

Pacific Pharmaceuticals Ltd.

Lahore, Pakistan



Levopraid® 25

Relieves GERD, Functional dyspepsia & IBS
with better safety profile

GERD Makes Their Life Miserable

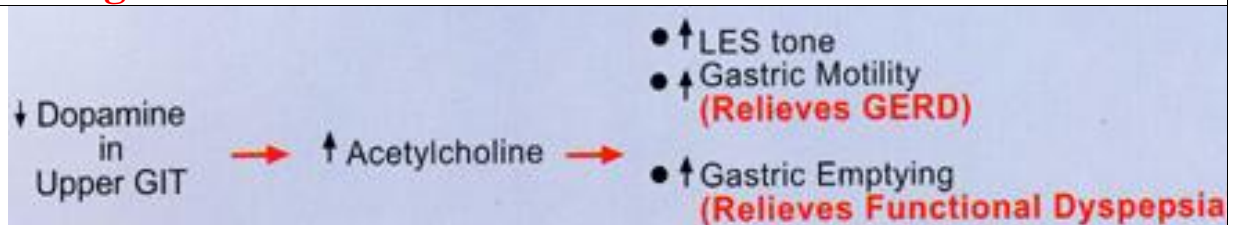
Due to Poor Lower Esophageal Sphincter Tone

When the esophageal sphincter is weak, it lacks the strength necessary to hold back stomach contents. Thus erosive stomach contents are allowed to backup (or reflux) into the esophagus.

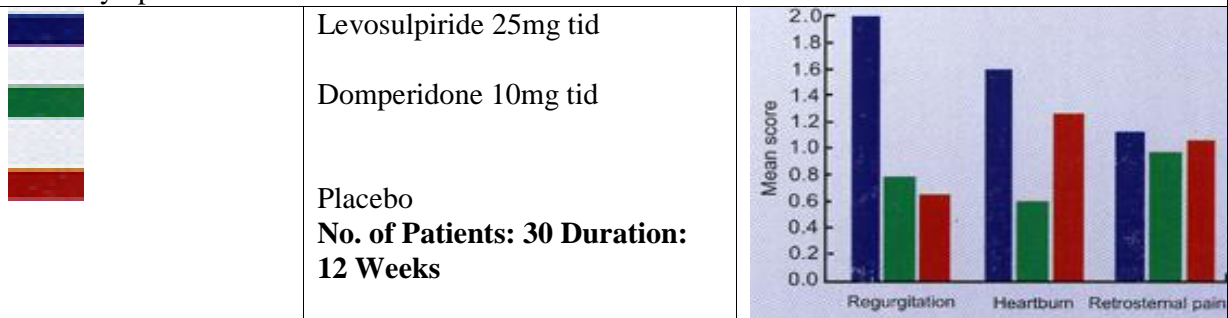
Poor Esophageal Clearance

Normally when an episode of reflux occurs the esophagus has mechanism that quickly push the refluxed materials back into the stomach. If these mechanism malfunction the erosive stomach contents may remain in the esophagus for prolonged periods. This can result in irritation and even damage to the esophageal lining.

Levopraid® 25 A Selective Dopamine DA2 Receptor Antagonist



Levopraid 25 is more effective than domperidone and placebo to improve the severity of main reflux symptoms.



Demonstrate better safety profile

The incidence of side effects with Levopraid 25 is significantly less than Domperidone and Metoclopramide.²

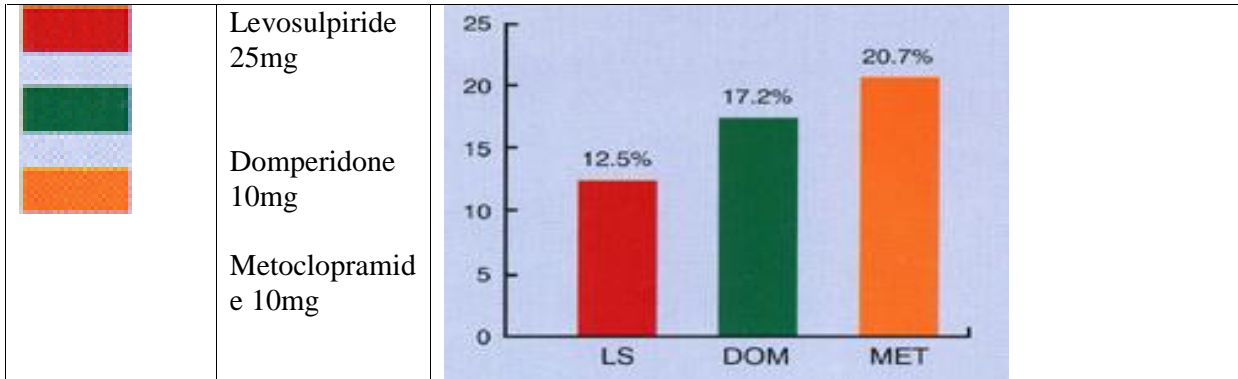
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Moreover...

Recent studies showed that Cisapride but not Levosulpiride has structural properties similar to those of class III antiarrhythmic drugs, which delays repolarization and prolong QT interval.³

Hence, **Levopraid 25** does not cause cardiac arrhythmias.

Relives GERD, Functional dyspepsia & IBS with better safety profile

**Effectively Relives
GERD, Functional
Dyspepsia & IBS**

**Better tolerability than
metoclopramide and
Domperidone.**

**Does not cause cardiac
arrhythmias and
diarrhoea.**

**No extrapyramidal
side effects.**

Indication	Dosage	Duration
GERD	1 Tab. TID	12 Weeks
Functional Dyspepsia	1 Tab. TID	4 Weeks
IBS	1 Tab. TID	4-6 Weeks

Ref 1: Masci et.al., current Therapeutic Research Vol-53, 1993

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Ref 2: Corazza GR, Biagi F, Albano O, et al. Levosulpiride in functional dyspepsia: a multicentric, double-blind, controlled trial. Ital J. Gastroenterol 1996; 28 317-23

Ref 3: Corazza GR and Tonini M Levosulpiride for Dyspepsia and emesis, Clin drug invest 2000 Feb. 19(2) 151-162

Prescribing Information

COMPOSITION: Levopraid -25 Tablets. Each tablet contains levosulpiride 25mg **CHEMICAL**

CLASSIFICATION: Levosulpiride is a substituted benzamide, chemically it is S-(-)-N(1-ethylpyrrolidine-2-yl)-1-methyl-5-sulfamoyl-benzamide **PHARMACOLOGICAL**

CLASSIFICATION: Antidopaminergic (A Selective DA₂ receptors) in the central nervous system and in the peripheral submucosal and myenteric plexus of the gastrointestinal tract.

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 increases the tone and range of gastric contractions in patients affected by gastric stasis and consequently retained gastric voiding relaxes the pyloric sphincter and increases the duodenal and jejunal peristalsis leading to accelerated gastric voiding and intestinal transit. Owing to these peculiar features, the pharmaceutical may be employed in endoscopic studies for overcoming spasm and primary or reflected pyloric hypermyotonia, in the radiology of the digestive tract for shortening examination time, for promoting antral ejection of the contrasting medium and for avoiding troublesome compressive motions. Levopraid exerts a regulation action both on the central and peripheral nervous circuits controlling the dynamics of the digestive system. Controlled clinical studies demonstrate that Levopraid is active for digestive disturbances (anorexia, nausea, vomiting etc.) of an organic, functional and heterogeneous nature. Levosulpiride considerably reduces the emesis induced by the most powerful antiemetic agents (cisplatin, antracycline). alone or in combination, in patients affected by metopodinia. It exerts a considerable pharmacological influence, by reducing the frequency, duration and intensity of crisis periods. Levopraid will generally not alter the cardio-respiratory parameters, the kidney or bladder functions or the emetic crisis,

PHARMACOKINETICS: After oral administration, the bioavailability of L-Sulpiride is about 30%. Peak-Plasma concentration occurs after about 3 hours and it has a plasma half-life of about 9.7 hours. It is mostly eliminated by the kidneys in the urine. **INDICATIONS:** 1. Gastroesophageal Reflux Disease (GERD) 2. Irritable Bowel syndrome (IBS) 3. Dyspeptic syndrome (anorexia, meteorism, sense of epigastric tension, postprandial cephalgia, pyrosis, eruptions, diarrhea, stipsis) due to retarded gastric voiding related to organic factors (diabetic gastroparesis, neoplasia etc.) and/or functional factors (visceral somatization in anxious depressive individuals): Essential Cephalgia: vasomotoric affections (classic, common, ophthalmic, cluster-type migraine) and muscular tension conditions: Vomiting and Nausea (post operatorial or induced by antiemetic pharmaceuticals) Vertigo of a Central and/or peripheral Origin. **DOSAGE AND**

ADMINISTRATION: Tablets; 1 tablet of 25 mg 3 times per day before meals, according to medical prescription. **CONTRAINDICATIONS:** Levosulpiride is contraindicated to patients affected by pheochromocytoma, as it may cause a hypertensive crisis, probably due to the release of catecholamines from the tumor. Such hypertensive crisis may be controlled by phentolamine,

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Levosulpiride is contraindicated in patients with a known hypersensitivity or intolerance to the drug, it must not be used in epilepsy, in manic conditions and in the manic stages of manic-depressive psychoses. In regard to the supposed correlations between the hyperprolactinemyzing effect of most psychotropic drugs and mammary dysplasias. It will be appropriate not to administer Levosulpiride in subjects affected by malignant mastopathies **SIDE EFFECTS:** For prolonged administrations, certain disturbances such as amenorrhea, gynocomastia, gaiactorrhea and aiterations of the libido, observed in particular occasions, are referable to a reversible effect of Levosulpiride on the functionality of the hypothalamus-pituitary gonadal axis, similar to that known for many neuroleptics. **PRECAUTIONS FOR USE:** No secondary effect have been observed at the dosage recommended in internai medicine, however at higher dosages somnolence, numbness and dyskinesia may occur, due to their potential dangers, patients under treatment must be made aware of these risks in order to avoid driving vehicals and attending to operations requiring total attention. Levosulpiride must not be used when stimulating gastrointestinal motifity may be harmful, for instance in the presence of gastrointestinal bleedings, mechanical obstructions or perforations. **USE DURING PREGNANCY AND LACTATION:** Not to be used during presumed or confirmed pregnancy and during the lactation period. **DRUG INTERACTION:** The affects of levosulpiride on the gastrointestinal motillty may be opposed by antichoiinergic, narcotic or analgesic-drugs. The association with psychopharmacological agents requires particular care and vigilance by the physician, in order to avoid any unexpected side effect due to interaction. The simultaneous intake of alcohol must be avoided. **OVERDOSAGE;** In internal medicine nor extrapyramidal or sleep disturbances have ever been observed, which may eventually occur at very high dosages. Interrupting the therapy or reducing the dosage depending on the physician's judgement will be sufficient in this case. **STORAGE:** Store at room temperature (15-30 C), away from children's reach . **SHELF LIFE:** 60 month (5 years) in undamaged packaging when stored properly. **PRESENTATION:** Cardboard box containing 2x 10's tablets of 25mg each in PVC/PVDC aluminium blisters.