adverse reactions occurring in more than one patient consisted of diarrhea 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**

Anaphylactoid reaction.

**Endocrine disorders**

Increased prolactin level and gynecomastia.

**Nervous system disorders**

Dizziness, headache, and tremor.

**Gastrointestinal disorders**

Diarrhea, 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.

**OVERDOSAGE**

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.

**CLINICAL PHARMACOLOGY**

**Mechanism of Action**

Itopride hydrochloride activates gastrointestinal propulsive motility due to its dopamine D2 antagonizing activity and acetylcholinesterase inhibitory activity. Itopride activates acetylcholine release and inhibits its degradation.

**Pharmacodynamics**

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.

Itopride hydrochloride does not affect serum gastrin levels.

**Pharmacokinetic Properties**

**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 efficacy 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 inductive 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.

**STORAGE**

Protect from excessive heat, light and moisture.

**HOW SUPPLIED**

Each Ganaton OD tablet contains 150 mg of itopride hydrochloride in sustained release form. One strip contains 10 tablets.

List No. P880

Manufactured by:
Abbott Laboratories (Pakistan) Ltd.
Landhi, Karachi.

CCDS: SOLID-1000318854 V2.0
25-Sep-2007

Abbott

01-20792
Ganaton® OD
(Itopride Hydrochloride)

150mg Tablets

Product Name
Itopride hydrochloride in sustained release form

Brand Name
Ganaton OD

Description
Itopride hydrochloride is an orally active gastropokinetic agent. Ganaton OD is a film-coated slow release tablet containing itopride hydrochloride 150 mg.

Indications
Ganaton OD 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.

Dosage and Administration
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.

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.

Warnings and Precautions
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.

Drug Interactions
Metabolic interactions are not expected since itopride is primarily metabolized by flavone 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 effects 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.

Pregnancy and Lactation
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.

Nursing Mothers
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.

Adverse Reactions
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...