SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the pharmaceutical product:

ITOKINE®

Itopride Hydrochloride Sustained Release Capsules 150 mg

2. Qualitative and Quantitative composition

Each hard gelatin capsule contains:

Itopride hydrochloride…..150 mg

(As sustained release pellets)

Excipients…..q.s

Approved colour used in empty hard gelatin capsule shell.

3. Pharmaceutical form:

Sustained Release Capsules.

A red/white colored, size '2' hard gelatin capsule containing white colored pellets.

4. Clinical particulars

4.1 Therapeutic indications

ITOKINE is indicated for the treatment of gastrointestinal symptoms caused by reduced gastrointestinal motility, like feeling of fullness, upper abdominal pain, anorexia, heartburn, nausea and vomiting; non-ulcer dyspepsia or chronic gastritis.

4.2 Posology and method of administration

Posology:

Adults:

The usual dose of itopride hydrochloride for adult patients is 150 mg daily before meals. The dose may be reduced according to the patient's age and symptoms (see PRECAUTIONS).

Duration of Treatment:

In clinical studies, itopride hydrochloride has been administered up to 8 weeks.

Method of administration:

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

4.3 Contraindications

Itopride hydrochloride is contraindicated in patients with known hypersensitivity to itopride hydrochloride or any of the excipients.

Itopride hydrochloride should not be used in patients in whom an increase in gastrointestinal motility could be harmful, e.g. gastrointestinal hemorrhage, mechanical obstruction or perforation.

4.4 Special warnings and precautions for use

General

Itopride hydrochloride enhances the action of acetylcholine and may produce cholinergic side effects.

Data on long-term use are not available.

Pediatric Use

Safety of itopride in children under the age of 16 has not been established.

Geriatric Use

In general, appropriate caution should be exercised in the administration and monitoring of Itopride hydrochloride in elderly patients reflecting the greater frequency of decreased hepatic, renal function, and of concomitant disease or other drug therapy.

4.5 Interaction with other medicinal products and other forms of interaction

Metabolic interactions are not expected since Itopride is primarily metabolized by flavine monooxygenase and not by CYP450.

No changes in protein binding have been seen with coadministration of warfarin, diazepam, diclofenac sodium, ticlopidine hydrochloride, nifedipine, and nicardipine hydrochloride.

Since itopride has gastrokinetic e_ects it could influence the absorption of concomitantly orally administered drugs. Particular caution should be taken with drugs with a narrow therapeutic index, sustained release or enteric-coated formulations.

Anti-ulcer drugs like cimetidine, ranitidine, teprenone and cetraxate do not affect the prokinetic action of itopride.

Anticholinergic drugs may reduce the action of itopride.

4.6 Pregnancy and lactation

Pregnancy: There are no adequate and well-controlled studies in pregnant women. Therefore, Itopride hydrochloride should not be used during pregnancy unless the benefits outweigh the potential risks.

Labor and Delivery: There are no known effects of itopride hydrochloride on labor or delivery.

Lactation: Because itopride is excreted in milk in rats, and because of the potential for adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines.

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. Care should be taken before driving or using machinery until the patient's individual reaction on the medicine has been established.

4.8 Undesirable effects Reactions

During Clinical Trials

In clinical trials (Phase I – Phase III) Itopride hydrochloride was well tolerated and no serious adverse reactions were reported. A total of 19 adverse drug reactions in 14 patients were reported out of 572 cases with an incidence of 2.4%. The majority of these adverse reactions occurring in more than one patient consisted of diarrhoea in 4 cases (0.7%), headache in 2 cases (0.3%), and abdominal pain in 2 cases (0.3%).

Abnormal laboratory findings observed in the trials include decreased WBC (leukocytopenia) in 4 cases (0.7%), increased prolactin in 2 cases (0.3%).

Post-marketing Experience and Ongoing Clinical Studies

The following adverse events have been reported in patients receiving itopride hydrochloride:

Blood and lymphatic system disorders

Leukopenia and thrombocytopenia.

Immune system disorders

Hypersensitivity, Anaphylactoid reaction.

Endocrine disorders

Increased prolactin level and gynecomastia.

Nervous system disorders

Dizziness, headache, and tremor.

Gastrointestinal disorders

Diarrhoea, constipation, abdominal pain, increased saliva, and nausea.

Hepato-biliary disorders

Jaundice.

Skin and subcutaneous tissue disorders

Rash, redness, and itching.

Investigations

Increased AST (SGOT), increased ALT (SGPT), increased gamma-GTP, increased alkaline phosphatase, and increased bilirubin.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org.

4.9 Overdose.
There have been no reported cases of overdose in humans. In case of excessive overdose, the usual measures of gastric lavage and symptomatic therapy should be applied.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs for functional gastrointestinal disorders, propulsives; *ATC code:* A03FA07

Itopride hydrochloride also has antiemetic action through interaction with D2 receptors located in the chemoreceptor trigger zone. This was demonstrated by dose dependent inhibition of apomorphine-induced vomiting in dogs.
In conscious dogs, itopride hydrochloride activates propulsive gastric motility through dopamine D2-receptor antagonistic actions and dose-dependent inhibition of acetylcholinesterase.
Itopride hydrochloride has been shown to accelerate gastric emptying in humans, dogs and rats. In single-dose studies in dogs, itopride hydrochloride was shown to promote gastric emptying. The action of itopride hydrochloride is highly specific for the upper gastrointestinal tract.

5.2 Pharmacokinetic properties

Absorption
ltopride hydrochloride is rapidly and almost completely absorbed from the gastrointestinal tract. Relative bioavailability is calculated to be 60% due to liver first pass metabolism. There is no effect of food on bioavailability. Peak plasma levels (Cmax 0.28 μg/mL) are reached after 0.5 to 0.75 hours after 50 mg of itopride hydrochloride.
Following multiple oral doses ranging from 50 mg to 200 mg tid, itopride hydrochloride and its metabolites showed linear pharmacokinetics over a treatment
period of seven days, with minimal accumulation.
Distribution
Approximately 96% of itopride hydrochloride is bound to plasma proteins.
Albumin
accounts for most of the binding. Alpha-1-acid-glycoprotein accounts for less than
15% of binding.
In rats, itopride is distributed extensively ($V_{d\beta}$ = 6.1 L/kg) with high concentrations in
the kidneys, small intestines, liver, adrenal glands, and stomach. Protein binding in the rat was lower than that seen in humans (78 vs 96%). The transfer into the central

nervous system, including brain and spinal cord, was minimal. ltopride distributes into the breast milk of rats.

Metabolism

Itopride undergoes extensive hepatic metabolism in humans. Three (3) metabolites have been identified, of which only one exerts minor activity without pharmacological relevance (approximately 2-3% of that of itopride). The primary metabolite in humans is the N-oxide, generated by oxidation of the tertiary amine N-dimethyl group.

Itopride is metabolized by a flavin-dependent mono-oxygenase (FMO3). The abundance and effciency of the human FMO-isozymes can be subject to genetic polymorphisms, which can lead to a rare autosomal recessive condition known as trimethylaminuria (fish odor syndrome).

The half-life of itopride may therefore be longer in trimethylaminuria patients.

In vivo pharmacokinetic studies on CYP-mediated reactions revealed that itopride showed neither inhibitory nor inductory effect on CYP2C19 and CYP2E1. CYP content and uridine diphosphate glucuronosyl transferase activity were not altered with the administration of itopride.

Excretion

Itopride hydrochloride and its metabolites are primarily excreted in the urine. The urinary excretions of itopride and its N-oxide were 3.7% and 75.4%, respectively, in healthy subjects after oral administration of a single therapeutic dose.

5.3 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 are less sensitive to hormonal effects observed in animals.

High doses of itopride (30 mg/kg/day) caused hyperprolactinaemia and secondary reversible hyperplasia of uterine mucosa in rats. Nevertheless, this was not proved in dogs (dose up to 100 mg/kg/day) and monkeys (dose up to 300 mg/kg/day).

3-month toxicity study in dogs has revealed prostate 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 were observed. Prolonged precoital interval was observed at doses 300 mg/kg/day.

6. Pharmaceutical particulars

6.1 List of Excipients:

Hard Gelatin capsule shell

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store below 30°C, protect from light.

6.5 Nature and contents of container

ITOKINE® Capsules are available in the pack of 1 x 10's

6.6 Special precautions for disposal and other handling

Do not throw away any medicines via wastewater or house hold waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help with the environment.

7. Marketing authorization holder and manufacturing site addresses

Manufactured in India by:

RELAX BIOTECH PVT. LTD.

862/1, GIDC, Makarpura,
Vadodara – 390010, Gujarat,
India.

Manufactured For & Marketed by:

KRISHNA CHEMISTS LTD.

P.O. BOX 3328-00506
NAIROBI, KENYA.

8. Marketing authorisation number(s)

CTD5559

9. Date of first Registration/ Renewal of Registration

19/07/2026

10. Date of revision of text

19/07/2026