AGOG Pharma Ltd.
(WHO - GMP CERTIFIED - GOVT RECOGNISED EXPORT HOUSE)
CIN: 11-59615
**Regd. Office & Factory :** Plot No. 33, Sector II, The Vasai Taluka Industrial Co-op. Estate Ltd. Gauraipada, Vasai (E), Dist. Thane - 401 208. INDIA.
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# LEAFLET

## CLOM

(Clomipramine Tablets 25 mg)

Each film coated tablet contains:
Clomipramine Hydrochloride BP 25 mg
Excipients ..... q.s.

**Indications:**
**Adults**
Antidepressant: Symptoms of depressive illness especially where sedation is required. Obsessional and phobic states. Adjunctive treatment of cataplexy associated with narcolepsy.

**Children and adolescents:**
In children and adolescents, there is not sufficient evidence of safety and efficacy of Clomipramine Hcl in the treatment of depressive states of varying aetiology and symptomatology, phobias and panic attacks, cataplexy accompanying narcolepsy and chronic painful conditions. The use of Clomipramine Hcl in children and adolescents (0-17 years of age) in these indications is therefore not recommended.

**Dosage & administration:**
Adults: Oral - 10mg/day initially, increasing gradually to 30-150mg/day, if required, in divided doses throughout the day or as a single dose at bedtime. Many patients will be adequately maintained on 30-50mg/day. Higher doses may be needed in some patients, particularly those suffering from obsessional or phobic disorders. In severe cases this dosage can be increased up to a maximum of 250mg per day. Once a distinct improvement has set in, the daily dosage may be adjusted to a maintenance level averaging either 2-4 tablets of 25mg or 1 tablet of 75 mg.

Elderly: The initial dose should be 10mg/day, which may be increased with caution under close supervision to an optimum level of 30-75mg daily which should be reached after about 10 days and then maintained until the end of treatment.

Children and adolescents (0-17 years of age): Not recommended
Obsessional/phobic states: The maintenance dosage of Clomipramine Hcl is generally higher than that used in depression. It is recommended that the dose be built up to 100-150mg Clomipramine Hcl daily, according to the severity of the condition. This should be attained gradually over a period of 2 weeks starting with 1 x 25mg Clomipramine Hcl daily. In elderly patients and those sensitive to tricyclic antidepressants a starting dose of 1 X 10 mg Clomipramine Hcl daily is recommended.

**Treatment discontinuation:**hdrawal should be avoided because of possible adverse reactions. If the dec n is made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms.

**Contraindications:**
Known hypersensitivity to clomipramine or any of the excipients, or cross-sensitivity to tricyclic antidepressants of the dibenzazepine group. Recent myocardial infarction. Any degree of heart block or other cardiac arrhythmias. Mania, severe liver disease, narrow angle glaucoma. Retention of urine. Clomipramine Hydrochloride tablet must not be given in combination with or within 3 weeks before or after treatment with an MAO inhibitor The concomitant treatment with selective, reversible MAO-A inhibitors such as moclobemide, is also contraindicated.

**Special warnings & precautions:**
**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.

Other psychiatric conditions for which Clomipramine Hydrochloride tablet is prescribed can also be associated with an increased risk of suicide-related events. In addition, these conditions may be co-morbid with major depressive disorder. The same precautions observed when treating patients with major depressive disorder should therefore be observed when treating patients with other psychiatric disorders.

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.

Use in Children and Adolescents (0-17 years of age) Clomipramine Hydrochloride tablets should not be used in the treatment of depressive states, phobias and cataplexy associated with narcolepsy in children and adolescents under the age of 18 years.

Antidepressants increase the risk of suicide-related behaviours (suicide attempt and suicidal thoughts), and hostility (predominately aggression, oppositional behaviour and anger) were more frequently observed in clinical trials among children and adolescents treated with antidepressants compared to those treated with placebo. If based on clinical need, a decision to treat is nevertheless taken; the patient should be carefully monitored for the appearance of suicidal symptoms. In addition, long term safety data in children and adolescents concerning growth, maturation and cognitive behavioural development are lacking.

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Families and care givers of both paediatric and adult patients being treated with antidepressants for both psychiatric and non psychiatric indications, should be alerted about the need to monitor patients for the emergence of other psychiatric symptoms as well as the emergence of suicidality, and to report such symptoms immediately to health care providers.

Prescriptions for Clomipramine Hydrochloride should be written for the smallest quantity of tablets and capsules consistent with good patient management, in order to reduce the risk of overdose.

**Other Psychiatric Effects**

Many patients with panic disorders experience intensified anxiety symptoms at the start of the treatment with antidepressants. This paradoxical initial increase in anxiety is most pronounced during the first few days of treatment and generally subsides within two weeks.

Activation of psychosis has occasionally been observed in patients with schizophrenia receiving tricyclic antidepressants.

**Cardiac and Vascular Disorders**

Clomipramine Hydrochloride should be administered with particular precaution in patients with cardiovascular disorders, especially those with cardiovascular insufficiency, conduction disorders, (e.g. atrioventricular block grades I to III), arrhythmias. Monitoring of cardiac function and the ECG is indicated in such patients.

**Drug Interactions:**

Diuretics

Diuretics may lead to hypokalemia, which increases the risk of QTc prolongation and Torsade de Pointes, Hypokalaemia should therefore be treated prior to administration of Clomipramine Hydrochloride.

**Quinidine**

Tricyclic antidepressants should not be employed in combination with antiarrhythmic agents of the quinidine type. Oral antifungal, terbinafine

Coadministration of Clomipramine Hydrochloride with terbinafine, a strong inhibitor of CYP2D6, may result in increased exposure and accumulation of clomipramine and its N-demethylated metabolite. Therefore, dose adjustments of Clomipramine Hydrochloride may be necessary when coadministered with terbinafine.

**Cimetidine**

Coadministration with the histamine2 (H2)-receptor antagonist, cimetidine (an inhibitor of several P450 enzymes, including CYP2D6 and CYP3A4), may increase plasma concentrations of tricyclic antidepressants, whose dosage should therefore be reduced.

**Rifampicin**

Rifampicin (CYP3A and CYP2C inducer), may decrease clomipramine concentrations as concomitant administration of drugs known to induce cytochrome P450 enzymes, particularly CYP3A4, CYP2C19 may accelerate the metabolism and decrease the efficacy of Clomipramine Hydrochloride.

**Overdosage :**

The signs and symptoms of overdose with Clomipramine Hydrochloride are similar to those reported with other tricyclic antidepressants. Cardiac abnormalities and neurological disturbances are the main complications. In children accidental ingestion of any amount should be regarded as serious and potentially fatal.

**Signs and symptoms:**

Symptoms generally appear within 4 hours of ingestion and reach maximum severity after 24 hours. Owing to delayed absorption (anticholinergic effect), long half-life, and enterohepatic recycling of the drug, the patient may be at risk for up to 4-6 days. The following signs and symptoms may be seen:

**Central nervous system:**

Drowsiness, stupor, coma, ataxia, restlessness, agitation, enhanced reflexes, muscular rigidity, choreoathetoid movements, convulsions, serotonin syndrome (e.g. hypertensive crisis, hyperpyrexia, myoclonus, delirium and coma) may be observed.

Cardiovascular system:

Hypotension, tachycardia, QTc prolongation and arrhythmia including Torsade de Pointes, conduction disorders, shock, heart failure; in very rare cases cardiac arrest.

Respiratory depression, cyanosis, vomiting, fever, mydriasis, sweating and oliguria or anuria may also occur.

**Treatment:**

There is no specific antidote, and treatment is essentially symptomatic and supportive. Anyone suspected of receiving an overdose of Clomipramine Hydrochloride particularly children, should be hospitalised and kept under close surveillance for at least 72 hours.

**Storage :**

Store under normal storage conditions (15°C to 30°C).
Protect from light .
Keep all medicines out of reach of children.

**Shelf life :** 36 month

**Presentation:**

Blister Pack of 10 X 10 Tablets.
Jar Pack of 1000 Tablets

Manufactured in India by:
AGOG PHARMA LTD.
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