



SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product

Levosulpiride Tablets 25mg

Micropride-25

2. Quality and Quantitative Composition

Each uncoated tablet contains Levosulpiride..... 25 mg

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

Tablet

White, circular, flat, beveled uncoated tablets

4. Clinical Particulars

4.1 Therapeutic indications:

- Short-term treatment of dyspeptic syndrome (anorexia, bloating, a feeling of epigastric tenderness, postprandial headache, heartburn, belching, diarrhoea, constipation) from delayed gastric emptying related to organic factors (diabetic gastroparesis, cancer, etc.) and / or functional factors (visceral somatisation in anxious subjects -depressants) in patients who failed to respond to other therapy.
- Symptomatic short-term treatment of nausea and vomiting (induced by anticancer drugs) after failure of first-line therapy.
- Symptomatic short-term treatment of dizziness, tinnitus, hearing loss and nausea associated with Meniere's syndrome.

4.2 Posology and method of administration:

Adult: 25 mg t.i.d.



Elderly: Dose reductions may be necessary

Oral administration

Pediatric population

No data are available.

4.3 Contraindications:

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

- Levosulpiride 25 mg should be used with caution in epilepsy, manic states, in the manic phase of manic-depressive disorder
- Levosulpiride 25 mg is contraindicated in patients with pheochromocytoma because it can cause a hypertensive crisis probably due to the release of catecholamines from the tumor. Such hypertensive crises may be controlled by phentolamine.
- Regarding the supposed correlation between the hyperprolactinemic effect of most psychotropic medicines and mammary dysplasia, levosulpiride should not be used in subjects who are already carriers of a malignant mastopathy.
- Levosulpiride 25 mg is contraindicated in pregnancy and during the breastfeeding period (see section 4.6).

4.4 Special warning and precautions:

In randomized clinical trials versus placebo performed in a population of patients with dementia treated with some atypical antipsychotics, an increase of about three times of the cerebrovascular events risk was observed. The mechanism for this increased risk is not known. An increased risk for other antipsychotics and other patient populations can not be ruled out. Levosulpiride should be used with caution in patients with risk factors for stroke.

A complex symptoms disorder, potentially fatal, called Neuroleptic Malignant Syndrome has been reported with use of neuroleptics (in general in the course of treatment with antipsychotic



drugs). Clinical manifestations of this syndrome are hyperpyrexia, muscle rigidity, akinesia, vegetative disorders (irregular pulse or blood pressure, sweating, tachycardia, arrhythmias), altered state of consciousness that may progress to stupor and coma. The treatment of Neuroleptic Malignant Syndrome consists of immediate discontinuation of the antipsychotic medicines and other not essential medicines and setting of an intensive symptomatic treatment (care must be taken in reducing hyperthermia and in correcting dehydration). In case the resumption of the treatment with antipsychotics is held to be essential, the patient should be carefully monitored. Concomitant therapy with other neuroleptics must be avoided.

- Levosulpiride should not be used when the stimulation of gastrointestinal motility can be detrimental, for example in the presence of gastrointestinal bleeding, mechanical obstructions or perforations.
- The effects of levosulpiride on gastrointestinal motility may be antagonized by anticholinergic drugs, narcotics and analgesics.
- Levosulpiride should be used with caution in patients with cardiovascular disease or with a family history of QT prolongation.
- There have been reports of venous thromboembolism (VTE) with antipsychotic medicines use. Since patients treated with antipsychotics often present with acquired risk factors for VTE, these factors need to be identified before and during treatment with Levosulpiride, in order to take appropriate preventive measures.
- Simultaneous intake of alcohol must be avoided.

4.5 Interactions with Other Medicaments

The association with other medicines requires special caution and vigilance from the physician, in order to avoid unexpected effects from unwanted interaction.

- Concomitant administration of neuroleptics with medicines that prolong the QT interval increases the risk of cardiac arrhythmias.
- Levosulpiride should not be administered concomitantly with medicines that cause electrolyte disturbances.



4.6 Pregnancy and lactation:

There are no adequate and well-controlled studies on pregnant women and during the breastfeeding. Patients should be advised of the need to inform their doctor in case of current or planned pregnancy during treatment with levosulpiride.

Do not use in pregnancy, possible pregnancy and during the breastfeeding period.

Neonates exposed to conventional or atypical antipsychotics included levosulpiride during the third trimester of pregnancy are at risk for side effects including extrapyramidal symptoms or withdrawal symptoms that may vary by severity and duration following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, and feeding disorder. Therefore, new-borns should be carefully monitored.

4.7 Effects on ability to drive and use machine:

High doses of levosulpiride may cause drowsiness, numbness, dizziness and dyskinesia, therefore they should be advised to avoid driving or operating machine and to be engaged in activities where a full alertness is required for their possible hazard.

4.8 Undesirable effects:

Tabulated list of adverse reactions

According to MedDRA system, organ classification, frequency categories are defined as follows: Very common ($\geq 1/10$), Common ($\geq 1/100$ to $< 1/10$), Uncommon ($\geq 1/1,000$ to $< 1/100$), Rare ($\geq 1/10,000$ to $< 1/1,000$), Very rare ($< 1/10,000$), Not known (cannot be estimated from the available data).

<i>System Organ Class</i>	<i>Rare</i>	<i>Very Rare</i>	<i>Frequency not known</i>
<i>Nervous system disorders</i>		Somnolence, Parkinsonism ¹ , Dyskinesia ¹ , Tremor ¹ , Dystonia ¹ , Neuroleptic Malignant	



		Syndrome (see section 4.4) ¹	
<i>Reproductive system and breast disorders</i>			Amenorrhea, Gynaecomastia, Galactorrhea, Changes in libido ²
<i>Cardiac disorders</i>	QT prolongation, Ventricular arrhythmias such as torsades de pointes, Ventricular tachycardia, Ventricular fibrillation, Cardiac arrest ³	Sudden death ²	
<i>Vascular disorders</i>			Thromboembolism (including cases of pulmonary embolism and deep venous thrombosis) (see section 4.4) ³
<i>Pregnancy, puerperium and perinatal conditions</i>			Neonatal withdrawal syndrome, extrapyramidal symptoms (see section 4.6)
<i>Investigations</i>			Hyperprolactinaemia ²

¹Observed in case of prolonged administration and/or with other drugs of the same therapeutic class.



²Observed in special cases, due to prolonged administration and due to a reversible effect of levosulpiride on the functionality of the hypothalamic-pituitary-gonadal axis, similar to that known for many neuroleptics.

³Observed with other drugs of the same therapeutic class.

4.9 Overdose:

The medicine can induce extrapyramidal effects and sleep disorders, at higher doses and in patients sensitive to neuroleptics.

In these cases it will be advisable to reduce the dosage or discontinue the treatment, according to the physician decision.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties:

Pharmacotherapeutic group: Psycholeptics, antipsychotics, ATC code: N05AL07.

Biochemical, pharmacological and clinical data obtained with the two isomers of sulpiride, indicates that the antidopaminergic activity, both at central and local levels, is due to levo-rotatory enantiomer.

5.2 Pharmacokinetic Properties:

When levo sulpiride is administered orally, the peak plasma concentration is reached in 3 hours, in an average of 94.183 ng/ml.

The $t_{1/2}$ of elimination calculated after administration of Levosulpiride is 4.305 hours. The elimination of the medicine occurs mainly via the urine.

5.3 Preclinical safety Data:

The values expressed as LD₅₀ acute toxicity after oral administration in mice, rats and rabbits were 2450 mg / kg, 2600 mg / kg and greater than 1500 mg / kg.

LD 50 values:

- In the mouse : 210 mg / kg, via i.p,



- In the rat via i.p. And i.v. :to 270 mg / kg and 53 mg / kg, respectively,
- In the rabbit via i.v.: to 42 mg / kg.

Sub acute toxicity tests were conducted by administering the active ingredient in rat, rabbit and dog, daily, for 12-13 weeks. The appearance of any toxic symptoms was not observed at doses of:

- 25 mg / kg sc and 300 mg / kg p.o. in the rat,
- 250 mg / kg p.o. and 12.5 mg / kg i.m. in rabbits,
- 50 and 100 mg / kg p.o. in the dog.

To evident ate the chronic toxicity after administration of the drug for 180-190 days, the following doses were well tolerated:

- mg / kg p.o. in the dog100 mg / kg p.o. and 20 mg / kg s.c. in the rat,
- 10 mg / kg i.m. in rabbits and
- 20.

Studies performed in rats and mice, administering the medicine at a dose higher than that expected for man, have shown that Levosulpiride do not possess carcinogenic properties.

Studies carried out in rats and rabbits have shown that the medicine is not teratogenic.

In vitro tests have ruled out that the medicine possesses mutagenic properties.



6. Pharmaceutical Particulars

6.1 List of excipients:

Maize Starch

Microcrystalline Cellulose

Croscarmellose Sodium

Povidone K-30

Colloidal Silicon Dioxide

Magnesium Stearate

6.2 Incompatibilities:

Not applicable

6.3 Shelf life:

36 Months from the date of Manufacturing.

6.4 Special precautions for storage:

Store below 30°C. Keep medicine away from the reach of children

6.5 Nature and contents of container:

Blister pack of 10 tablets

7. Marketing Authorization Holder:

MICRO LABS LIMITED

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INDIA