

SEAPRIDE

(Itopride Hydrochloride)

50mg

Tablets

COMPOSITION

Each tablet contains:
Itopride hydrochloride..... 50mg
(As per Innovator's Specification)

THERAPEUTIC INDICATIONS

Treatment of gastrointestinal symptoms of functional, non-ulcer dyspepsia, like feelings of bloating, gastric fullness, discomfort to pain in epigastrium, anorexia, heartburn, nausea and vomiting.

The medicinal product is intended for adults

DOSAGE AND ADMINISTRATION

The recommended dose for adults is 150 mg daily, i.e. 1 tablet 3 times a day before meal. This dose can be reduced if required in the course of disease. The exact dosage and duration of treatment depends on the clinical state of the patient. The duration of the administration in clinical studies was maximally 8 weeks.

Paediatric population

The safety and efficacy of itopride in pediatric population has not been established.

Patients with hepatic or renal impairment

Itopride is metabolized in liver. Itopride and its metabolites are excreted mainly via kidneys. Patients with reduced hepatic or renal functions should be carefully monitored and in case of adverse reactions it is necessary to take appropriate measures, as e.g. to reduce the dosage or to discontinue the therapy.

Elderly

It was shown in clinical studies that the incidence of adverse effects in patients aged 65 years and older was not higher than in younger patients. Itopride should be administered in elderly patients with adequate caution because of increased incidence of hepatic and renal function disorders, other diseases or treatment with additional drugs.

Method of administration

Tablets should be swallowed whole with a sufficient amount of liquid.

CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients.

Itopride 50 mg must not be used in patients in whom increased gastrointestinal motility could be harmful, e.g., in patients with gastrointestinal haemorrhage, mechanical obstruction or perforation.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Itopride potentiates acetylcholine action and can induce side anticholinergic effects.

Data about long-term administration of itopride is not available. This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine

DRUG INTERACTIONS

No interaction was detected when itopride was administered concomitantly with warfarin, diazepam, diclofenac, ticlopidine, nifedipine and nicardipine.

Drug-drug interactions that arise due to cytochrome P450 metabolism are not assumed because itopride is metabolized mainly by flavine monooxygenase.

Itopride has gastrokinetic effect that could influence the absorption of concomitantly orally administered medicines. Particular attention should be paid to medicines with a narrow therapeutic index, medicines with prolonged-release of the active substance and enteric-coated drug formulations.

Anticholinergic agents may reduce the action of itopride. Substances as cimetidine, ranitidine, teprenone and cetrexate do not affect prokinetic activity of itopride.

EFFECTS ON ABILITY TO DRIVE

Although no effects on ability to drive and use machines have been found, impairment of alertness cannot be ruled out since dizziness may occur very rarely

FERTILITY, PREGNANCY AND LACTATION

Pregnancy

Safety of itopride in pregnancy was not verified. Therefore, itopride can be used in pregnant women or women in that pregnancy cannot be excluded only if therapeutic benefits outweigh possible risks considerably.

Breast-feeding

Data about excretion in mother milk is known only in animals. Because of lack of experience with use of itopride during breast-feeding itopride it is not recommended for breast-feeding women.

ADVERSE DRUG REACTIONS

Adverse reactions have been ranked according to MedDRA terminology under headings of frequency using the following convention: very common (1/10); common (1/100 to < 1/10); uncommon (1/1,000 to < 1/100); rare (1/10,000 to < 1/1,000); very rare (< 1/10,000), not known (cannot be estimated from the available data).

Blood and lymphatic system disorders

Uncommon: Leucopenia*.

Not known: Thrombocytopenia.

* Careful observation should be made through haematological examination. The treatment should be

discontinued when any abnormality is observed.

Immune system disorders

Not known: Anaphylactoid reaction.

Endocrine disorders

Uncommon: Hyperprolactinaemia**.

Not known: Gynecomastia.

** If e.g. galactorrhoea or gynecomastia appears the treatment must be interrupted or terminated.

Psychiatric disorders

Uncommon: Irritability.

Nervous system disorders

Uncommon: Headache, sleep disorders, dizziness.

Not known: Tremor.

Gastrointestinal disorders

Uncommon: Diarrhoea, constipation, abdominal pain, hypersalivation.

Not known: Nausea.

Hepatobiliary disorders

Not known: Jaundice.

Skin and subcutaneous tissue disorders

Rare: Rash, erythema, pruritus.

Musculoskeletal and connective tissue disorders

Uncommon: Chest or back pain.

Renal and urinary disorders

Uncommon: BUN (blood urea nitrogen) and creatinine increased.

General disorders and administration site conditions

Uncommon: Fatigue.

Investigations

Not known: AST increased, ALT increased, gamma-GTP increased, alkaline phosphatase increased,

bilirubin increased.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at pv@searlecompany.com

OVERDOSE

Overdose was not experienced in humans. In case of overdose the usual measures of gastric lavage and symptomatic therapy should be applied.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group: Drugs for functional gastrointestinal disorders, propulsives; ATC code:

A03FA07.

Mechanism of action

Itopride activates the gastrointestinal propulsive motility by dopamine D2 receptors antagonistic action and acetylcholine esterase inhibitory action. Itopride activates acetylcholine release and inhibits its degradation.

In addition, itopride has an antiemetic action which is based on interaction with dopamine D2 receptors in chemoreceptor zone. This action was demonstrated by dose dependent inhibition of apomorphine induced vomiting in dogs.

Itopride accelerates stomach emptying in humans. In animal studies in dogs with a single dose administration itopride supported stomach emptying. Itopride has high specific action in upper part of gastrointestinal tract. Itopride does not influence plasma concentrations of gastrin.

Pharmacokinetic properties

Absorption

Itopride is absorbed rapidly and almost completely from gastrointestinal tract. Relative bioavailability about 60% is due to first-pass effect. Food does not affect bioavailability of the product. Maximum plasma concentrations are reached in 30 to 50 minutes after administration of 50 mg of itopride. After repeated administration of doses in the range of 50 to 200 mg 3 times a day for period of 7 days, itopride and its metabolites have shown pharmacokinetics of linear type with minimal accumulation.

Distribution

About 96% of itopride is bound on plasma proteins, mainly albumin. Less than 15% of itopride bound part is bound on alpha-1-acid-glycoprotein.

In rats itopride is distributed extensively in the tissues ($Vd\beta = 6.1$ l/kg) except for central nervous system; high concentrations are reached in kidneys, small intestine, liver, adrenal glands and stomach. Protein binding in rats was lower than in humans (78% contrary to 96%). Penetration into the central nervous system was minimal. Itopride is excreted in milk of lactating rats.

Biotransformation

Itopride is extensively metabolised in liver in humans. Three metabolites were identified of which only one manifests minor activity without pharmacological

significance (about 2 to 3% of itopride effect). Itopride is metabolized by flavine monooxygenase (FMO3). The amount and efficacy of human FMO isoenzymes can be associated with genetic polymorphism which can result in rare autosomal recessive condition known as trimethylaminuria (fish odour syndrome). Biological half-life in patients with trimethylaminuria can be longer.

Pharmacokinetic in vivo studies of CYP-mediated reactions did not prove inhibition or induction CYP2C19 and CYP2E1 caused by itopride. Administration of itopride did not influence content of CYP or the activity of uridine-diphosphate-glucuronyl transferase.

Elimination

Itopride and its metabolites are primarily excreted by urine. The amount of excreted itopride and Noxide after oral single therapeutic dose to healthy volunteers was 3.7% and 75.4%, respectively Half-life of itopride is about 6 hours.

PRECLINICAL SAFETY DATA

Oral single lethal dose was 2,000 mg/kg in mice and rats and approximately 600 mg/kg in dogs. Preclinical safety studies were carried out only with doses multiplicatively overrunning therapeutic human doses and found effect have only little importance for use of itopride in humans. In addition to it humans s atrophy after oral administration in dose 30 mg/kg/day. This effect was induced neither after 6-month administration of higher doses (100 mg/kg/day) in rats nor more higher doses (300 mg/kg/day) in monkeys.

Long-term studies of cancerogenity in animals have not been carried out. In series of in vitro and in vivo tests no clastogenic and mutagenic effects of itopride were found. In fertility studies in female rats who were administered doses 30 mg/kg/day and higher hyperprolactinaemia and secondary prolongation of oestral cycle after were observed. Prolonged precoital interval was observed at doses 300 mg/kg/day. No side effect on copulation and fertility was proved.

PRESENTATION

Seapride 50mg tablets are available in blister pack of 10's.

INSTRUCTIONS

-Protect to be sold on the prescription of a registered medical practitioner only.

-Protect from sunlight, moisture and heat.

-Store below 30°C.

-Keep all medicines out of sight and reach of children.

REGISTRATION NUMBER

Seapride 50mg Tablets: 084566

Manufacturing license Number: 000647

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

Manufactured by:

The Searle Company Limited.

32-Km, Multan Road, Lahore - Pakistan.

Marketed by:

IBL HEALTHCARE LIMITED,

One IBL Center, 2nd Floor, Plot # 1, Block 7 & 8, D.M.C.H.S,

Tipu Sultan Road, Off Shahra-e-Faisal, Karachi – Pakistan

DATE OF PUBLICATION OF THE PACKAGE INSERT

June 2021

SPL/SPC-SEA.T/621-000(001)

