eurolife healthcare pvt. ltd.	YELLOW LOPERAMIDE CAPSULES (Loperamide Capsule BP 2mg)

PACKAGE LEAFLET: INFORMATION FOR THE USER

YELLOW LOPERAMIDE CAPSULES

(Loperamide Capsule BP 2mg)

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to you doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Yellow Loperaide Capsules are and what they are used for

For the symptomatic treatment of acute diarrhoea, in adults and children 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.

2. What you need to know before you take Yellow Loperamide Capsules

Only take Loperamide Capsules 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

3. How to take Yellow Loperamide Capsules

Oral use. The capsules should be taken with liquid.

4. Possible side effects

Headache

Constipation

Nausea

Flatulence

5. **How to store Yellow Loperamide Capsule**

Store in cool & dry place.

Keep all medicines out of rech of children.

1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC)

1. Name of the medicinal product:

Brand Name: YELLOW LOPERAMIDE CAPSULES

Generic Name: Loperamide Capsules BP 2mg

2. Qualitative and quantitative composition:

Each had gelatin capsule contain:
Loperamide Hydrochloride BP ……2 mg.
Excipients ….q.s.

For a full list of excipients, see section 6.1

3. Pharmaceutical form: Capsules

4. Clinical particulars:

4.1 Therapeutic indications:

For the symptomatic treatment of acute diarrhoea, in adults and children 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

Posology:
Acute Diarrhoea
Adults and children over 12:
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 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 hydrochloride 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:

• 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 must be discontinued promptly when ileus, constipation or abdominal distension develop.

4.4 Special warnings and precautions for use:

Only take Loperamide Capsules 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

4.5 Interaction with other medicinal products and other forms of interaction:

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-glucoprotein 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, is unknown.

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 central nervous system (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. This increase was not associated with increased pharmacodynamic effects as measured by pupillometry. 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 and that drugs that accelerate gastrointestinal transit may decrease its effect.

4.6 Pregnancy and lactation:

Pregnancy

Safety in human pregnancy has not been established, although from animal studies there are no indications that loperamide hydrochloride possesses any teratogenic or embryotoxic properties. As with other drugs, it is not advisable to administer this medicine in pregnancy, especially during the first trimester.

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.

4.7 Effects on ability to drive and use machines:

Loss of consciousness, depressed level of consciousness, tiredness, dizziness, or drowsiness may occur when diarrhoea is treated with this medicine. Therefore, it is advisable to use caution when driving a car or operating machinery. See Section 4.8, Undesirable Effects.

4.8 Undesirable effects:

Constipation
Nausea
Flatulence
Headache

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.

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.

Management:

If 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:

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 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.

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.

5.3 Preclinical safety data:

Not applicable.

6 Pharmaceutical particulars:

6.1 List of Excipients:

Maize Starch	BP
Microcrystalline cellulose	BP
Sodium Lauryl Sulphate	BP
Cross Carmellose Sodium	BP
Purified Water	BP
Talc	BP
Magnesium Staerate	BP
Colloidal Anhydrous Silica	BP

6.2 Incompatibilities:

None known

6.3 Shelf life: 48 months from the date of manufacture.

6.4 Special precautions for storage:

Store below in a cool & dry place.

Keep all medicines out of reach of children.

6.5 Nature and contents of container

10X10 Capsules

6.6 Special precautions for disposal:

Not applicable

7 Registrant:

Eurolife Healthcare Pvt. Ltd.

8 Manufacturer:

EUROLIFE HEALTHCARE PVT.LTD.

Unit II, Khasra No. 242, Bhagwanpur,

Roorkee, Distt. Haridwar,(Uttarakhand)

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9 Date of revision of the text:

Not Applicable

1.9 Information printed on the primary, secondary packaging and instructions

Attached