1.3 PRODUCT INFROMATION

1.3.1 Summary of product Characteristic

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of drug Prodcut

Loperamide capsule BP 2mg

2. Qualitative and quantitative composition

Each Hard Gelatin Capsule contains:

Loperamide Hydrochloride capsule BP...2mg
Excipients …….... Q.S
For a full list of excipients, refer section 6.1

3. Pharmaceutical form

Hard Gelatin Capsule
Green /Yellow hard gelatin size '2' capsule "YELLOW" printed on cap and "LOPERA" printed on body contains white granular powder.

4. Clinical particulars

4.1 Therapeutic indications

For symptomatic treatment of acute diarrhoea in adults and children aged 12 years and over.

For the symptomatic treatment of acute episodes of diarrhoea associated with Irritable Bowel Syndrome in adults aged 18 years and over following initial diagnosis by a doctor.

4.2 Posology and method of administration

ACUTE DIARRHOEA

Adults and children over 12 years of age:

Two capsules (4 mg) initially, followed by one capsule (2 mg) after each loose stool. The usual dose is 3-4 capsules (6 mg − 8 mg) a day. The total daily dose should not exceed 6 capsules (12 mg).

SYMPTOMATIC TREATMENT OF ACUTE EPISODES OF DIARRHOEA ASSOCIATED WITH IRRITABLE BOWEL SYNDROME IN ADULTS AGED 18 YEARS AND OVER

Two capsules (4 mg) to be taken initially, followed by 1 capsule (2 mg) after every loose stool, or as previously advised by your doctor. The maximum daily dose should not exceed 6 capsules (12 mg).

Paediatric population

Loperamide hydrochloride is contraindicated in children less than 12 years of age.

Elderly

No dose adjustment is required for the elderly.

Renal impairment

No dose adjustment is required for patients with renal impairment.

Hepatic impairment

Although no pharmacokinetic data are available in patients with hepatic impairment Loperamide should be used with caution in such patients because of reduced first pass metabolism (see section 4.4 Special warnings and precautions for use).

Method of administration

Oral use. The capsules should be taken with liquid.

4.3 Contraindications

This medicine is contraindicated:

• Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

• In children less than 12 years of age.

• In patients with acute dysentery, which is characterised by blood in stools and high fever.

• 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 hydrochloride must not be used when inhibition of peristalsis is to be avoided due to the possible risk of significant sequelae including ileus, megacolon and toxic megacolon. Loperamide hydrochloride must be discontinued promptly when ileus, constipation or abdominal distension develop.

4.4 Special warnings and precautions for use

Treatment of diarrhoea with loperamide is only symptomatic. Whenever an underlying etiology can be determined, specific treatment should be given when appropriate. 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 hydrochloride 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 hydrochloride should not be used for prolonged periods until the underlying cause of the diarrhoea has been investigated.

In acute diarrhoea, if clinical improvement is not observed within 48 hours, the administration of loperamide hydrochloride should be discontinued and patients should be advised to consult their doctor.

Patients with AIDS treated with loperamide hydrochloride for diarrhoea should have therapy stopped at the earliest signs of abdominal distension. There have been isolated reports of obstipation with an increased risk of toxic megacolon in AIDS patients with infectious colitis from both viral and bacterial pathogens treated with loperamide hydrochloride.

Although no pharmacokinetic data are available in patients with hepatic impairment, this medicine should be used with caution in such patients because of reduced first pass metabolism, as it may result in a relative overdose leading to CNS toxicity.

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.

If patients are taking this medicine to control episodes of diarrhoea associated with Irritable Bowel Syndrome previously diagnosed by their doctor, and clinical improvement is not observed within 48 hours, the administration of loperamide HCl should be discontinued and they should consult with their doctor. Patients should also return to their doctor if the pattern of their symptoms changes or if the repeated episodes of diarrhoea continue for more than two weeks.

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 (see section 4.9). Overdose can unmask existing Brugada syndrome. Patients should not exceed the recommended dose and/or the recommended duration of treatment.

Caution is needed in patients with a history of drug abuse. Abuse and misuse of loperamide, has been described (see section 4.9). Loperamide is an opioid with low bioavailability and limited potential to penetrate the blood brain barrier at therapeutic doses. However, addiction is observed with opioids as a class.

Special Warnings to be included on the leaflet:

Only take Loperamide to treat acute episodes of diarrhoea associated with Irritable Bowel Syndrome if your doctor has previously diagnosed IBS.

If any of the following now apply, do not use the product without first consulting your doctor, even if you know you have IBS:

• If you are aged 40 or over and it is some time since your last IBS attack

• If you are aged 40 or over and your IBS symptoms are different this time

• If you have recently passed blood from the bowel

• If you suffer from severe constipation

• If you are feeling sick or vomiting

• If you have lost your appetite or lost weight

• If you have difficulty or pain passing urine

• If you have a fever

• If you have recently travelled abroad

Consult your doctor if you develop new symptoms, if your symptoms worsen, or your symptoms have not improved over two weeks.

4.5 Interaction with other medicinal products and other forms of interaction

Non-clinical data have shown that loperamide is a P-glycoprotein substrate. Furthermore, loperamide is mainly metabolised by CYP3A4 and CYP2C8.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 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.

Possible interactions may occur with drugs that delay intestinal peristalsis (for instance anti-cholinergic drugs) because the effects of loperamide could be enhanced.

Administration of itraconazole with loperamide (4 mg single dose) increased loperamide plasma levels 3- to 4-fold. In addition, gemfibrozil, a CYP2C8 inhibitor, increased the AUC of loperamide 2-fold. Concomitant use of itraconazole and gemfibrozil with loperamide raised the mean Cmax and AUC of loperamide about 2- and 13-fold, respectively. This increase did not lead to measurable CNS effects.

The concomitant administration of loperamide (16mg 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.

The clinical relevance of these pharmacokinetic interactions, when loperamide is given at recommended dosages (2 mg, up to 12 mg maximum daily dose), is unknown.

4.6 Pregnancy and lactation

Pregnancy

A limited amount of data from the use of loperamide in pregnant women is available. In one of two epidemiological studies the use of loperamide during early pregnancy suggested a possible moderate increased risk for hypospadia, however, an increased risk for major malformations could not be identified. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). Safety in human pregnancy has not been established, although from animal studies there are no indications that loperamide HCl possesses any teratogenic or embryotoxic properties.

If possible the use of loperamide should be avoided during the first trimester of pregnancy, however, it may be used during the second and third trimester of pregnancy

Breast-feeding

Small amounts of loperamide may appear in human breast milk. Therefore, this medicine is not recommended during breast-feeding. Women who are pregnant or breast feeding infants should therefore be advised to consult their doctor for appropriate treatment.

Fertility

Only high doses of loperamide hydrochloride affected female fertility in non-clinical studies (see section 5.3).

4.7 Effects on ability to drive and use machines

Loperamide hydrochloride has moderate influence on the ability to drive and use machines. Loss of consciousness, depressed level of consciousness, tiredness, dizziness or drowsiness may occur when diarrhoea is treated with loperamide hydrochloride.

Therefore, it is advisable to use caution when driving or operating machinery. (See section 4.8 Undesirable effects).

4.8 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 hydrochloride 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%).

Table 1 displays ADRs that have been reported with the use of loperamide hydrochloride from either clinical trial (acute diarrhoea) or post-marketing experience.

The frequency categories use the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); and very rare (<1/10,000) and not known (cannot be estimated from the available data).

Table 1 Adverse Drug reactions

System Organ Class	**Indication**			
	Common	**Uncommon**	**Rare**	**Not known**
Immune System Disorders			Hypersensitivity reaction[a] Anaphylactic reaction (including Anaphylactic shock)[a] Anaphylactoid reaction[a]	
Nervous System Disorders	Headache Dizziness	Somnolence[a]	Loss of consciousness[a] Stupor[a] Depressed level of consciousness[a] Hypertonia[a] Coordination abnormality[a]	
Eye Disorders			Miosis[a]	
Gastrointestinal Disorders	Constipation Nausea Flatulence	Abdominal pain Abdominal discomfort Dry mouth Abdominal pain upper Vomiting Dyspepsia[a]	Ileus[a] (including paralytic ileus) Megacolon[a] (including toxic megacolon[b]) Glossodynia[a] Abdominal distension	Acute pancreatitis
Skin and Subcutaneous Tissue Disorders		Rash	Bullous eruption[a] (including Stevens-Johnson syndrome, toxic epidermal necrolysis and erythema multiforme) Angioedema[a] Urticaria[a]	

			Pruritus[a]	
Renal and Urinary Disorders			Urinary retention[a]	
General Disorders and Administration Site Conditions			Fatigue[a]	

a: Inclusion of this term is based on post-marketing reports for loperamide hydrochloride. As the process for determining post marketing ADRs did not differentiate between chronic and acute indications or adults and children, the frequency is estimated from all clinical trials with loperamide hydrochloride (acute and chronic), including trials in children ≤ 12 years (N=3683).

b: See section 4.4 Special Warnings and Special Precautions for use.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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), urinary retention and ileus may occur. Children may be more sensitive to CNS effects than adults.

In individuals who have ingested overdoses of loperamide HCl, cardiac events such as QT interval prolongation, torsades de pointes, other serious ventricular arrhythmias, cardiac arrest and syncope have been observed (see section 4.4). Fatal cases have also been reported. Overdose can unmask existing Brugada syndrome.

Upon cessation, cases of drug withdrawal syndrome have been observed in individuals abusing, misusing, or intentionally overdosing with excessively large doses of loperamide.

Treatment

In cases of overdose, ECG monitoring for QT interval prolongation should be initiated.

If CNS symptoms of overdose occur, 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 possible CNS depression.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Antipropulsives;

ATC code: A07DA03

Loperamide hydrochloride is a synthetic opioid which inhibits gut motility by binding to opiate receptors in the gut wall and may also reduce gastrointestinal secretions, resulting in improvement in diarrhoea symptoms.

Loperamide also increases the tone of the anal sphincter. Onset of antidiarrhoeal effect occurred as soon as one hour after intake of a 4 mg dose of loperamide.

In a double blind randomised 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.

5.2 Pharmacokinetic properties

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.

Biotransformation: Loperamide is almost completely extracted by the liver, where it is predominantly metabolised, 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.

Paediatric Population: No pharmacokinetic studies were performed in the paediatric population. It is expected that pharmacokinetic behaviour of loperamide and drug-drug interactions with loperamide will be similar to those in adults.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

Acute and chronic studies on loperamide showed no specific toxicity.

Loperamide had no effect on fertility in male rats when administered orally prior to mating at doses up to approximately 40 mg/kg. No pregnancy occurred in females dosed with approximately 40 mg/kg. Lower doses (approximately 10 and 2.5mg/kg) did not affect female fertility. In rabbits no differences in pregnancy rate were observed when females were administered orally up to 40mg/kg.

No malformations of offspring were noted in rats and rabbits dosed up to 40 mg/kg. Loperamide did no show genotoxic potential.

In an 18-month carcinogenicity study in rats, with doses up to 100 times the maximum human dose no evidence of carcinogenesis was found.

Non-clinical in vitro and in vivo evaluation of loperamide indicates no significant cardiac electrophysiological effects within its therapeutically relevant concentration range and at significant multiples of this range (up to 47-fold. However, at extremely high concentrations associated with overdoses (see section 4.4), loperamide has cardiac electrophysiological actions consisting of inhibition of potassium (hERG) and sodium currents, and arrhythmias.

6. Pharmaceutical particulars

6.1 List of excipients

MCCP
Starch
Talcum
Magnesium Stearate
Aerosil
CCS

6.2 Incompatibilities

Not applicable

6.3 Shelf life

4 years

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container
10x1x10 Capsule per carton.

6.6 Special precautions for disposal and other handling
No special requirements.

7. Marketing authorization holder

EUROLIFE HEALTHCARE PVT. LTD.
UNIT-2, Khasra No- 520,
Bhagwanpur, Roorkee
Distt. Haridwar 247667 Uttarakhand (India).

9 Marketing authorization number

C4- 1575

10 Date of first of authorization/ renewal of authorization

25.02.2021

11 Date of revision of the text

Sep. 2026