Data Sheet

SURMONTIL

trimipramine (as maleate) 25 mg tablets and 50 mg capsules

Presentation

SURMONTIL *tablets* are compression coated, white or cream, circular, biconvex, containing the equivalent of 25mg trimipramine (as maleate) with a diameter of about 8.0mm. The face is indented with the name and strength, reverse plain.

SURMONTIL *capsules* are opaque white with opaque green cap, printed SU50, each containing the equivalent of 50mg trimipramine (as maleate).

Uses

Actions

SURMONTIL has a potent anti-depressant action similar to that of other tricyclic anti-depressants. The mechanism of action is not fully understood but it is thought to be via inhibition of neuronal re-uptake of noradrenalin, thereby increasing availability. SURMONTIL also possesses a pronounced sedative action.

Pharmacokinetics

SURMONTIL is readily absorbed after oral administration, reaching a mean peak plasma level after 3 hours. High first pass hepatic clearance results in a mean bioavailability of about 41% of the oral dose, and trimipramine is extensively protein bound in plasma. Elimination half-life is 24 hours. Metabolism is in the liver to its major metabolite, desmethyltrimipramine, which is excreted mainly in the urine.

Indications

SURMONTIL is indicated in the treatment of depressive illness, especially where sleep disturbance, anxiety or agitation is a presenting symptom. Sleep disturbance is controlled within 24 hours and true anti-depressant action follows within 7-10 days.

Dosage and Administration

Adults

Mild/Moderate Depression in General Practice:

The recommended dosage is 50-75 mg orally given two hours before bedtime, the larger dose (75 mg) being preferable for those patients with more marked sleep disturbance. Treatment should be continued for at least three weeks.

Moderate/Severe Depression (Patients under psychiatric supervision):
Initial dosage – 75 mg orally per day. This is best given as a single dose late in the evening or as 25mg midday and 50mg late in the evening. Dosage should then be increased as necessary until the optimal therapeutic level is reached, usually 150-300 mg per day. Treatment at this dosage should be continued for four to six weeks, dosage then being reduced to a maintenance level, usually within the range of 75-150 mg per day, for two to three months.

Giving most of the total daily dosage at night induces a rapid return to normal sleep, reduces the need for night-time sedation and minimises daytime drowsiness.

Elderly
Initially 10-25 mg three times a day. The initial dose should be increased with caution under close supervision. Half the normal maintenance dose may be sufficient to produce a satisfactory clinical response.

Impaired Liver Function:
As trimipramine is metabolised in the liver, patients with liver disease may require a reduced dosage.

Renal Failure:
Trimipramine should be used with caution in patients with chronic renal failure.

Cyclothymic patients with recurrent depression may require maintenance therapy for up to one year or even longer.

Children
Not recommended.

Adolescents
Not recommended for use in adolescent patients 13-18 years of age for the treatment of depression, unless under the supervision of a specialist.

When discontinuing treatment with SURMONTIL - this should be done with a gradually reducing dosage regimen. If during this regimen there are signs of a relapse, patients should be maintained on the therapy for a further 3 - 6 months before a second attempt at treatment discontinuation is made.

Contraindications

Recent myocardial infarction. Any degree of heart block or other cardiac arrhythmia. Mania, severe liver disease. During breastfeeding.

Treatment should be avoided, if possible, in patients with narrow angle glaucoma, symptoms suggestive of prostatic hypertrophy and a history of epilepsy.

SURMONTIL is contraindicated for the treatment of depression in patients 12 years of age and under.

SURMONTIL is contraindicated for the treatment of nocturnal enuresis.

Warnings and Precautions

Clinical worsening and suicide risk: Patients of any age with major depressive disorder may experience worsening of their depression and/or the emergence of suicidal ideation and behaviour (suicidality), whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Patients should be closely monitored, especially at the beginning of therapy or when the dose is changed, until such improvement occurs.

There has been a long-standing concern that some antidepressants may have a role in the emergence of suicidality in some patients. The possible risk of increased suicidality in patients applies to all classes of antidepressant medicines, as available data are not adequate to exclude this risk for any antidepressant. Therefore, consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse or whose emergent suicidality is severe, abrupt in onset, or was not part of the patient's presenting symptoms.

Because of the possibility of co-morbidity between major depressive disorder and other psychiatric and non-psychiatric disorders, the same precautions observed when treating patients with major depressive disorder should be observed when treating patients with other psychiatric and non-psychiatric disorders.

Symptoms including anxiety, agitation, panic attacks, insomnia, irritability, hostility (aggressiveness), impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and paediatric patients being treated with antidepressants for major depressive disorders as well as for other indications, both psychiatric and non-psychiatric. Although a causal link between the emergence of such symptoms and worsening of depression an/or the emergence of suicidal impulses has not been established, consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients for whom such symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

The patient has the right to treatment meeting appropriate ethical and professional standards, and the patient needs to be fully informed with frank discussion of risk/benefit issues relating to this medicine's efficacy and safety when used in the treatment regimen proposed.

Mania and bipolar disorder: A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with any antidepressant alone may increase the likelihood of a mixed/manic episode in patients at risk for bipolar disorder. Prior to initiating treatment with an antidepressant, patients should be adequately screened to determine if they are at risk for bipolar disorder. It should be noted that SURMONTIL is not approved for use in treating bipolar depression.

Information for patients and families: Patients and their families should be alerted about the need to monitor for the emergence of anxiety, agitation, panic attacks, insomnia, irritability, hostility, impulsivity, akathisia, hypomania, mania, worsening of depression, and suicidal ideation, especially early during antidepressant treatment. Such symptoms should be reported to the patient's doctor, especially if they are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

The elderly are particularly liable to experience adverse reactions, especially agitation, confusion and postural hypotension. (See 'Dosage & Administration').

Patients posing a high suicidal risk require close initial supervision.

Patients should be monitored closely during the initial stages of treatment, as improvement may not occur during the first 2-4 weeks. Trimipramine may initially impair alertness. Patients should be warned of the possible hazard when driving or operating machinery. Cardiac arrhythmias and severe hypotension are likely to occur with high dosage or in deliberate overdosage. They may also occur in patients with pre-existing heart disease taking normal dosage. It may be advisable to monitor liver function in patients on long-term treatment with SURMONTIL.

Pregnancy and Lactation:
Category C: Do not use during pregnancy especially during the first and last trimester, unless there are compelling reasons. Breast-feeding mothers should not receive SURMONTIL.

Epidemiological studies have suggested an increased risk of congenital abnormalities associated with use of tricyclics antidepressants in pregnancy.

Neonates should be observed if maternal use of trimipramine has continued into the later stages of pregnancy, particularly into the third trimester.

Neonates exposed to tricyclics antidepressants, late in the third trimester have showed drug withdrawal symptoms such as dyspnoea, lethargy, colic irritability, hypotension or hypertension and tremor or spasms.

Epidemiological data suggests that the use of tricyclics antidepressants in pregnancy may be associated with an increase in pre-term delivery.

Adverse Effects

Side-effects are similar to those of other tricyclic anti-depressants; they are usually more evident during the first few days of treatment and are invariably controlled by modification of dosage. Drowsiness may occur, but this is minimised by giving the total daily dosage at night. Atropine-like side-effects including dry mouth, disturbances of accommodation, tachycardia, constipation and hesitancy of micturition are common early in treatment, but usually lessen. Other adverse effects including sweating, postural hypotension, tremor and skin rashes.

Interference with sexual function may occur.

Serious adverse effects are rare; the following have been reported: depression of the bone marrow including agranulocytosis, cholestatic jaundice, hypomania, convulsions and peripheral neuropathy. Psychotic manifestations, including mania and paranoid delusions, may be exacerbated during treatment with tricyclic anti-depressants. Withdrawal symptoms may occur on abrupt cessation of therapy and include insomnia, irritability and excessive perspiration. Adverse effects such as withdrawal symptoms, respiratory depression and agitation have been reported in neonates whose mothers had taken trimipramine during the last trimester of pregnancy.

Interactions

The central nervous depressant action of alcohol is potentiated by SURMONTIL.

Anaesthetics given during tricyclic anti-depressant therapy may increase the risk of arrhythmias and hypotension. If surgery is necessary, the anaesthetist should be made aware that a patient is being so treated.

Trimipramine should not be given concurrently with or within 2 weeks of cessation of therapy with monoamine oxidase inhibitors. The anti-hypertensive effect of guanethidine, debrisoquine, bethanidine and possibly clonidine may be decreased by trimipramine. It would be advisable to review all anti-hypertensive therapy during treatment with tricyclic anti-depressants. Trimipramine should not be given with sympathomimetic agents such as adrenaline, ephedrine, isoprenaline, noradrenaline, phenylephrine and phenylpropanolamine.

Barbiturates may increase the rate of metabolism of SURMONTIL.

SURMONTIL should be administered with care in patients receiving therapy for hyperthyroidism.

Overdosage

Acute overdosage may be accompanied by hypotensive collapse, convulsions and coma. Provided coma is not present, gastric lavage should be carried out without delay even although some time may have passed since the drug was ingested. Patients in coma should have an endotracheal tube passed before gastric lavage is started. Absorption of trimipramine is slow but, as cardiac effects may appear soon after the drug is absorbed, a saline purge should be given. Electrocardiography monitoring is essential.

It is important to treat acidosis as soon as it appears with, for example, 20mL per kg of M/6 sodium lactate injection by slow intravenous injection. Intubation is necessary and the patient should be ventilated before convulsions develop; convulsions should be treated with diazepam administered intravenously.

Ventricular tachycardia or fibrillation should be treated by electrical defibrillation; if supraventricular tachycardia develops, pyridostigmine bromide 1mg (adults) intravenously or propranolol 1mg (adults) intravenously should be administered at intervals as required.

Treatment should be continued for at least three days even if the patient appears to have recovered.

Pharmaceutical Precautions

Protect from light. SURMONTIL capsules should be stored in a dry place below 25°C.

Medicine Classification

Prescription Medicine.

Package Quantities

Tablets: 25 mg in containers of 50
Capsules: 50 mg in containers of 50

Further Information

Excipients

Tablets
Wheat starch, kaolin light, dextrin, indigo carmine, magnesium stearate, sodium lauryl sulfate, calcium hydrogen phosphate.

Capsules
Maize starch, microcrystalline cellulose, magnesium stearate, colloidal silicon dioxide, gelatin, titanium dioxide, indigo carmine, iron oxide yellow, black ink.

Name & Address

Distributed by:
Pharmacy Retailing New Zealand Limited
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Date of Preparation

14 October 2010.