

# Scipride™

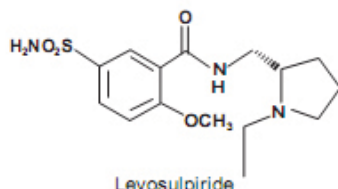
(Levosulpiride)

25mg, 50mg TABLETS

سائپرائڈ

## 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-sulfamoyl]benzamide. Its molecular formula is  $C_{17}H_{23}N_3O_2S$  and structure is following:



Levosulpiride

## QUALITATIVE & QUANTITATIVE COMPOSITION

SCIPRIDE (Levosulpiride) is available for oral administration as:

1. Scipride Tablets 25mg  
Each tablet contains:  
Levosulpiride ... 25mg
2. Scipride Tablets 50mg  
Each tablet contains:  
Levosulpiride ... 50mg

## CLINICAL PHARMACOLOGY

### Mechanism of Action

Levosulpiride is a selective antagonist at dopamine (D<sub>2</sub>) 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 D<sub>2</sub> receptor family (which includes D<sub>2</sub>, D<sub>3</sub>, and D<sub>4</sub> receptors), the affinity of levosulpiride for the D<sub>2</sub> receptor is only 2-3 times greater than that for the D<sub>3</sub> receptor (this contrasts with typical antipsychotics, which are 10-20 times more potent at D<sub>2</sub> than at D<sub>3</sub>).
- At low doses levosulpiride preferentially blocks dopamine autoreceptors, which are located on presynaptic neurons (this is because the dopamine autoreceptor has a greater affinity for ligands than the dopamine postsynaptic receptor, and because D<sub>3</sub> ligands show greater preference for autoreceptors).
- Low dose levosulpiride increases dopaminergic neurotransmission by increasing the presynaptic synthesis and release of dopamine (this is because it blocks the dopamine autoreceptor, 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 D<sub>2</sub> 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 symptom 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-HT<sub>2</sub> serotonergic and H<sub>1</sub> 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.

## THERAPEUTIC INDICATIONS

SCIPRIDE (Levosulpiride) tablets are indicated for oral administration:

SCIPRIDE (Levosulpiride) 25mg tablets are indicated for treatment of the following:

- Gastroesophageal reflux disease.
- Irritable bowel syndrome.
- Dyspeptic syndrome due to delayed gastric emptying linked to organic factor (diabetic gastroparesis, neoplasias, etc.) and/or to functional disorder.
- Essential cephalgia.
- Vertigo of a central and/or peripheral origin.

SCIPRIDE (Levosulpiride) 50mg tablets are indicated for treatment of the following:

- Endogenous and reactive depressive states
- Stomach disorder.
- Acute and chronic schizophrenia especially recommended for negative symptoms (after disorder).

## DOSAGE AND ADMINISTRATION

The usual adult oral dose of SCIPRIDE (Levosulpiride) 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 cephalgia - 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 prescribe, 3 tablets of 50mg per day. This dose can be reduced gradually.
- Acute and chronic schizophrenia	2-3 tablets of 100 mg 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.

#### 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 were observed psychomotor excitation, autonomic disturbance and allergic reactions extrapyramidal effects such as tremors, parkinsonism and dystonia. All these effects are modest in scale and reversible.

Some disorders, such as amenorrhea, gynecomastia, galactorrhoea, hyperprolactinemia and changes in libido observed in particular cases are attributable to a reversible effect on the functionality levosulpiride hypothalamus-pituitary-gonadal axis, similar to that known for many neuroleptic. Ventricular arrhythmias such as torsades de pointes, ventricular tachycardia, ventricular fibrillation arrest may also be observed.

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

#### PRECAUTIONS

Levosulpiride should be used with care in the following conditions:

- Patients receiving levosulpiride should be warned that at higher doses 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.

#### 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 analgesic 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.

#### OVERDOSAGE

In internal medicine neither extrapyramidal nor sleep disturbances have ever been observed, which may eventually occur at very high dosages. Interrupting the therapy or reducing the dosages depending on physician's judgement will be sufficient in this case.

#### STORAGE

Store at room temperature between 15-30°C.

Protect from sunlight and moisture.

The expiration date refers to the product correctly stored at the required conditions.

#### HOW SUPPLIED

SCIPRIDE tablets 25mg are available in blister packs of 20's.

SCIPRIDE tablets 50mg are available in blister packs of 20's.

**Keep out of reach of children.**

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

Please read the contents carefully before use.  
This package insert is continually updated from time to time.

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Getz Pharma (Pvt.) Limited, 29-30/27,  
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**SCILIFE**

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