SUMMARY PRODUCT CHARACTERISTICS (SPC)

1. Name of the Finished Pharmaceutical Product

Product Name: Komide (Loperamide Tablets BP 2mg)

1.1 Strength: 2 mg

1.2 Pharmaceutical Dosage Form: Tablets

2. Qualitative and Quantitative Composition

2.1 Qualitative declaration:

Each film coated tablet contains:

Loperamide Hydrochloride BP 2 mg

2.2 Quantitative declaration:

Composition of unit dose is given below:

S.No	Ingredients
1.	Loperamide Hydrochloride
2.	Lactose monohydrate
3.	Microcrystalline Cellulose
4.	Pregelatinised starch
5.	PurifiedTalc
6.	Magnesium Stearate
7.	Hydroxypropyl methylcellulose
8.	Propylene glycol
9.	Polyethylene glycol
10.	Titanium dioxide
11.	Purified water

2.3 Salts and hydrates

Loperamide Hydrochloride

3. Pharmaceutical form

Description: White to off white, round shape biconvex film coated tablets plain on both sides .

4 Clinical Particulars

4.1 Therapeutic indications-

For the symptomatic treatment of acute diarrhoea of any aetiology including acute exacerbations of chronic diarrhoea for periods of up to 5 days in adults and children 9 years and over. For the symptomatic treatment of chronic diarrhoea in adults.

4.2 Posology and Method of Administration

Posology

Acute diarrhea

Adults and children over 12 years :Two tablets initially, followed by one tablet after each loose stool. The usual dose is 3-4 tablets a day. The total daily dose should not exceed 8 tablets.

Method of Administration

Oral

4.3 Contraindications

Loperamide is contraindicated in:

•Patients with a known hypersensitivity to loperamide hydrochloride or to any of the excipients.

•Children less than 4 years of age.

•When inhibition of peristalsis is to be avoided due to the possible risk of significant sequelae including ileus, megacolon and toxic megacolon, in particular:

−when ileus or constipation are present or when abdominal distension develops, particularly in severely dehydrated children,

−in patients with acute ulcerative colitis, −in patients with bacterial enterocolitis caused by invasive organisms including Salmonella, Shigella, and Campylobacter,

−in patients with pseudomembranous colitis associated with the use of broad-spectrum antibiotics.

Loperamide should not be used alone in acute dysentery, which is characterised by blood in stools and elevated body temperatures.

4.4 Special warnings and precautions for use

Precautions

The priority in acute diarrhoea is the prevention or reversal of fluid and electrolyte depletion. This is particularly important in young children and in frail and elderly patients with acute diarrhoea. Use of Loperamide does not preclude the administration of appropriate fluid and electrolyte replacement therapy. Since persistent diarrhoea can be an indicator of potentially more serious conditions, Loperamide should not be used for prolonged periods until the underlying cause of the diarrhoea has been investigated. Loperamide must be used with caution when the hepatic function necessary for the drug's metabolism is defective (eg in cases of severe hepatic disturbance), as this might result in a relative overdose leading to CNS toxicity. Patients with AIDS treated with Loperamide for diarrhoea should have therapy stopped at the earliest signs of abdominal distension. There have been isolated reports of toxic megacolon in AIDS patients with infectious colitis from both viral and bacterial pathogens treated with loperamide hydrochloride. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine because it contains lactose.

4.5 Interactions with other medicinal products and other forms of interactions:

Non-clinical data have shown that loperamide is a P-glycoprotein substrate. 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. The clinical relevance of this pharmacokinetic interaction with P-glycoprotein inhibitors, when loperamide is given at recommended dosages (2 mg, up to 16 mg maximum daily dose), is unknown. The results of one published pharmacokinetic study suggested that the concomitant administration of loperamide with oral desmopressin may result in a 3-fold increase of desmopressin plasma concentrations, although no clinical effects were reported.

4.6 Pregnancy and Lactation

Fertility

There is no relevant data to demonstrate the effect of Loperamide on human fertility.

Pregnancy

Safety in human pregnancy has not been established although studies in animals have not demonstrated any teratogenic effects. As with other drugs, it is not advisable to administer Loperamide in pregnancy.

Lactation

Small amounts of loperamide may appear in human breast milk. Therefore, Loperamide is not recommended during breast-feeding.

4.7 Effects on ability to drive and use machine

Loss of consciousness, depressed level of consciousness, tiredness, dizziness, or drowsiness may occur when diarrhoea is treated with loperamide. Therefore, it is advisable to use caution when driving a car or operating machinery.

4.8 Undesirable effects

Commonly reported: Headache, Dizziness, Nausea.

Uncommonly reported: Somnolence, Abdominal pain and discomfort, vomiting, dyspepsia.

Rarely reported: Anaphylactic reaction, CNS depression, miosis, abdominal distension, megacolon, angioedema, urinary retention, fatigue.

4.9 Overdose

Symptoms

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 than adults.

In individuals who have ingested overdoses of loperamide, cardiac events such as QT interval and QRS complex prolongation, torsades de pointes, other serious ventricular arrhythmias, cardiac arrest and syncope have been observed. Fatal cases have also been reported.

Management

In cases of overdose, ECG monitoring for QT interval prolongation should be initiated. If the patient develops respiratory depression, airway

obstruction, vomiting with impaired consciousness or other CNS symptoms of overdose, naloxone can be given as an antidote. Since the duration of action of loperamide is longer than that of naloxone (1 to 3 hours), repeated treatment with naloxone might be indicated. Therefore, the patient should be monitored closely for at least 48 hours in order to detect any possible CNS depression. Other measures should be as indicated by the patient's clinical condition.

5.0 Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antipropulsives

ATC code: A07DA03

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.

5.2 Pharmacokinetic properties

Absorption

Most ingested loperamide is absorbed from the gut, but as a results of significant first pass metabolism, systemic bioavailability is only approximately 0.3%.

Distribution

Studies on distribution in rats show high affinity for the gut wall with a preference for binding to the receptors in 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.

Biotransformation

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 effects, 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.

5.3 Pre-clinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to those already included in other sections. Non-clinical data reveal no special hazards for humans based on conventional studies of safety, pharmacology, repeat–dose toxicity or genotoxicity.

6.0 Pharmaceutical Particulars

6.1 List of Excipients

Lactose monohydrate, Microcrystalline Cellulose PH-102, Pregelatinised starch, Purified Talc, Magnesium Stearate, Hydroxypropyl methylcellulose, Propylene glycol, Polyethylene glycol, Titanium dioxide, Purified water.

6.2 Incompatibilities

None

6.3 Shelf life

Shelf life of the medicinal products as Packaged for sale : 36 Months

Shelf life after dilution or reconstitution according to directions:

Not applicable

Shelf life after opening of the container: Not applicable.

6.4 Special precautions for storage:

Store below 30 °C in a dry place.

6.5 Nature and contents of container

Primary Packaging : Tablets are packed in a Printed Aluminium foil/Plain PVC-PVDC blisters.10 tablets are packed in 1 blister.

Secondary Packaging :

10 blisters are packed in 1 carton along with pack insert.

6.6 Special precaution for disposal

No special requirements. Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder.

Kopran Limited,
1076, Parijat House, Dr. E. Moses Road,
Worli, Mumbai - 400 018, India,

Manufacturer

Kopran Limited,
Village Savroli, Taluka Khalapur,
District Raigad – 410202, India.

8. Marketing authorization registration number(s).

09362/10177/NMR/2022

9. Date of first authorization registration/renewal of the authorization

Dec 25, 2023

10. Date of revision (if any) of this text.

Not applicable

11. DOSIMETRY (IF APPLICABLE)

Not applicable

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IFAPPLICABLE)

Not applicable