Ganaton®
(Itopride Hydrochloride)
50mg Tablets

Composition
- Ganaton (Itopride hydrochloride) is an orally active Gastroprokinetic agent.
- Ganaton film coated tablets contain 50 mg of itopride hydrochloride. Abbott specs
- The tablet has been formulated to provide immediate release.
- It is chemically designated as N-[4-[2 (Dimethylamino)ethoxy]benzyl]-3,4-dimethoxybenzamide hydrochloride. Itopride hydrochloride is a substituted benzamide. It has an empirical formula of C_{20}H_{26}N_{2}O_{3}·HCl, molecular weight of 394.89 g/mol.

INDICATIONS
Ganaton (Itopride hydrochloride) is used in the treatment of
- Functional Dyspepsia
- Non-Ulcer Dyspepsia (chronic gastritis) i.e.,
  - Sensation of bloating,
  - Early satiety,
  - Upper abdominal pain or discomfort,
  - Anorexia, o Heartburn,
  - Nausea and
  - Vomiting.

DOSAGE AND ADMINISTRATION
Adults
The recommended dose of Ganaton (Itopride hydrochloride) for adult patients is 150 mg daily [one tablet (50 mg) taken orally three times a day before meals].

The dose may be reduced according to the patient's age and symptoms (see PRECAUTIONS).

PHARMACOLOGICAL PROPERTIES
Mechanism of Action
Ganaton (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
- Ganaton (Itopride hydrochloride) also has antiemetic action through interaction with D2 receptors located in the chemoreceptor trigger zone.
- Ganaton (Itopride hydrochloride) has been shown to accelerate gastric emptying in humans.
- The action of Ganaton is highly specific for the upper gastrointestinal tract. Ganaton does not affect serum gastrin levels.

Pharmacokinetic Properties
Absorption: Ganaton (Itopride 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 Ganaton (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.

Metabolism
Ganaton (Itopride hydrochloride) 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. Ganaton is metabolized by a flavin-dependent mono-oxygenase (FMO3). The abundance and efficiency 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 Ganaton may therefore be longer in trimethylaminuria patients. In vivo pharmacokinetic studies on CYP-mediated reactions revealed that Ganaton 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
Ganaton (itopride hydrochloride) and its metabolites are primarily excreted in the urine. The urinary excretions of Ganaton 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 Ganaton was approximately six (6) hours.

CONTRAINDICATIONS
Ganaton (itopride hydrochloride) is contraindicated in patients with known hypersensitivity to itopride hydrochloride or any of the excipients. Ganaton should not be used in patients in whom an increase in gastrointestinal motility could be harmful, e.g. gastrointestinal hemorrhage, mechanical obstruction or perforation.

PRECAUTIONS
General
Ganaton (itopride hydrochloride) enhances the action of acetylcholine and may produce cholinergic side effects.

DRUG INTERACTIONS
Metabolic interactions are not expected since Ganaton (itopride hydrochloride) is primarily metabolized by flavine monoxygenase 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 Ganaton 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, tretinoin and cetrexate do not the prokinetic action of itopride. Anticholinergic drugs may reduce the action of Ganaton.

PREGNANCY & LACTATION
There are no adequate and well-controlled studies in pregnant women. Therefore, Ganaton (itopride hydrochloride) should not be used during pregnancy unless the benefits outweigh the potential risks.

There are no known effects of Ganaton on labor or delivery. Because Ganaton is excreted in milk, 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.

PEDiatric USE
Safety of this product 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 Ganaton (itopride hydrochloride) in elderly patients reflecting the greater frequency of decreased hepatic, renal function, and of concomitant disease or other drug therapy.

ADVERSE REACTIONS
The following adverse events have been reported in patients receiving Ganaton (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 of overdose the usual measures of gastric lavage and symptomatic therapy should be applied.

STORAGE
Store between 15ºC - 30ºC.

DO NOT USE AFTER EXPIRATION DATE.

HOW SUPPLIED
Ganaton (itopride hydrochloride) 50 mg tablets film-coated.

List No. P160 1x10’s
List No. P160 3x10’s

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

Abbott

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