SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

GENEITH LOPERAMIDE CAPSULES

(LOPERAMIDE HYDROCHLORIDE CAPSULES BP 2 MG)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Batch size: 1,00,000 Capsules

Sr. No.	Ingredients	Specification	Qty. (mg/ Tab)	Ovg.	Qty/ batch (in kg)
1.	Loperamide HCL	BP	2.000	--	0.200
2.	Lactose Monohydrate	BP	104.600	--	10.460
3.	Maize Starch	BP	5.400	--	0.540
4.	Sodium Starch Glycolate	BP	18.400	--	1.840
5.	Colloidal Anhydrous Silica	BP	3.000	--	0.300
6.	Microcrystalline Cellulose	BP	46.600	--	4.660
7.	Ehg.Caps. Size"3" (Green Colour Cap & Ivory Colour Body)	IHS	1 No	--	1,00,000 No
	TOTAL		**180.000 mg**		

Note:

BP : British Pharmacopoeia

IHS : In House Specification

Average net content per capsule : 180 mg ± 7.5%

Average Weight of filled capsules: 231.00 mg ± 7.5%

3. PHARMACEUTICAL FORM

Capsules

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the control and symptomatic relief of acute and chronic non specific diarrhoea when inhibition of peristalsis is indicated. Also indicated for the reduction of the volume of discharge from ileostomies.

4.2 Posology and method of administration

Route of administration: Oral

Acute diarrhoea:

Adults and children older than 12 years:

Initially 2 capsules orally followed by 1 capsule after each subsequent loose stool. Maximum dose is 16 mg daily. Discontinue if no improvement occurs in 48 hours.

Children ages 9 to 11: 1 capsule taken orally three times daily on first day
Children ages 6 to 8: 1 capsule taken orally twice daily on first day

Children ages 2 to 5: 1 capsule taken orally once daily on first day

Chronic diarrhoea:

Adults:

Initially 2 capsules orally followed by 1 capsule after each subsequent loose stool until diarrhoea subsides. Adjust dose to individual response. Discontinue if 16 mg is used for at least 10 days.

4.3 Contraindications

Contraindicated in children under 2 years, acute dysentery, acute ulcerative colitis or pseudo membranous colitis associated with broad spectrum antibiotics, conditions in which inhibition of peristalsis should be avoided such as acute diarrhoea due to ingestion of poison. Also, OTC use in contraindicated in patients with a fever exceeding 38.3°C or if blood is present in the stool.

4.4 Special warnings and precautions for use

In acute diarrhoea, discontinue therapy and consult a physician if no improvement occurs within 48 hours. Therapy for chronic diarrhoea should not exceed 10 days.
Children should be monitored for signs of dehydration (appropriate fluid and electrolyte replacement should be given). Use cautiously in patients with hepatic impairment (monitor closely for CNS toxicity)

4.5 Interaction with other medicinal products and other forms of interaction

i) Concomitant administration of loperamide (16 mg single dose) with quinidine, or ritonavir, which are both P-glycoprotein inhibitors, resulted in a 2 to 3-fold increase in loperamide plasma levels.
ii) 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. This increase was not associated with increased pharmacodynamic effects as measured by pupillometry.
iii) Concomitant treatment with oral desmopressin resulted in a 3-fold increase of desmopressin plasma concentrations, presumably due to slower gastrointestinal motility.
iv) It is expected that drugs with similar pharmacological properties may potentiate loperamide's effect and that drugs that accelerate gastrointestinal transit may decrease its effect.

4.6 Pregnancy and lactation

Use with caution

4.7 Undesirable effects

Adults and children aged ≥12 years

The safety of loperamide hydrochloride was evaluated in 2755 adults and children aged ≥ 12 years who participated in 26 controlled and uncontrolled clinical trials of loperamide HCl used for the treatment of acute diarrhoea.

The most commonly reported (i.e., ≥1% incidence) adverse drug reactions (ADRs) in clinical trials with loperamide hydrochloride in acute diarrhoea were: constipation (2.7%), flatulence (1.7%), headache (1.2%) and nausea (1.1%).

4.8 Overdose

In case of overdose (including relative overdose due to hepatic dysfunction), CNS depression (stupor, coordination abnormality, somnolence, miosis, muscular hypertonia and respiratory depression), constipation, urinary retention and ileus may occur. Children and patients with hepatic dysfunction may be more sensitive to CNS effects.

4.9 Pharmacodynamic properties

Mechanism of action:

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, which helps reduce faecal incontinence and urgency.

In a double blind randomized clinical trial in 56 patients with acute diarrhoea receiving Loperamide, onset of anti-diarrhoeal action was observed within one hour following a single 4 mg dose. Clinical comparisons with other antidiarrhoeal drugs confirmed this exceptionally rapid onset of action of Loperamide.

5.1 Pharmacokinetic properties

Pharmacokinetics of Loperamide

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%.

Distribution: Studies on distribution in rats show a high affinity for the gut wall with a preference for binding to receptors of the longitudinal muscle layer. The plasma protein binding of loperamide is 95%, mainly to albumin. Non-clinical data have shown that loperamide is a P-glycoprotein substrate.

Metabolism: loperamide is almost completely extracted by the liver, where it is predominantly metabolized, conjugated and excreted via the bile. Oxidative N-demethylation is the main metabolic pathway for loperamide, and is mediated mainly through CYP3A4 and CYP2C8. Due to this very high first pass effect, plasma concentrations of unchanged drug remain extremely low.

Elimination: The half-life of loperamide in man is about 11 hours with a range of 9-14 hours. Excretion of the unchanged loperamide and the metabolites mainly occurs through the faeces.

5.2 Preclinical safety data

Nonclinical data reveal no special hazard for humans based on studies of safety pharmacology, genotoxicity and toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

NO.	INGREDIENTS	SPECIFICATION
1.	Lactose Monohydrate	BP
2.	Maize Starch	BP
3.	Sodium Starch Glycolate	BP
4.	Colloidal Anhydrous Silica	BP
5.	Microcrystalline Cellulose	BP

6.2 Shelf life

3 years

6.3 Special precautions for storage

Store at a temperature below 30ºC. Protect from light and moisture.

6.4 Nature and contents of container

Blister Pack of 10 Capsules

6.5 Special precautions for disposal and other handling

No special requirements

7. **Applicant/Manufacturer**

MANUFACTURER BY:
Head Office Address:
FREDUN PHARMACEUTICALS LIMITED.
26, Manoj Industrial Premises, G. D. Ambekar Marg,
Wadala, Mumbai- 400 031. India

Plant Address:
FREDUN PHARMACEUTICALS LIMITED.
PLOT NO. 14,15,16, ZORABIAN INDUSTRIAL COMPLEX,
VILLAGE VEVOOR, TAL. PALGHAR, THANE - 401404,
MAHARASHTRA STATE

APPLICANT NAME:
GENEITH PHARM. LTD.,
NO. 12 ADEWALE CRESCENT,
OFF EWENLA STREET,
OSHODI-APAPA EXPRESSWAY,
OSHODI, NIGERIA.