and/or gastric lavage together with supportive and symptomatic measures.

External cooling is recommended for hyperpyrexia. Treat hypotension with fluid replacement; if severe or persistent, noradrenaline may be considered.

Hypertension, if it occurs, may be relieved by slow intravenous injection of phentolamine mesylate. Pancuronium with mechanical ventilation may help reverse muscle spasm and pyrexia. Beta-adrenergic receptor blockade has been used successfully.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

Tranlycypromine is a non-hydrazone monoamine oxidase inhibitor.

5.2. Pharmacokinetic Properties

Tranlycypromine is well and rapidly absorbed. The drug is extensively metabolised in the liver and eliminated mainly in urine with a $T_{1/2}$ of about 2 hours. Recovery from the inhibition of the monoamine oxidase is usually achieved by 14 days.

5.3 Preclinical safety data

None stated

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cores

Sucrose

Maize Starch

Calcium sulphate dihydrate

Carmellose sodium

Magnesium Stearate (E 572)

Coating

Gelatin

Sucrose

Docusate sodium

Purified talc (E 553[b])

Light Kaolin (E 559)

Calcium carbonate (E 170)

Ethylcellulose

Acacia (E 414)

Carmoisine (E 122)

Ponceau 4R (E 124)

Maize starch

Titanium dioxide (E171)

Carnauba wax (E 903)

Edible ink (shellac, iron oxide black (E172), soya lecithin (E322) and trace amounts of dimethyl siloxane)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Parnate Tablets 10mg

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Clean copy

The shelf life is 2 years.

6.4 Special precautions for storage

Do not store above 25°C. Keep the container in the outer carton to protect from light and tightly closed to protect from moisture.

6.5 Nature and content of container

Polypropylene tablet container with cap and security tag containing desiccant cartridge and 28 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Goldshield Pharmaceuticals Ltd
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CR0 0XT

8. MARKETING AND AUTHORISATION NUMBER

PA 899/16/1

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

1 April 1978 / 1 April 1998

10. DATE OF (PARTIAL) REVISION OF THE TEXT

May 2009