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Zuclopenthixol Decanoate Injection BP 200 mg/ml

AMERICAN
ZUXOL DEPOT 200
Injection 1ml

For deep Intramuscular injection only

Composition:

Each ml contains:

Zuclopenthixol Decanoate BP ..... 200 mg

Medium-chain Triglycerides BP..... q.s

Pharmacodynamic:

Pharmacotherapeutic group: Neuropleptics (antipsychotics),
The action of zuclopenthixol, as with other antipsychotics is mediated through dopamine receptor blockade. Zuclopenthixol has a high affinity for D_1 and D_2 receptors and activity has been demonstrated in standard animal models used to assess antipsychotic action. Serotonergic blocking properties, a high affinity for alpha-adrenoreceptors and slight antihistamine properties have been observed.

Pharmacokinetic:

After deep intramuscular injection of Zuclopenthixol decanoate, 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.

Indications:

The maintenance treatment of schizophrenia and paranoid psychoses.

Dosage & Administration:

Route of Administration- For Deep Intramuscular Injection Only
Dosage: 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 stabilised 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.
Paediatric population
Zuclopenthixol decanoate is not recommended for use in children due to lack of clinical experience.
Patients with renal impairment
Zuclopenthixol decanoate 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.

Contraindications:

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.

Warnings and Precautions:

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 hypokalaemia, 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 randomised 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.
Zuclopenthixol decanoate Conc. Injection and Injection are not licensed for the treatment of dementia-related behavioural disturbances.

Pregnancy and Lactation:

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.
Animal studies have shown reproduction toxicity.
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 hyperprolactinaemia, galactorrhoea, amenorrhoea, erectile dysfunction and ejaculation failure have been reported. These events may have a negative impact on female and/or male sexual function and fertility.

Effects on ability to drive and use machines:

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.

Drug Interaction & Incompatibilities:

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.

Side effects:

Erythema . nodules. pain at injection site. swelling.
If the dose needs to be reduced to alleviate side-effects, it is important to recognise that the plasma-drug concentration may not fall for some time after reducing the dose, therefore it may be a month or longer before side-effects subside.
Hepatic Impairment Can precipitate coma.
Renal impairment Start with small doses in severe renal impairment because of increased cerebral sensitivity.

Overdose & Treatment:

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.

Storage: Store below 30°C. Protect from light.Do not freeze.

Presentation: 1ml Ampoule and disposable syringe with needle packed in a carton along with insert.

Keep the medicine out of reach of children.

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