Imotil® Plus

Loperamide Hydrochloride USP 2 mg &
Simethicone USP 125 mg

COMPOSITION
Imotil® Plus Tablet: Each tablet contains Loperamide Hydrochloride USP 2 mg & Simethicone USP 125 mg.

PHARMACOLOGY
Loperamide HCl: Loperamide binds to the opiate receptor in the gut wall, reducing propulsive peristalsis, increasing intestinal transit time and enhancing resorption of water and electrolytes. Loperamide increases the tone of the anal sphincter.
Simethicone: Simethicone is an inert surface-active agent with anti-foaming properties thereby potentially relieving gas related symptoms associated with diarrhoea.
Absorption: Most ingested Loperamide is absorbed from the gut, but as a result of significant first pass metabolism, systemic bioavailability is only approximately 0.3%. The Simethicone is not absorbed. *Distribution:* The plasma protein binding of Loperamide is 95%, mainly to albumin. *Metabolism:* Loperamide is almost completely extracted by the liver, where it is predominantly metabolized, conjugated and excreted via the bile. *Elimination:* The half-life of Loperamide in man is about 11 hours. Excretion of the unchanged Loperamide and the metabolites mainly occurs through the faeces.

INDICATION
It is indicated for the symptomatic treatment of acute diarrhea in adults and adolescents over 12 years when acute diarrhea is associated with gas-related abdominal discomfort including bloating, cramping or flatulence.

DOSAGE & ADMINISTRATION
Adults over 18 years: Take two tablets initially, followed by one tablet after every loose stool. Not more than 4 tablets should be taken in a day, limited to no more than 2 days.
Adolescents between 12 and 18 years: Take one tablet initially, followed by one tablet after every loose stool. Not more than 4 tablets should be taken in a day, limited to no more than 2 days.

USE IN PREGNANCY AND LACTATION
Pregnancy: Safety in human pregnancy has not been established, although from animal studies there are no indications that Loperamide or Simethicone possesses teratogenic or embryotoxic properties. Loperamide Hydrochloride & Simethicone should not be given during pregnancy, especially during the first trimester, unless clinically justified.
Lactation: Small amounts of Loperamide may appear in human breast milk. Therefore, it is not recommended during breast feeding.

PRECAUTIONS & WARNING
Treatment of diarrhea with Loperamide-Simethicone is only symptomatic. Whenever an underlying etiology can be determined, specific treatment should be given when appropriate. If clinical improvement is not observed within 48 hours, the administration of Loperamide-Simethicone must be discontinued. Patients should be advised to consult their physician. This medicine must be used with caution in patients with hepatic impairment as it may result in a relative overdose leading to central nervous system (CNS) toxicity. Loperamide-Simethicone should be used under medical supervision in patients with severe hepatic dysfunction. Cardiac events including QT interval and QRS complex prolongation, and torsades de pointes have been reported in association with overdose. Some cases had a fatal outcome. Patients should not exceed the recommended dose and/or the recommended duration of treatment.

SIDE EFFECTS
The safety of Loperamide-Simethicone was evaluated in 2040 patients with acute diarrhea with gas related discomfort in five clinical trials. The most commonly reported (i.e., ≥1% incidence) ADRs: dysgeusia (2.6%) and nausea (1.6%).

CONTRAINDICATIONS
Patients with known hypersensitivity to the active substance or to any of the excipients.

DRUG INTERACTIONS
Loperamide is a P-glycoprotein substrate. Concomitant administration of Loperamide (16 mg single dose) with P-glycoprotein inhibitors (Quinidine, or Ritonavir) resulted in a 2 to 3-fold increase in Loperamide plasma concentrations. The concomitant administration of Loperamide (4 mg single dose) and Itraconazole, an inhibitor of CYP3A4 and P-glycoprotein, resulted in a 3 to 4-fold increase in Loperamide plasma concentrations. In the same study a CYP2C8 inhibitor, Gemfibrozil, increased Loperamide by approximately 2-fold. The combination of Itraconazole and Gemfibrozil resulted in a 4-fold increase in peak plasma levels of Loperamide and a 13-fold increase in total plasma exposure. These increases were not associated with measured CNS effects, as measured by psychomotor tests (i.e. subjective drowsiness and the Digit Symbol Substitution Test). The concomitant administration of Loperamide (16 mg single dose) and ketoconazole, an inhibitor of CYP3A4 and P-glycoprotein, resulted in a 5-fold increase in Loperamide plasma concentrations. Concomitant treatment with oral desmopressin resulted in a 3-fold increase of desmopressin plasma concentrations, presumably due to slower gastrointestinal motility. It is expected that drugs with similar pharmacological properties may potentiate Loperamide's effect & drugs that accelerate gastrointestinal transit may decrease its effect.
Since Simethicone is not absorbed from the gastrointestinal tract, no relevant interactions between Simethicone and other drugs are expected.

STORAGE CONDITION
Store below 30°C. Protect from light and moisture. Keep out of reach of children.

How Supplied
Imotil® Plus Tablet: Each box contains 50's tablets in blister packs.

Manufactured by
SQUARE
PHARMACEUTICALS PLC.
BANGLADESH