IPRIDE

COMPOSITION:

Ipride 50mg Tablets
Each tablet contains:
Itopride HCl (M.S) 50mg
Ipride SR 150mg Capsule
Each capsule contains:
Itopride HCl sustained release pellets
containaing Itopride HCl (M.S) 150mg

Product conforms to the Manufacturer's Specifications.

DESCRIPTION:

Itopride Hydrochloride (Ipride/Ipride SR) is an AChE (Acetylcholinesterase) inhibitor and Dopamine Receptor D2 (D2DR) inhibitor. Itopride is used as a gastroprokinetic agent. Its chemical name is N-[4-[2-(Dimethylamino) ethoxy] benzyl]-3,4-dimethoxybenzamide Hydrochloride. Its empirical formula is C20H26N2O4. HCl and molecular weight is 394.88.

MECHANISM OF ACTION:

Itopride HCl (Ipride/Ipride SR) has three way actions:
It inhibits the dopamine D2 receptor at the parasympathetic nerve ends and thereby increases the release of acetylcholine and decreases the metabolism of acetylcholine by inhibiting the enzyme acetylcholinesterase (AChE). By maintaining higher acetylcholine levels, Itopride increases the oesophageal and gastrointestinal peristalsis, increases the lower oesophageal sphincter pressure, stimulates gastric motility, accelerates gastric emptying and improves gastrodoudenal coordination. Itopride exerts antiemetic actions because of its dopamine D2 receptor antagonistic action at CTZ.

PHARMACOKINETICS:

Absorption:
Itopride HCl is rapidly and almost completely absorbed from the gastrointestinal tract. Relative bio-avalbility is calculated to be 60% due to liver first pass metabolism.There is no effect of food on bio-availability. Peak plasma levels (Cmax 0.2 µg/ml) and reached after 0.5 to 0.75 hours after 50mg of Itopride Hydrochloride (Ipride). Following multiple over doses ranging from 50 to 200mg t.i.d. Itopride Hydrochloride (Ipride/Ipride SR) and its metabolite showed linear pharmacokinetics over a treatment period of seven days, with minimal accumulation.
Distribution:
Approximately 96% of Itopride HCl is bound to plasma proteins. Albumin accounts for most of the binding.Alpha -1 acid glycoprotein accounts for less than 15% of binding.
Metabolism:
Itopride Hcl undergoes extensive hepatic metabolism in humans three metabolites have been identified of which only one exerts minor activity without pharmacological relevance (approximately 2-3% of that Itopride) the primary metabolite in human is the n-oxide,generally by oxidation of the tertiary amine N-dimethyl group. Itopride HCl is metabolized by a Flavine dependent mono oxygenase (FMO3). The abundance and efficacy of the human FMO isoenzyme can be subjected to genetic polymorphism,which can lead to a rare autosomal recessive condition known as trimethylamin

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uria(fish ordor syndrome). The half life of Itopride HCl may therefore be longer in trimethylaminuria patients.In vivo pharmacikontics studies on cyp-mediated reactions revealed that Itopride HCl showed neither inhibitory nor inductory effect on cyp2c19 and CYP2E1.CYP potent and uridine diphosphate glucuronosyl transferase activity were not altered with administration of Itopride HCl.
EXCRETION:
Itopride HCl and its metabolites are mainly excreted in the urine. The urinary excretion of Itopride HCl and its n-oxide were 3.7% and 75.4% respectively, in healthy subjects after oral administration of a single therapeutic dose. The terminal phase half life of Itopride HCl was approximately six hours.

INDICATIONS:

Itopride HCl (Ipride/Ipride SR) is indicated in various digestive conditions giving rise to symptoms such as heart burn, regurgitation, epigastric pain, esophagitis etc. These conditions include GERD, non ulcer dyspepsia, chronic gastritis and a very important complication seen in diabetics wherein the gastric emptying is markedly reduced i.e. diabetic gastroparesis.

DOSAGE & ADMINISTRATION:

Adult Dose:
The recommended dose of Itopride HCl is 150mg daily i.e. one tablet (Ipride 50mg) taken orally three times a day before meal or one capsule Ipride SR 150mg once a day before meal.
The dose may be reduced according to patient's age and symptoms.

CONTRAINDICATIONS:

Itopride HCl (Ipride/Ipride SR) is contraindicated in patients with known history of Itopride HCl or any of the excipient. Itopride HCl should not be used in patients in whome an increase in gastrointestinal motility could be harmful e.g. gastrointestinal hemorrhage, mechanical obstruction or perfusion.

PRECAUTIONS:

Itopride HCl (Ipride/Ipride SR) enhances the action of acetylcholine and may produce cholinergic side effects.

PREGNANCY AND LACTATION:

Pregnancy: Safety of Itopride HCl 50mg in pregnancy was not verified. Therefore it can be used in pregnant women or women in that pregnancy cannot be excluded only if therapeutic benefits outweigh possible risks considerably.
Lactation: Because of lack of experience with use of Itopride HCl during breastfeeding it is not recommended for breast feeding. women.

DRUG-DRUG INTERACTIONS:

Coadministration of Cisapride with such CYP3A4 inhibitors impairs CYP3A4 dependent presystemic extraction, causing greatly elevated plasma concentrations of unchanged Cisapride compared with those after administration of Cisapride alone. The resultant high levels of Cisapride produce adverse effects, such as QT interval prolongation, leading to the risk of ventricular arrhythmias.
Itopride N-oxide formation was inhibited in the presence of Methimazole and Thiourea, alternative substrate competitive inhibitors of FMO. In addition, the decrease in Itopride N-oxide formation to 0% of the control caused by treatment at 45°C for 5 min suggests a heat mediated inactivation of FMO that was delayed when NADPH was included.

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Pre retreatment with Ketoconazole did not alter the metabolism of Itopride in rats, whereas it caused accumulation of unmetabolized Cisapride and Mosapride. In addition, Itopride showed no inhibitory effect on five specific CYP-mediated reactions in human liver microsomes. It is concluded that Itopride is unlikely to cause clinically significant pharmacokinetic drug interactions.

ADVERSE DRUG REACTIONS:

Following side effects can occur during the treatment with Itopride HCl (Ipride/Ipride SR).
Uncommon: Affects1 to 10 users in 1,000
Diarrhea, abdominal pain, hypersalivation, headache, irritability, sleep disorders, dizziness, chest pain or back pain, fatigue, increased levels of hormone prolactin, change in laboratory blood values (Reduced white cell count, increased urine and creatinine).
Rare: Affects 1 to 10 users in 10,000
Rash formation, redness and itching of the skin.
Frequency not known:

- Increased laboratory blood values (AST, ALT, gamma-GTP, alkaline phosphatase, bilirubin)
- Decreased amount of platelets (it can manifest with contusions and increased bleeding)
- Tremor
- Nausea
- Jaundice
- Enlarged breasts in men.

If galactorrhea (production and secretion of breast milk not associated with breast feeding) ogyneco-mastia (enlarged breasts in men) occurs, the treatment must be discontinued or terminated.

OVERDOSAGE:

There have been no reported causes of overdose in human. In case of excessive overdose the usual measure of gastric lavage and symptomatic therapy should be applied.

INSTRUCTIONS:

Store in a cool and dry place below 25°C.
Protect from light, heat and moisture.
Keep out of reach of children.

PRESENTATION:

Ipride 50mg tablets are available in a blister pack of 30's
Ipride SR 150mg capsules are available in a blister pack of 20's