SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Loperamide 2mg Capsules

Numark Diarrhoea Relief 2 mg capsules, hard

Max Healthcare Acute Diarrhoea Relief 2mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Loperamide Hydrochloride 2mg

3 PHARMACEUTICAL FORM

Capsules, hard

Green and grey hard capsules marked with 'Max' on the green cap and 'Lop' on the grey body.

For a full list of excipients, see section 6.1.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the 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 (IBS) in adults aged 18 years and over following initial diagnosis by a doctor.

4.2 Posology and method of administration

The capsules should be taken with liquid. For oral administration.

a) Acute diarrhoea

Adults and children over 12 years of age

Two capsules (4mg) initially followed by 1 capsule (2mg) after every loose stool (motion). The usual dose is 3-4 capsules (6mg – 8mg) a day. The total daily dose should not exceed 6 capsules (12mg).

b) Symptomatic treatment of acute episodes of diarrhoea associated with irritable bowel syndrome in adults aged 18 years and over.

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

USE IN 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 4.4 Special warnings and special precautions for use).

4.3 Contraindications

This medicine is contraindicated:

- In patients with known hypersensitivity to Loperamide hydrochloride or to any of the excipients.
- In children less than 12 years of age.
- In patients with acute dysentery, which is characterised by blood in the 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 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 Hydrochloride is only symptomatic. Whenever an underlying aetiology 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 this medicine does not preclude the administration of appropriate fluid and electrolyte replacement therapy.

Since persistent diarrhoea can be an indicator of potentially more serious conditions, this medicine 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 this medicine for diarrhoea should have therapy stopped at the earliest signs of abdominal distension. There have been isolated reports of obstipation with an increased risk for 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 Hydrochloride should be discontinued and they should consult 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.

Special Warnings to be included on the leaflet:

Only take this medicine to treat acute episodes of diarrhoea associated with Irritable Bowel Syndrome (IBS) 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 has been 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 of lose 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, or if symptoms worsen, or if your symptoms have not improved over two weeks.

Keep all medicines out of the sight and reach of children.

Ponceau 4R (E124) can cause allergic-type reactions including asthma. Allergy is more common in those people who are allergic to aspirin.

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.

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 (16mg 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, is unknown.

The concomitant administration of Loperamide (4mg 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 intraconazole and gemfibrozil resulted in a 4-fold increase in the peak levels of Loperamide and a 13-fold increase in the 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 (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.

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 Fertility, Pregnancy and lactation

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

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

Women who are pregnant of breast feeding infants should therefore be advised to consult their doctor for appropriate treatment.

Fertility

The effect on human fertility has not been evaluated.

4.7 Effects on ability to drive and use machines

Loss of consciousness, depressed level of consciousness, tiredness, dizziness and drowsiness may occur. Patients should be advised that if affected they should not drive, operate machinery or take part in activities where such symptoms could put themselves or others at risk.

See section 4.8, Undesirable effects.

SUMMARY OF PRODUCT CHARACTERISTICS

4.8 Undesirable effects

Adults and children aged 12 years and over.

The safety of Loperamide hydrochloride was evaluated in 2755 adults and children aged 12 years and over 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); Very Rare (1/10,000).

Table 1: Adverse Drug Reactions

System Organ Class	Indication		
	Common	Uncommon	Rare
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 Stupor[a] Depressed level of consciousness[a] Hypertonia[a] Coordination abnormality[a]
Eye Disorders			Miosis[a]
Gastrointestinal	Constipation	Abdominal Pain	Ileus[a] (including

Disorders	Nausea Flatulence	Abdominal Discomfort Dry Mouth Abdominal pain upper Vomiting Dyspepsia[a]	paralytic ileus) Megacolon[a] (including toxic megacolon[b]) Abdominal distension. Acute pancreatitis (frequency not known)
Skin & Subcutaneous Tissue Disorders		Rash	Bullous eruption[a] (including Stevens-Johnson syndrome, Toxic epidermal necrolysis & Erythema multiforme) Angloedema[a] Urticaria[a] Pruritus[a]
Renal & Urinary Disorders			Urinary retention[a]
General Disorders & 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 & chronic), including trials in children aged 12 years or less (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 the Yellow Card Scheme at:
www.mhra.gov.uk/yellowcard or in the Google Play or Apple App Store.

4.9 Overdose

Large doses of loperamide may cause features of opioid poisoning. The following patients should be referred for medical assessment:

- All patients who have taken a deliberate overdose.
- All children
- Symptomatic adults
- Adults who have ingested 0.4mg/kg of Loperamide or more

Adults who have accidentally ingested less than 0.4mg/Kg and who have no new symptoms since the time of ingestion should be advised to seek medical attention if symptoms develop.

The effects of overdose will be potentiated by concurrent ingestion of alcohol and/or other centrally active drugs.

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. If untreated deep coma and respiratory arrest can occur. Children, and patients with hepatic dysfunction, may be more sensitive to CNS effects.

Pin point pupils are often present but are not a reliable clinical sign. Their absence does not exclude opiate toxicity.

Treatment:

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

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.

In individuals who have ingested overdoses of loperamide HCl, cardiac events such as QT interval and QRS complex 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, orintentionally overdosing with excessively large doses of loperamide.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antidiarrhoeals, Intestinal Anti-inflammatory/ Anti-infective Agents - 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.

In a double blind randomised trial in 213 patients with acute diarrhoea, loperamide (56 patients) was compared with two other common antidiarrhoeal agents and placebo. Onset of antidiarrhoeal effect occurred as soon as one hour after intake of a 4mg dose of loperamide.

5.2 Pharmacokinetic properties

More than 65% of a dose of loperamide is reported to be absorbed from the gastrointestinal tract. The drug undergoes considerable first pass metabolism in the liver and excretion via the bile in the faeces as the inactive conjugate. As a result of the drug's high affinity for the gut wall and its high first pass metabolism very little loperamide reached the systemic circulation and therefore there is only a small amount of urinary excretion. The elimination half life is reported to be about 10 hours.

5.3 Preclinical safety data

Acute and chronic studies on loperamide showed no specific toxicity. Results of in vivo and in vitro studies carried out indicated that loperamide is not genotoxic. In reproduction studies, very high doses (40 mg/kg/day – 20 times the maximum human use level (MHUL)), based on body surface area dose comparison (mg/m2), loperamide impaired fertility and fetal survival in association with maternal toxicity in rats. Lower doses (≥ 10mg/kg/day – 5 times MHUL) revealed no effects on maternal or fetal health and did not affect peri- and post-natal development.

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

Capsule contents

Lactose monohydrate

Magnesium stearate

Starch, pregelatinised

Capsule shell

Gelatin

Ponceau 4R E124

Indigo carmine E132

Titanium dioxide E171

Yellow iron oxide E172

Black iron oxide E172

Printing Ink

Black iron oxide E172

Shellac

Propylene glycol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 30°C. Store in the original package.

6.5 Nature and contents of container

Blisters of 250µm PVC/ 40gsm PVdC/ 20µm Aluminium foil**.**
Pack sizes of 2, 4, 6, 8, 10, 12 capsules.

Blisters of 250µm PVC/ 20µm Aluminium foil**.**
Pack sizes of 2, 4, 6, 8, 10, 12 capsules.

Blisters of 250µm PVC/ 40gsm PVdC/ 25µm Aluminium foil**.**
Pack sizes of 2, 4, 6, 8, 10, 12 capsules.

Blisters of 250µm PVC/ 25µm Aluminium foil**.**
Pack sizes of 2, 4, 6, 8, 10, 12 capsules.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Max Remedies Ltd
William Nadin Way
Swadlincote
Derbyshire
DE11 0BB

8 MARKETING AUTHORISATION NUMBER(S)

PL 31308/0002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13/10/2008

10 DATE OF REVISION OF THE TEXT

12/09/2024