zunorma™ Quik

1. Generic Name

Zuclopenthixol Acetate IP 50 mg/ml

2. Qualitative and Quantitative Composition

Each ml contains:

Zuclopenthixol Acetate IP…… 50 mg

Oily base…….. q.s.

3. Dosage form and strength

Solution containing Zuclopenthixol Acetate 50 mg for injection.

4. Clinical particulars

4.1 Therapeutic indication

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

4.2 Posology and method of administration

Posology:

Adults

Dosage should be adjusted according to the severity of the patient's illness.

The usual dosage is 50-150 mg (1-3 ml), repeated, if necessary, after 2 or 3 days. Some patients may need an additional injection between 1 and 2 days after the first injection.

Zunorma Quik is not intended for long-term use and duration of treatment should not be more than two weeks. The maximum accumulated dosage should not exceed 400 mg and the number of injections should not exceed four.

Older patients

The dosage may need to be reduced in older patients owing to reduced rates of metabolism and elimination. Maximum dosage per injection should be 100 mg.

Method of administration:

Deep intramuscular injection into the upper outer buttock or lateral thigh. Injection volumes exceeding 2 ml should be distributed between two injection sites.

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.
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 acetate should be used with caution in patients with organic brain syndrome, convulsions or advanced hepatic, renal or cardiovascular 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 acetate may cause QT prolongation. Persistently prolonged QT intervals may increase the risk of malignant arrhythmias. Therefore, zuclopenthixol acetate 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 acetate and preventive measures undertaken.

Concomitant treatment with other antipsychotics should be avoided (see section 4.5).
As described for other psychotropics, zuclopenthixol acetate may modify insulin and glucose responses calling for adjustment of the antidiabetic therapy in diabetic patients.

Older people
Older people require close supervision because they are especially prone to experiencing 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 acetate 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 elderly people with dementia who are treated with antipsychotics are at a small increased risk of death compared with those who are not treated. There is 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 Quik 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 anesthetics 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.

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 (see section 4.4).

Antipsychotics may antagonize 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 metabolized 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

Pediatric population

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

Patients with renal impairment

Zunorma Quik 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 hepatic disease. Patients with compromised hepatic function should receive half the recommended dosages. Serum-level monitoring is advised.

Pregnancy

Zuclopenthixol acetate 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 acetate) 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 acetate 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, amenorrhea, 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 hyperprolactinemia, galactorrhea, amenorrhea 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 dyskinesia and may aggravate it. 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
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**.**

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions.

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 D_1 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 behavior 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 benzamides 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

By esterification of zuclopenthixol with acetic acid, zuclopenthixol has been converted to a more lipophilic substance, zuclopenthixol acetate. When dissolved in oil and injected intramuscularly this substance diffuses slowly into the surrounding body water, where enzymatic breakdown occurs releasing the active component zuclopenthixol.

Maximum serum concentrations of zuclopenthixol are usually reached 36 hours after an injection, after which the serum levels decline slowly. The average maximum serum level corresponding to the 100 mg dose is 41 ng/mL. Three days after the injection the serum level is about one third of the maximum.

Zuclopenthixol is distributed in the body in a comparable way to other neuroleptics, with the higher concentrations of drug and metabolites in liver, lungs, intestines and kidneys and lower concentrations in heart, spleen, brain, and blood. The apparent volume of distribution is about 20 L/kg and the protein binding about 98%.
Zuclopenthixol crosses the placental barrier in small amounts. Zuclopenthixol is excreted in small amounts with the milk - the ratio milk concentration/serum concentration in women is on average 0.3.
The metabolism of zuclopenthixol proceeds via three main routes - sulphoxidation, side chain N-dealkylation and glucuronic acid conjugation. The metabolites are devoid of psychopharmacological activity. The excretion proceeds mainly with the faeces but also to some degree with the urine. The systemic clearance is about 0.9 L/min.
The kinetics seem to be linear, since highly significant correlation exist between the dose and the area under the serum concentration curve.

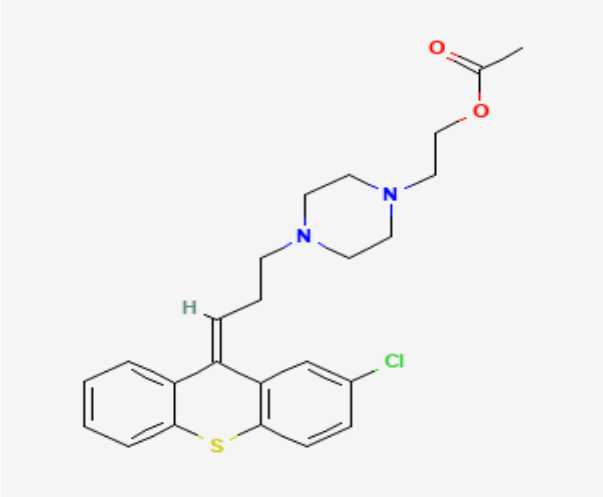
6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Not available

7. Description

Zuclopenthixol acetate is a member of thioxanthenes.
Its chemical name is 2-[4-[(3Z)-3-(2-chlorothioxanthen-9-ylidene)propyl]piperazin-1-yl]ethyl acetate.
The empirical formula and molecular weight are $C_{24}H_{27}ClN_2O_2S$ and 443.0 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