

Pacific Pharmaceuticals Ltd.

Lahore, Pakistan

LEVOPRAID ® 100



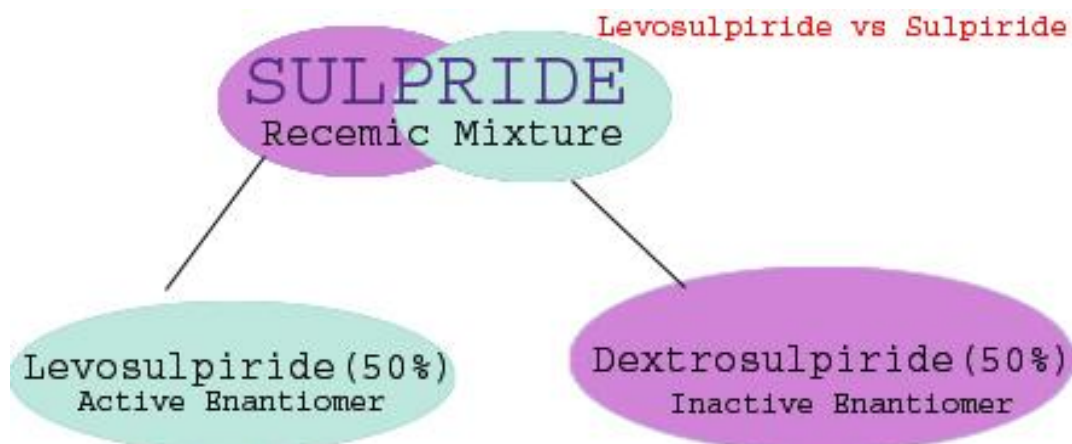
A Selective Dopamine DA₂ Receptor Antagonist

Negative Symptoms Of Schizophrenia

	Dulled Emotions		Social withdrawal		Loss of interest in life
		Apathy or lack of motivation		Lack of spontaneity and flow of conversation	

Dopamine hypoactivity leads to negative symptoms

"Dopamine hyperactivity seems to lead to the positive symptoms of schizophrenia and dopamine under activity to negative symptoms, therefore, there seems to be inverse level of cortical-sub-cortical dopaminergic function." (Harrison 1999)



More Potent than Sulpiride. 3 Half daily dose than Sulpiride. 3 Fewer Side effects than sulpiride. 3

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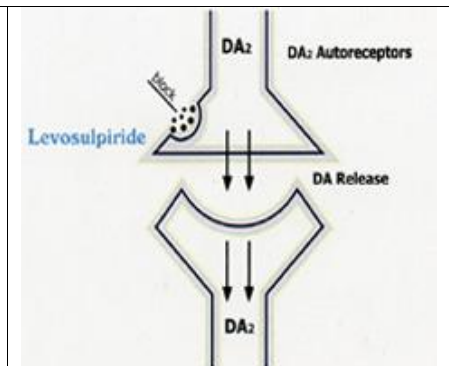


A Selective Dopamine DA₂ Receptor Antagonist

A Breakthrough in the Treatment of Schizophrenia with Predominant Negative Symptoms

Mechanism of Action

LEVOPRAID 100 (Levosulpiride) provides good control of the negative symptoms of Schizophrenia through selective action on central dopaminergic hypofunction. This involves specific inhibitory interaction on presynaptic DA₂ autoreceptors, with an increase in dopaminergic activity and consequent clinical and behavioral activation.



Better response than depot neuroleptics

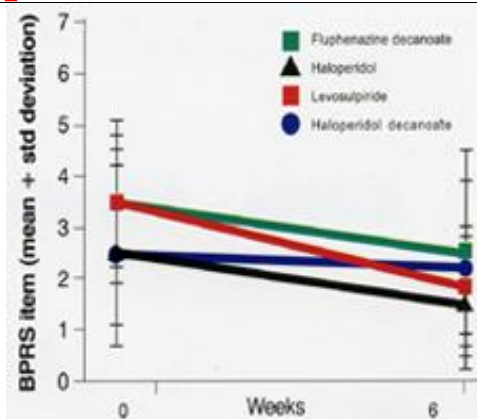
Study Design: Open, comparative.

No. of Patients: 144

Duration: Six weeks.

Results:

Levosulpiride showed a trend to be more effective on depressive symptomatology in comparison to the other neuroleptics.



A Breakthrough in the Treatment of Schizophrenia with Predominant Negative Symptoms

- ❖ Exhibits Better Therapeutic Response than Depot Neuroleptics.
- ❖ Demonstrates High Efficacy & Safety Profile in Young and Elderly Negative Schizophrenics.
- ❖ Extrapyramidal/antimuscarinic effects, Sedation & Hypotension appear to be Generally Less Frequent and Mild than with Typical Antipsychotics.1-2
- ❖ Good Tolerability is Ensured in Elderly Patients.1

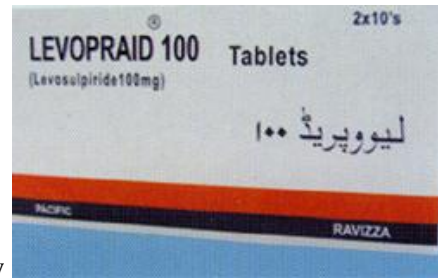
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DOSAGE: 1 Tablet of LEVOPRAID 100® 2 - 3 times daily

Composition: LEVOPRAID - 100 Tablets: Each tablet contains Levosulpiride.....100mg.
Chemical Classification: Levosulpiride is a substituted benzamide, chemically it is S-(-)-N(1-ethylpyrrolidine-2-yl-methyl)-5- sulfamoyl-benzamide. Therapeutic Classification: Atypical Neuroleptic with stereoselective antidopaminergic action. Properties: The biochemical, pharmacological and clinical data obtained from the two sulpiride isomers indicate that the Antidopaminergic action, both on a central and peripheral level, is due to the levogyre enantiomer (levosulpiride) LEVOPRAID exhibits a clear antidepressive, anticenesthopathic, Uninhibiting and resocializing action. Due to its hallucinolytic and deliriolytic action it is effective against acute and chronic schizophrenia. For depression, LEVOPRAID is administered at lower dosages than those used on patients with schizophrenia. It is suggested that these low dosages involve a preferential action on the presynaptic DA-receptors, thus producing a functional increase of dopaminic transmission and stimulating motoric and psychic action. The antipsychotic effects of LEVOPRAID generated at high dosages may be due to a Blocking of the post synaptic DA-receptors, although these effects are not a characteristic as those produced by classic neuroleptic agents. LEVOPRAID exerts its action at dosages which are 2-3 times lower than those of the racemic molecule, which entails a better tolerability and a reduced occurrence of collateral effects. Sedation, antimuscarinic effects, hypotension and extrapyramidal disorders are less of a problem than with most other neuroleptics. Pharmacokinetics: After oral administration, the bioavailability of L-sulpiride is about 30%. Peak-plasma concentration occurs after about 3 hours and it has plasma half life of about 9.7 hours. It is mostly eliminated by the kidneys in the urine. Indications: LEVOPRAID is indicated in the treatment of Endogenous and reactive depressive states, Somatic disturbances, acute and chronic schizophrenia with predominant negative symptoms {After disorders). Dosage: Endogenous and reactive depressive states / somatic disturbances: For Adults 2-3 tablets of 50mg in divided doses daily. Acute and chronic schizophrenia: For Adults 2-3 tablets of 100mg daily. Maintenance Therapy: The dosages may be progressively lowered. When treating aged patients the dosage must be carefully established by the physician who must consider a possible reduction in the dosage mentioned above. Contraindications: As with other neuroleptics, levosulpiride is also contraindicated in patients with hyperprolactinemic tendency, mammary dysplasias and malignant mastopathies. Precautions: LEVOPRAID is to be applied with caution in epilepsies, manic states, manic stages of manic-depressive psychoses, cases of hypertension in patients suspected to be carriers of phaeochromocytoma and in patients showing signs of cardiac insufficiency. Warnings: As with other neuroleptics, the association of levosulpiride with typical

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neuroleptics demands particular medical care and attention. In case of potentially fatal complex of symptoms, known as Malignant Neuroleptic Syndrome (hyperpyrexia, muscular rigidity, akinesia, vegetative disturbances, irregularities of pulse and arterial pressure, perspiration, arrhythmias, alterations of the conscious conditions, or numbness and coma). Under such circumstances, the treatment may be suspended, or should be continued if considered essential and patients must be carefully monitored. Drug interaction: As with other neuroleptics or substituted benzamide, 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. Side Effect: Numbness, a sense of vertigo and asynchronisms may occur; patients under treatment must be made aware of these risks in order to avoid driving vehicles and attending to operations demanding total attention, due to their potential dangers. In very rare cases, psychomotoric excitement, neurovegetative disturbances and allergic phenomena have been observed. Isolated cases of an increase in body weight have been reported following prolonged treatment, All these effects are of a modest and reversible nature, Galactorrhoea and alterations of the libido, observed on particular occasions, are reconducible to a reversible effect of levosulpiride on the functionality of the hypothalamus-pituitary-gonadic axis.which are similar to that known in many neuroleptics. Packing: LEVOPRAID 100 is available in a box of 2x10's tablets. M.R.P. Rs.763.05 KEEP OUT OF THE REACH OF CHILDREN.