150mm

180mm

Dowsul™
25mg Tablets
50mg Tablets
(Levosulpiride)

ڈاؤسل ۲۵ ملی گرام ٹیبلیٹس
۵۰ ملی گرام ٹیبلیٹس

DESCRIPTION
Levosulpiride is a substituted benzamide antipsychotic which is reported to be a selective antagonist of central dopamine (D-2, D-3 and D-4) receptors. Chemically it is N-[[(2S)-1-Ethylpyrrolidin -2-yl] methyl]-2-methoxy -5-sulfamoylbenzamide. Its molecular formula is $C_{15}H_{23}N_3O_4S$.

COMPOSITION
Each tablet contains:-
Levosulpiride ……. 25 mg
Each tablet contains:-
Levosulpiride ……. 50 mg

THERAPEUTIC INDICATIONS
Dowsul (Levosulpiride) tablets are indicated for oral administration.
Dowsul 25mg tablets are indicated for the treatment of the following:
• Gastroesophageal Reflux Disease
• Irritable bowel syndrome
• Dyspeptic syndrome due to delayed gastric emptying linked to organic factor (diabetic gastroparalysis, neoplasias, etc.) and/or functional disorder.
Essential Cephalagia.
• Vertigo of a central and/or peripheral origin.

Dowsul 50mg tablets are indicated for the treatment of the following:
• Endogenous and reactive depressive states.
• Somatoform disorders
• Acute and chronic schizophrenia, especially recommended for negative symptoms (after disorder).

CLINICAL PHARMACOLOGY
Mechanism of action
Levosulpiride is a selective antagonist at dopamine (D2) receptors. Levosulpiride exerts a regulation action both on the central and peripheral nervous circuits controlling the dynamics of digestive system.
Action on dopamine autoreceptors
• In the D2 receptor family (which includes D2, D3 and D4 receptors), the affinity of levosulpiride for the D2 receptor is only 2-3 times greater than that for the D3 receptor (this contrasts with typical antipsychotics, which are 10-20 times more potent at D2 than at D3).
• At low doses levosulpiride preferentially blocks dopamine auto receptors, which are located on presynaptic neurons (this is because the dopamine auto receptor has a greater affinity for ligands than the dopamine postsynaptic receptor, and because D3 ligands show greater preference for auto receptors).
• Low doses levosulpiride increases dopaminergic neurotransmission by increasing the presynaptic synthesis and release of dopamine (this is because it blocks the dopamine auto receptor, which inhibits the presynaptic synthesis and release of dopamine).
• Low doses of levosulpiride generally refer to doses of 50-200mg/day. At these doses, levosulpiride is therapeutic for negative and cognitive symptoms of schizophrenia and for depressive and somatoform disorders.
Action on dopamine postsynaptic receptors
In high doses, levosulpiride also blocks D2 dopamine postsynaptic receptors. The result is decreased dopaminergic neurotransmission. In humans high doses of levosulpiride generally refer to doses of 400-800mg/day. At these doses, levosulpiride is therapeutic for positive symptoms of schizophrenia.
Indirect action on adrenergic receptors
Levosulpiride down regulates cortical beta adrenoceptors. This action may contribute to the antidepressant action of the drug.
Absence of binding to other receptors
• Levosulpiride does not block 5-HT2 serotonergic and H1 histaminic receptors, therefore, it is unlikely to cause occasional adverse effects such as sedation, increased appetite, and increased weight.
• Levosulpiride does not block alpha-1 adrenergic receptors, and is therefore unlikely to cause postural hypotension.
• Levosulpiride does not block muscarinic cholinergic receptors, and is therefore unlikely to cause adverse effects such as dry mouth, blurred vision, impaired accommodation, constipation and difficulty in passing urine.
Pharmacokinetics
Levosulpiride is slowly absorbed from the gastrointestinal tract, bioavailability is about 30%. Levosulpiride is less than 40% bound to plasma proteins. Peak plasma concentration occurs after 3 hours and it has plasma half-life of about 9-7 hours. It is mostly eliminated by the kidneys in the urine, chiefly as unchanged drug.

DOSAGE AND ADMINISTRATION
The usual adult oral dose of Dowsul is given before meals as mentioned in the following table:

Indications	Dosage	Maintenance Therapy
• Gastroesophageal Reflux Disease (GERD) • Irritable Bowel Syndrome (IBS) • Dyspeptic syndrome • Essential Cephalagia • Vertigo of a central and/or peripheral origin	1 tablet of 25mg 3 times a day	—
• Endogenous reactive depressive states • Somatic disorder	2-3 tablets 50mg a day	Unless otherwise prescribed, 3 tablets of 50mg per day. This dose can be reduced gradually.
• Acute and chronic schizophrenia	2-3 tablets 100mg a day	

Geriatric Use:
The dosage may be progressively lowered. In treating aged patients the dosage must be carefully established by the physician who must consider a possible reduction in the dosage mentioned above.

CONTRAINDICATIONS
Levosulpiride is contraindicated in following conditions:
• Patients with known hypersensitivity to levosulpiride or any component of this product.
• In epilepsy, in manic conditions and in the manic stages of manic-depressive psychoses.
• Patients with hyperprolactinemic tendency, mammary dysplasia, malignant mastopathy.
• Patients affected by pheochromocytoma as it may cause a hypertensive crisis, probably due to release of catecholamine

150mm

180mm

from the tumor.
• In the presence of gastrointestinal bleeding, mechanical obstruction or perforations.
• Pregnant women or nursing mothers.
• Pediatric population.

DRUG INTERACTIONS
General:
• When neuroleptics are administered concomitantly with drugs that prolong the QT risk of cardiac arrhythmias increase.
• Not to be administered concomitantly with the drugs that cause electrolyte disturbance.

Antacids: The concomitant use of levosulpiride with therapeutic doses of sucralfate or an antacid containing aluminium and magnesium hydroxide may reduce mean oral bioavailability of levosulpiride.

Anticholinergics, narcotics or analgesics agents: The effect of levosulpiride on the gastrointestinal motility may be opposed by anticholinergics, narcotics or analgesic agents.

Psychopharmacological agents: Concomitant use with other psychopharmacologic agents requires particular care and vigilance by the physician, in order to avoid any unexpected side effect or drug-drug interaction.

WARNING AND PRECAUTIONS
Levosulpiride should be used with care in the following conditions:
• Patients receiving levosulpiride should be warned that at higher dose somnolence, numbness and dyskinesia might occur, therefore patients should avoid driving vehicles or operate machineries.
• If held to be essential for re-treatment with antipsychotics, the patient should be carefully monitored.
• Avoid concomitant therapy with other neuroleptics.
• Use with caution in patients with cardiovascular disease or with a family history of QT prolongation.
• Avoid the simultaneous consumption of alcohol.

USE IN SPECIAL POPULATION
Pregnancy and lactation
Not to be used in established or presumed pregnancy and during the lactation period.

ADVERSE REACTIONS
The adverse effects of levosulpiride are particularly marked in the elderly and include sedation and hypotension as well as precocious dyskinesia. Very rarely psychomotor excitation, autonomic disturbance and allergic reactions, extrapyramidal effects such as tremors, parkinsonism and dystonia are observed. All these effects are modest in scale and reversible. Some disorders, such as amenorrhea, gynecomastia, galactorrhea, hyperprolactinemia and changes in libido, observed in particular cases, are attributable to a reversible effect of levosulpiride on the functionality of hypothalamus-pituitary-gonadal axis, similar to what is known for many neuroleptics. Ventricular arrhythmias such as torsades de pointes, ventricular tachycardia, ventricular fibrillation and cardiac arrest may also be observed.

OVERDOSAGE
Extrapyramidal or sleep disturbance may occur at higher doses. Interrupting the therapy or reducing the dose depending on physician's judgment will be sufficient in this case.

STABILITY
See expiry on pack

PACKS
Dowsul is supplied in following dosage form, strengths and pack sizes:

Tablets 25mg	20's
Tablets 50mg	20's

INSTRUCTIONS
Keep all medicines out of the reach of children.
Protect from light, heat and moisture.
Store below 30°C.

To be sold on prescription of a registered medical practitioner only.

ہدایات:

تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔
روشنی، گرمی اور نمی سے محفوظ رکھیں۔
۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

صرف رجسٹرڈ ڈاکٹر کے نسخے پر فروخت کی جائے۔

Manufactured by:
Martin Dow Limited
Plot No. 37, Sector 19, Korangi Industrial Area,
Karachi-74900, Pakistan.

Martin Dow