zunorma™ Max

1. Generic Name

Zuclopenthixol Decanoate IP 200 mg/ml

2. Qualitative and Quantitative Composition

Each ml contains:
Zuclopenthixol Decanoate IP……. 200 mg
Oily base……... q.s.

3. Dosage form and strength

Solution containing Zuclopenthixol decanoate 200 mg/ml for injection.

4. Clinical particulars

4.1 Therapeutic indication

By psychiatrist only for the treatment of acute psychosis including mania & exacerbation of chronic psychosis acute & chronic schizophrenia.

4.2 Posology and method of administration

Posology:

Adults

Dosage and dosage interval should be adjusted according to the patient's symptoms and response to treatment.

The usual dosage range of zuclopenthixol decanoate is 200 - 500 mg every one to four weeks, depending on response, but some patients may require up to 600 mg per week. The maximum single dose at any one time is 600 mg. For example, 1200 mg every 2 weeks should not be given. In patients who have not previously received depot antipsychotics, treatment is usually started with a small dose (e.g. 100 mg) to assess tolerance. An interval of at least one week should be allowed before the second injection is given at a dose consistent with the patient's condition.

Adequate control of severe psychotic symptoms may take up to 4 to 6 months at high enough dosage. Once stabilized lower maintenance doses may be considered, but must be sufficient to prevent relapse.

Injection volumes of greater than 2 ml should be distributed between two injection sites.

Older patients

In accordance with standard medical practice, initial dosage may need to be reduced to a quarter or half the normal starting dose in the frail or older patients.

Method of administration

By deep intramuscular injection into the upper outer buttock or lateral thigh.

Note: As with all oil-based injections it is important to ensure, by aspiration before injection, that inadvertent intravascular entry does not occur

4.3 Contraindication

Hypersensitivity to the active substance or to any of the excipients.

Circulatory collapse, depressed level of consciousness due to any cause (e.g. intoxication with alcohol, barbiturates or opiates), coma.

4.4 Special warnings and precautions for use

Caution should be exercised in patients having: liver disease; cardiac disease, or arrhythmias; severe respiratory disease; renal failure; epilepsy (and conditions predisposing to epilepsy, e.g. alcohol withdrawal or brain damage); Parkinson's disease; narrow angle glaucoma; prostatic hypertrophy; hypothyroidism; hyperthyroidism; myasthenia gravis; phaeochromocytoma and patients who have shown hypersensitivity to thioxanthenes or other antipsychotics.

Acute withdrawal symptoms, including nausea, vomiting, sweating and insomnia have been described after abrupt cessation of antipsychotic drugs. Recurrence of psychotic symptoms may also occur, and the emergence of involuntary movement disorders (such as akathisia, dystonia and dyskinesia) has been reported. The plasma concentrations of zuclopenthixol decanoate gradually decrease over several weeks which make gradual dosage tapering unnecessary.

When transferring patients from oral to depot antipsychotic treatment, the oral medication should not be discontinued immediately but gradually withdrawn over a period of several days after administering the first injection.
The possibility of development of neuroleptic malignant syndrome (hyperthermia, muscle rigidity, fluctuating consciousness, instability of the autonomous nervous system) exists with any neuroleptic. The risk is possibly greater with the more potent agents. Patients with pre-existing organic brain syndrome, mental retardation and opiate and alcohol abuse are over-represented among fatal cases.

Treatment:
Discontinuation of the neuroleptic. Symptomatic treatment and use of general supportive measures. Dantrolene and bromocriptine may be helpful. Symptoms may persist for more than a week after oral neuroleptics are discontinued and somewhat longer when associated with the depot forms of the drugs.

Like other neuroleptics, zuclopenthixol decanoate should be used with caution in patients with organic brain syndrome, convulsions or advanced hepatic disease.
Blood dyscrasias have been reported rarely. Blood counts should be carried out if a patient develops signs of persistent infection.

As with other drugs belonging to the therapeutic class of antipsychotics, zuclopenthixol decanoate may cause QT prolongation. Persistently prolonged QT intervals may increase the risk of malignant arrhythmias. Therefore, zuclopenthixol decanoate should be used with caution in susceptible

individuals (with hypokalemia, hypomagnesaemia or genetic predisposition) and in patients with a history of cardiovascular disorders, e.g. QT prolongation, significant bradycardia (<50 beats per minute), a recent acute myocardial infarction, uncompensated heart failure, or cardiac arrhythmia.

Cases of venous thromboembolism (VTE) have been reported with antipsychotic drugs. Since patients treated with antipsychotics often present with acquired risk factors for VTE, all possible risk factors for VTE should be identified before and during treatment with zuclopenthixol decanoate and preventive measures undertaken.

Concomitant treatment with other antipsychotics should be avoided.
As described for other psychotropics, zuclopenthixol decanoate may modify insulin and glucose responses calling for adjustment of the antidiabetic therapy in diabetic patients.
Leukopenia, neutropenia and agranulocytosis have been reported with antipsychotics, including zuclopenthixol decanoate.

Long-acting depot antipsychotics should be used with caution in combination with other medicines known to have a myelosuppressive potential, as these cannot rapidly be removed from the body in conditions where this may be required.

Older people
Older people require close supervision because they are especially prone to experience such adverse effects as sedation, hypotension, confusion and temperature changes.

Cerebrovascular
An approximately 3-fold increased risk of cerebrovascular adverse events has been seen in randomized placebo controlled clinical trials in the dementia population with some atypical antipsychotics. The mechanism for this increased risk is not known. An increased risk cannot be excluded for other antipsychotics or other patient populations.
Zuclopenthixol should be used with caution in patients with risk factors for stroke.

Increased Mortality in Older People with Dementia
Data from two large observational studies showed that older people with dementia who are treated with antipsychotics are at a small increased risk of death compared with those who are not treated. There are insufficient data to give a firm estimate of the precise magnitude of the risk, and the cause of the increased risk is not known.

Zunorma Max injection is not licensed for the treatment of dementia-related behavioral disturbances.

4.5 Drug interactions

In common with other antipsychotics, zuclopenthixol enhances the response to alcohol, the effects of barbiturates and other CNS depressants.

Zuclopenthixol may potentiate the effects of general anaesthetics and anticoagulants and prolong the action of neuromuscular blocking agents.

The anticholinergic effects of atropine or other drugs with anticholinergic properties may be increased.

Concomitant use of drugs such as metoclopramide, piperazine or antiparkinson drugs may increase the risk of extrapyramidal effects such as tardive dyskinesia.

Combined use of antipsychotics and lithium or sibutramine has been associated with an increased risk of neurotoxicity.

Antipsychotics may enhance the cardiac depressant effects of quinidine; the absorption of corticosteroids and digoxin.

The hypotensive effect of vasodilator antihypertensive agents such as hydralazine and α blockers (e.g. doxazosin), or methyl-dopa may be enhanced.

Concomitant use of zuclopenthixol and drugs known to cause QT prolongation or cardiac arrhythmias, such as tricyclic antidepressants or other antipsychotics should be avoided.

Increases in the QT interval related to antipsychotic treatment may be exacerbated by the co administration of other drugs known to significantly increase the QT interval. Co-administration of such drugs should be avoided.

Relevant classes include:

• class Ia and III antiarrhythmics (e.g. quinidine, amiodarone, sotalol, dofetilide)

• some antipsychotics (e.g. thioridazine)

• some macrolides (e.g. erythromycin)

• some antihistamines

• some quinolone antibiotics (e.g. moxifloxacin)

The above list is not exhaustive and other individual drugs known to significantly increase QT interval (e.g. cisapride, lithium) should be avoided. Drugs known to cause electrolyte disturbances such as thiazide diuretics (hypokalemia) and drugs known to increase the plasma concentration of zuclopenthixol should also be used with caution as they may increase the risk of QT prolongation and malignant arrhythmias.

Antipsychotics may antagonise the effects of adrenaline and other sympathomimetic agents, and reverse the antihypertensive effects of guanethidine and similar adrenergic-blocking agents.

Antipsychotics may also impair the effect of levodopa, adrenergic drugs and anticonvulsants.

The metabolism of tricyclic antidepressants may be inhibited and the control of diabetes may be impaired.

Since zuclopenthixol is partly metabolised by CYP2D6 concomitant use of drugs known to inhibit this enzyme may lead to higher-than-expected plasma concentrations of zuclopenthixol, increasing the risk of adverse effects and cardiotoxicity.

4.6 Use in special population

Paediatric population

Zunorma Max is not recommended for use in children due to lack of clinical experience.

Patients with renal impairment

Zunorma Max can be given in usual doses to patients with reduced renal function. Where there is renal failure dosage should be reduced to half the normal dosage.

Patients with hepatic impairment

Use with caution in patients with liver disease. Patients with compromised hepatic function should receive half the recommended dosages. Serum-level monitoring is advised.

Pregnancy

Zuclopenthixol decanoate should not be administered during pregnancy unless the expected benefit to the patient outweighs the theoretical risk to the foetus.

Neonates exposed to antipsychotics (including zuclopenthixol decanoate) during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or withdrawal symptoms that may vary in severity and duration following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, newborns should be monitored carefully.

Breast-feeding

As zuclopenthixol is found in breast milk in low concentrations it is not likely to affect the infant when therapeutic doses are used. The dose ingested by the infant is less than 1% of the weight related maternal dose (in mg/kg). Breast-feeding can be continued during zuclopenthixol decanoate therapy if considered of clinical importance, but observation of the infant is recommended, particularly in the first 4 weeks after giving birth.

Fertility

In humans, adverse events such as hyperprolactinemia, galactorrhea, amenorrhoea, erectile dysfunction and ejaculation failure have been reported (see section 4.8). These events may have a negative impact on female and/or male sexual function and fertility.

If clinically significant hyperprolactinaemia, galactorrhoea, amenorrhoea or sexual dysfunctions occur, a dose reduction (if possible) or discontinuation should be considered. The effects are reversible on discontinuation.

4.7 Effects on ability to drive and use machine.

Zuclopenthixol is a sedative drug.

Alertness may be impaired, especially at the start of treatment, or following the consumption of alcohol; patients should be warned of this risk and advised not to drive or operate machinery until their susceptibility is known.

Patients should not drive if they have blurred vision.

4.8 Undesirable effects

The majority of undesirable effects are dose dependent. The frequency and severity are most pronounced in the early phase of treatment and decline during continued treatment.

Extrapyramidal reactions may occur, especially in the early phase of treatment. In most cases these side effects can be satisfactorily controlled by reduction of dosage and/or use of antiparkinsonian drugs. The routine prophylactic use of antiparkinsonian drugs is not recommended.

Antiparkinsonian drugs do not alleviate tardive dyskinsea and may aggravate them. Reduction in dosage or, if possible, discontinuation of zuclopenthixol therapy is recommended. In persistent akathisia a benzodiazepine or propranolol may be useful.

Blood and lymphatic system disorders	Thrombocytopenia, neutropenia, leukopenia, agranulocytosis.
Immune system disorders	Hypersensitivity, anaphylactic reaction.
Endocrine disorders	Hyperprolactinaemia.
Metabolism and nutrition disorders	Increased appetite, weight increased.
	Decreased appetite, weight decreased.
	Hyperglycaemia, glucose tolerance impaired, hyperlipidaemia.
Psychiatric disorders	Insomnia, depression, anxiety, nervousness, abnormal dreams, agitation, libido decreased.
	Apathy, nightmare, libido increased, confusional state.
Nervous system disorders	Somnolence, akathisia, hyperkinesia, hypokinesia.
	Tremor, dystonia, hypertonia, dizziness, headache, paraesthesia, disturbance in attention, amnesia, gait abnormal.
	Tardive dyskinesia, hyperreflexia, dyskinesia, parkinsonism, syncope, ataxia, speech disorder, hypotonia, convulsion, migraine.
	Neuroleptic malignant syndrome.
Eye disorders	Accommodation disorder, vision abnormal.
	Oculogyration, mydriasis.
Ear and labyrinth disorders	Vertigo.
	Hyperacusis, tinnitus.
Cardiac disorders	Tachycardia, palpitations.
	Electrocardiogram QT prolonged.
Vascular disorders	Hypotension, hot flush.
	Venous thromboembolism
Respiratory, thoracic and mediastinal disorders	Nasal congestion, dyspnoea.
Gastrointestinal disorders	Dry mouth.
	Salivary hypersecretion, constipation, vomiting, dyspepsia, diarrhoea.
	Abdominal pain, nausea, flatulence.
Hepato-biliary disorders	Liver function test abnormal.
	Cholestatic hepatitis, jaundice.
Skin and subcutaneous tissue disorders	Hyperhidrosis, pruritus.

	Rash, photosensitivity reaction, pigmentation disorder, seborrhoea, dermatitis, purpura.
Musculoskeletal and connective tissue disorder	Myalgia.
	Muscle rigidity, trismus, torticollis.
Renal and urinary disorders	Micturition disorder, urinary retention, polyuria.
Pregnancy, puerperium and perinatal conditions	Drug withdrawal syndrome neonatal (see 4.6)
Reproductive system and breast disorders	Ejaculation failure, erectile dysfunction, female orgasmic disorder, vulvovaginal dryness.
	Gynaecomastia, galactorrhoea, amenorrhoea, priapism.
General disorders and administration site conditions	Asthenia, fatigue, malaise, pain.
	Thirst, injection site reaction, hypothermia, pyrexia.

As with other drugs belonging to the therapeutic class of antipsychotics, rare cases of QT prolongation, ventricular arrhythmias - ventricular fibrillation, ventricular tachycardia, Torsade de Pointes and sudden unexplained death have been reported for zuclopenthixol.

Cases of venous thromboembolism, including cases of pulmonary embolism and cases of deep vein thrombosis have been reported with antipsychotic drugs – Frequency unknown.

Abrupt discontinuation of zuclopenthixol may be accompanied by withdrawal symptoms. The most common symptoms are nausea, vomiting, anorexia, diarrhoea, rhinorrhoea, sweating, myalgias, paraesthesias, insomnia, restlessness, anxiety, and agitation. Patients may also experience vertigo, alternate feelings of warmth and coldness, and tremors. Symptoms generally begin within 1 to 4 days of withdrawal and abate within 7 to 14 days**.**

4.9 Overdose

Symptoms: somnolence, coma, extrapyramidal symptoms, convulsions, hypotension, shock, hyper or hypothermia. ECG changes, QT prolongation, Torsade de Pointes, cardiac arrest and ventricular arrhythmias have been reported when administered in overdose together with drugs known to affect the heart.

Treatment: treatment is symptomatic and supportive. Measures aimed at supporting the respiratory and cardiovascular systems should be instituted.

Adrenaline (epinephrine) must not be used in these patients. There is no specific antidote.

5. Pharmacological properties

5.1 Mechanism of action

Zuclopenthixol is a potent neuroleptic of the thioxanthene series with a piperazine side-chain. The antipsychotic effect of neuroleptics is related to their dopamine receptor blocking effect. The thioxanthenes have a high affinity for both the adenylate cyclase coupled dopamine D_1 receptors and for the dopamine D_2 receptors; in the phenothiazine group the affinity for D1 receptors is much lower than that for D_2 receptors, whereas butyrophenones, diphenylbutylpiperidines and benzamides only have affinity for D_2 receptors.

In the traditional tests for antipsychotic effect, e.g. antagonism of stereotypic behaviour induced by dopamine agonists, the chemical groups of neuroleptics mentioned reveal equal but dosage dependent activity. However, the antistereotypic effect of phenothiazines, butyrophenones, diphenylbutylpiperidines, and benzamindes is strongly counteracted by the anticholinergic drug, scopolamine, while the antisteriotypic effect of the thioxanthenes, e.g. zuclopenthixol, is not, or only very slightly, influenced by concomitant treatment with anticholinergics.

5.2 Pharmacodynamic properties

Zuclopenthixol has proven to be a potent neuroleptic in all the behavioural studies for neuroleptic (dopamine receptor blocking) activity, i.e. antagonism of stereotypic behaviour in rodents induced by dopamine agonists (methylphenidate, amphetamine, apomorphine), antiemetic and antistereotypic effect in dogs, antagonism of hyperactivity in rodents induced by 6,7-ADTN, antagonism of circling behaviour induced by DA agonists in unilaterally 6-OHDA lesioned rats, catalepsy and inhibition of conditioned avoidance response. The acute pharmacological effect of zuclopenthixol resembles that of perphenazine and haloperidol in many respects. Correlation is found between the potency of individual neuroleptics in the in vivo test models, the affinity for dopamine D2 binding sites in vitro and the average, daily oral antipsychotic doses.

Like most neuroleptics, zuclopenthixol possess α1-adrenolytic properties. The peripheral α1-adrenoceptor blockade is claimed to be responsible for cardiovascular side effects such as orthostatic hypotension and tachycardia. Zuclopenthixol is approximately half as potent as chlorprothixene. The antihistaminic potency is of the same order of magnitude as that of diphenhydramine and, therefore, zuclopenthixol possibly may diminish the alcohol-disulfiram reaction. The anticholinergic activity is very weak. Inhibition of locomotor activity, inhibition of electrically induced EEG arousal reaction and prolongation of alcohol- and barbiturate-induced sleeping time indicate a sedative action of zuclopenthixol. Like most other neuroleptics, zuclopenthixol increases the serum prolactin level.

5.3 Pharmacokinetic properties

After deep intramuscular injection of Zunorma Max, serum levels of zuclopenthixol increase during the first week and decline slowly thereafter. A linear relationship has been observed between Zuclopenthixol decanoate dosage and serum level. Metabolism proceeds by sulphoxidation, dealkylation and glucuronic acid conjugation. Sulphoxide metabolites are mainly excreted in the urine while unchanged drug and the dealkylated form tend to be excreted in the faeces.

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

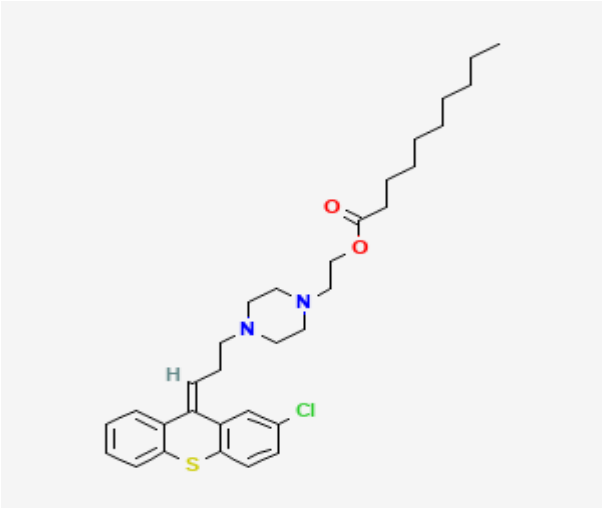
Not available

7. Description

Zuclopenthixol decanoate is a member of thioxanthenes.

Its chemical name is 2-[4-[(3*Z*)-3-(2-chlorothioxanthen-9-ylidene)propyl]piperazin-1-yl]ethyl decanoate.

The empirical formula and molecular weight are $C_{32}H_{43}ClN_2O_2S$ and 555.2 g/mol and its structural formula is:



8. Pharmaceutical particulars

8.1 Incompatibilities
No known incompatibilities

8.2 Shelf-life
24 months

8.3 Packaging Information:
Ampoule of 1ml with sterile disposable Syringe

8.4 Storage and handling instructions:
Store in a cool and dry place below 30º C. Protect from light. Do not allow to freeze.
Keep out of reach of children.

9. Patient Counselling Information

9.1 Adverse Reactions
Refer part 4.8

9.2 Drug Interactions
Refer part 4.5

9.3 Dosage
Refer part 4.2

9.4 Storage
Refer part 8.4

9.5 Risk Factors
Refer part 4.4

9.6 Self-monitoring information
N/A

9.7 Information on when to contact a health care provider or seek emergency help.

Patient is advised to be alert for the emergence or worsening of the adverse reactions and contact the prescribing physician.

9.8 Contraindications

Refer part 4.3

10. Details of the manufacturer:

Maya Biotech Pvt Ltd,
Village Kondi, P.O, Thana,
Baddi- 173205 (H.P.), India.

11. Details of permission or license number with date:

Mfg.Lic.No.: MB/08/725; dated- 12/11/2023

12. Date of revision

June 2026