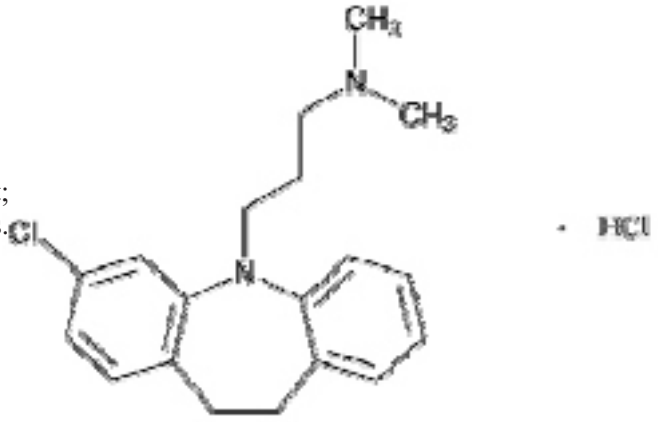
Taj Pharmaceuticals Ltd.

Clomipramine HCL

CAS No. : 17321-77-6

Synonym:

Anafranil hydrochloride,3-Chloro-10,11-dihydro-N,N-dimethyl-5H-dibenz[b,f]azepine-5-propanamine hydrochloride
CAS Number: 17321-77-6
Linear Formula: C19H23ClN2 HCl
Molecular Weight: 351.31
EC Number: 241-344-3
MDL number: MFCD00069234



Description
Biochem/physiol Actions Tricyclic antidepressant; inhibits serotonin and norepinephrine transporters.

Properties

Assay: 98% (HPLC)
Form: Powder
Color: White to off-white
Solubility: H2O: soluble25 mg/mL 0.1 M HCl: soluble

$C_{19}H_{23}ClN_2 \bullet HCl$ MW = 351.31

DOSAGE

Initial doses are usually 25 mg 2 or 3 times daily or 75 mg once daily in slow released form. The dose may be increased in regular intervals (the usual dose per day is 100 to 225 mg). Doses up to 300 mg may be used, but these are associated with an increased risk of seizures. This medication may be taken with food to prevent stomach upset. In hospitalized patients initial intramuscular injections and very slow intravenous infusions can be used, but the risk of hypotension and seizures may be increased with parenteral drug use. The advantage is that the onset of action may be faster.

Usually, clomipramine needs some weeks to reach its maximum effects and needs to be given as longterm treatment, sometimes for life (narcolepsy). Sometimes, in patients with narcolepsy the full effect of clomipramine is not sufficient. In these cases treatment with clomipramine should be terminated gradually and a commonly used central stimulant (e.g. modafinil, methylphenidate or methamphetamine) tried instead.
Clomipramine is not able to elevate the mood of non-depressive persons and any unindicated use may be dangerous.

Dosage should be individualized according to the requirements of each patient. Treatment should be initiated at the lowest recommended dose and increased gradually, noting carefully the clinical response and any evidence of into lerance. During the initial dose titration phase, the total daily dose of clomipramine should be divided and served with meals to reduce gastrointestinal side-effects.

Owing to the long elimination half-lives of clomipramine and its active metabolite, desmethylclomipramine, steady-state plasma levels may not be achieved until 2 to 3 weeks after a dosage adjustment. It may thus be advisable to wait 2 to 3 weeks after the initial dose titration phase, before attempting further dosage adjustments. It should be kept in mind that a lag in therapeutic response usually occurs at the onset of therapy, lasting from several days to a few weeks. Increasing the dosage does not normally shorten this latent period and may increase the incidence of side effects.

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SIDE EFFECTS

The most commonly observed adverse events associated with the use of clomipramine and not seen at an equivalent incidence among placebo-treated patients were gastrointestinal complaints, including dry mouth, constipation, nausea, dyspepsia, and anorexia; nervous system complaints, including somnolence, tremor, dizziness, nervousness and myoclonus; genitourinary complaints including changed libido, ejaculatory failure, impotence and micturition disorder; and other miscellaneous complaints, including fatigue, sweating, increased appetite, weight gain, and visual changes.The tabulations that follow list adverse reactions that have also been observed with clomipramine; these are categorized by organ system and listed in order of decreasing frequency.

Neurological:
Extrapyramidal effects such as ataxia, also headache, delirium, speech disorders, muscle weakness, muscle hypertonia, tinnitus, paresthesias of the extremities, convulsions, EEG changes, hyperpyrexia. Peripheral neuropathy has been reported with other tricyclic antidepressants.

Behavioral:
Drowsiness, fatigue, restlessness, confusion accompanied by disorientation (particularly in geriatric patients and patients suffering from Parkinson's disease), anxiety states, agitation, sleep disturbances, insomnia, nightmares, aggravated depression, hypomania or manic episodes, disturbed concentration, visual hallucinations, impaired memory, aggressiveness, yawning, depersonalization, activation of latent psychosis, delusions.

Autonomic:
Difficulty with accommodation, slurred speech, urinary retention, hot flushes, mydriasis, glaucoma, paralytic ileus.

Cardiovascular:
Hypotension, particularly orthostatic hypotension with associated vertigo, sinus tachycardia, palpitations. A quinidine-like effect and other reversible ECG changes in patients with normal cardiac status (such as flattening or inversion of T-waves, depressed S-T segments). Arrhythmias, hypertension, conduction disorders (e.g. widening of QRS complex, PQ changes, bundle-branch block), syncope.
Fibrillation, myocardial infarction, stroke and unexpected death in patients with cardiovascular disorders have been reported with tricyclic antidepressants.

Hematologic:
Leukopenia, agranulocytosis, thrombocytopenia, eosinophilia and purpura. One case of pancytopenia has been reported.

Gastrointestinal:
Vomiting, abdominal pain, diarrhea, taste perversion, elevated transaminases, obstructive jaundice, hepatitis with or without jaundice.

Endocrine:
Weight loss, breast enlargement and galactorrhea in the female, inappropriate antidiuretic hormone (ADH) secretion syndrome, gynecomastia in the male, changes in blood sugar levels, increase in prolactin levels, menstrual irregularity.

Allergic or Toxic:
Allergic skin reactions (skin rash, urticaria), photosensitization, pruritus, edema, drug fever.

Withdrawal Symptoms:
Abrupt cessation of treatment with tricyclic antidepressants after prolonged administration may occasionally

PRECAUTIONS

Epileptic seizures are the most important risk associated with clomipramine. Among patients taking the drug for six months or more, more than 1% may experience seizures. The risk of seizure increases with larger doses, and seizures have been reported to occur following abrupt discontinuation of the medication. Caution and physician supervision is required if the patient has a history of epilepsy or some other condition associated with seizures, such as brain damage or alcoholism.

Clomipramine and other tricyclic antidepressants often cause drowsiness. Activities requiring alertness, such as driving, should be avoided until patients understand how the drug affects them. Dizziness or light-headedness may occur on arising from a seated position, due to sudden decreases in blood pressure. Fainting may also occur. Some patients, especially men with prostate enlargement, may experience difficulty urinating. Glaucoma may be worsened. Sensitivity to ultraviolet light may increase, and sunburns may occur more easily.

Tricyclic antidepressants, including clomipramine, should be used with caution and physician supervision in patients with heart disease, because of the possibility of adverse effects on heart rhythm. Adverse effects on the heart occur frequently when tricyclics are taken in overdose. Only small quantities of these drugs should be given to patients who may be suicidal.

DRUG DESCRIPTION

Clomipramine is used to treat people with obsessive-compulsive disorder (a condition that causes repeated unwanted thoughts and the need to perform certain behaviors over and over). Clomipramine is in a group of medications called tricyclic antidepressants. It works by increasing the amount of serotonin, a natural substance in the brain that is needed to maintain mental balance.

Clomipramine is an antidepressant drug used primarily to alleviate obsessions and compulsions in patients with obsessive-compulsive disorder. Clomipramine is also used in the treatment of depressive disorders and in a number of other psychiatric and medical conditions.Long term treatment of depression, irrational fears and obsessive behaviour. Clomipramine can also be employed to treat phobias (feared) and obsessions, and cataplexy, which breaks down joined narcolepsy (extreme somnolence).

Changes the chemical balance in the brain to lift the mood, increases the appetite and stimulates an improved interest in day to-day living.

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