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For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.

LEVAZEO OD

(Levosulpiride Extended Release Tablets)

DOSAGE FORM

Levosulpiride Extended Release Tablet 100, 150 & 200 mg

COMPOSITION

LEVAZEO OD 100

Each uncoated extended release tablet contains :

Levosulpiride 100 mg

LEVAZEO OD 150

Each uncoated extended release tablet contains :

Levosulpiride 150 mg

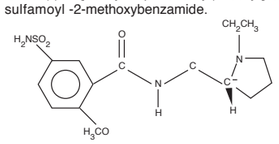
LEVAZEO OD 200

Each uncoated extended release tablet contains :

Levosulpiride 200 mg

DESCRIPTION

Levosulpiride is the levorotatory enantiomer of sulpiride. The chemical structure of levosulpiride is S-(-)-N-[l-ethyl-2-pirrolidinyl)methyl]-5-sulfamoyl -2-methoxybenzamide.



CLINICAL PHARMACOLOGY

Mechanism of action

The mechanism of action of levosulpiride is not fully understood. The drug is a selective though weak D_2 antagonist. It shows dose dependent regional specificity in receptor occupancy and behavioral effects. The preferential blockade of centrally located DA autoreceptors at lower doses and blockade of post synaptic DA receptors at higher doses seems to contribute to the anti-depressant and antipsychotic effects of levosulpiride.

Typical antipsychotics are 10-20 times more potent at the D_2 than at the D_3 receptor, while levosulpiride is only 2-3 times more potent at D_2. This lower D_2/D_3 affinity ratio might explain some of the regional preferences of levosulpiride and greater activity on autoreceptors and lower extrapyramidal side effects associated with D_2 blockade compared to other antipsychotics.

Pharmacokinetics

The bioavailability of levosulpiride, when given orally is low (about 27% to 34%) with incomplete absorption as opposed to presystemic metabolism. Food reduces absorption by 30%.

Bioequivalence between the IR (2□100mg) and ER 200 mg tablet has been demonstrated (AUC0-t mean ratio 98.5%, 90% confidence interval 85.01-114.12; AUC0-∞ mean ratio 97.6%, 90% confidence interval 85.56-111.21).

The time to peak concentration is 3 to 9 hours with median tmax 5.5 hours. The oral AUC values for levosulpiride extended release tablet for a dose of 200 mg is 6050 ng.hr/ml.

Levosulpiride displays a protein binding of about 14% and a volume of distribution of 1 to 2.7 L/kg which is similar in elderly and younger subjects.

Metabolism does not occur and the drug is excreted unchanged into the urine. The renal clearance is 15 to 30%. The drug is substantially excreted in the feces due to poor absorption. The lack of hepatic metabolism makes metabolic interactions with cytochrome P-450 related substrates very unlikely.

The elimination half life ranges from 4.7 to 14.6 hours for oral 200mg dose of levosulpiride ER tablet. The elimination half life is prolonged in patients with renal impairment. The peak concentrations, time to peak levels and the elimination half life is similar in younger and elderly patients.

INDICATIONS

It is indicated for the treatment of schizophrenia and depression in adults.

DOSAGE AND ADMINISTRATION

Dosage should be individualized.

Schizophrenia: The recommended dose for adults is 200-300mg daily. Treatment should be initiated with levosulpiride ER 100mg and it can be titrated up to 300 mg based on individual patient's response and recommendations by the doctor.

Maintenance therapy: The recommended maintenance dose of Levosulpiride is 150 mg daily. The dose can be reduced gradually on individual patient's response and recommendations by the doctor.

Depression: For adults the usually recommended dosage is 100-150mg of Levosulpiride daily.

Elderly: Caution is advised when used in the elderly patients and the dose should be carefully stabilized. A possible reduction in dosage should be considered as per the patient response and tolerance.

Renal impairment: Levosulpiride is primarily excreted renally, and dose adjustments have been suggested in renal insufficiency.

The following modifications are recommended

during long-term levosulpiride therapy: creatinine clearance 30 to 60 milliliters/minute: 70% of normal dose; creatinine clearance 10 to 30 milliliters/minute: 50% of normal dose; creatinine clearance less than 16 milliliters/ /minute: 34% of normal dose; alternatively, the dosage interval can be prolonged by a factor of 1.5, 2 and 3 respectively.

USE IN SPECIAL POPULATIONS

Pregnancy and Lactation

Not to be used during presumed or confirmed pregnancy and during the lactation period.

CONTRAINDICATIONS

- Hypersensitivity to the drug or any other excipients of the formulation.
- Pheochromocytoma as it can cause hypertensive attack probably due to release of catecholamine from tumor; such attacks can be controlled with phentolamine.
- Epilepsy.
- Concomitant prolactin dependent tumors like pituitary gland prolactinomas and breast cancer.
- Pregnancy and lactation.

WARNINGS AND PRECAUTIONS

Neuroleptic malignant syndrome (NMS), a potentially fatal symptom complex, has been reported in association with other antipsychotic drugs. NMS is associated with hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatinine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. In such an event, or with unexplained high fever without additional clinical manifestations of NMS, all antipsychotic drugs must be discontinued.

The treatment of NMS involves immediate discontinuation of administration of antipsychotic drugs and establishment of intensive symptomatic therapy (particular care should be taken to reduce hyperthermia and correct the dehydration). If resumption of treatment with antipsychotic drugs becomes essential, the patient should be carefully monitored.

Levosulpiride should be used with caution in patients with manic states such as in the manic phase of manic depressive psychosis.

Caution is advised when the drug is administered to patients with cerebrovascular events including risk factors for stroke.

Caution is also advised when levosulpiride is given to patients with cardiac insufficiency.

Levosulpiride should not be used when gastrointestinal stimulation of motility can be harmful, e.g., in presence of gastrointestinal hemorrhage, mechanical obstructions or perforations. Levosulpiride may cause drowsiness in some patients especially at higher doses, thus patients should be advised to exercise caution when driving or operating machinery.

ADVERSE EFFECTS

With prolonged administration of levosulpiride, disturbances such as amenorrhea, gynecomastia, galactorrhea, hyperprolactinemia and changes in libido are observed; in particular cases, reversible effects of levosulpiride on functioning of hypothalamic pituitary gonadal axis are observed.

Very rarely neuroleptic malignant syndrome associated symptoms, allergic and extra-pyramidal side effects like tremor, Parkinsonism like symptoms, dystonia may occur.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY

No data regarding carcinogenesis, mutagenesis, impairment of fertility is available

DRUG INTERACTIONS

Caution is advised when levosulpiride is taken concomitantly with other centrally acting drugs. It can potentiate the cognitive and motor effects of alcohol. The effect of levosulpiride on gastrointestinal motility can be antagonized by anti-cholinergic drugs; narcotics and analgesic drugs.

OVERDOSAGE

Extrapyramidal disturbances and sleep disorders may occur with higher doses and in patients who are sensitive to dopamine antagonists. In such cases therapy should be stopped or the dose should be reduced as dictated by the clinical condition of the patient.

EXPIRY DATE

Do not use later than expiry date.

STORAGE

Store at a temperature not exceeding 30°C, protected from light and moisture.

Keep out of reach of children

PRESENTATION

Levazeo OD 100, Levazeo OD 150 and Levazeo OD 200 are available in strips of 10 tablets.

torrent

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