PROFESSIONAL INFORMATION

SCHEDULING STATUS: S2

1. NAME OF THE MEDICINE

ADCO LOPERAMIDE, 2 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains loperamide hydrochloride 2 mg.

Contains sugar: Lactose 43,9 mg

For a full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Tablets

White, round, tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Children 2 to 5 years:

Loperamide is not indicated for acute and chronic nonspecific diarrhoea but for inhibition of peristalses and slowing of intestinal transit time.

Adults and children 6 years and older:

Loperamide is indicated for the symptomatic relief of acute and chronic nonspecific diarrhoea and to inhibit peristalsis and slow intestinal transit time in patients with ileostomies, colostomies and other intestinal resections.

4.2 Posology and method of administration:

Posology

Dosage should not exceed four to six tablets per day.

For inhibition of peristalses and slowing of the intestinal transit time:

For children 2 to 5 years: ½ a tablet eight hourly.

Acute diarrhoea:

Adults: Two tablets initially, followed by one tablet after each loose stool.

Children of 6 years and older: One tablet initially, followed by one tablet after each loose stool.

The initial dose should be adjusted until solid stools are obtained. This is usually achieved on a maintenance dose of one to six tablets.

Chronic diarrhoea:

The dosage should be adjusted individually.

Adults: The initial dose is two tablets daily.

Children of 6 years and older: The initial dose is one tablet daily.

The initial dose should be adjusted until solid stools are obtained. This is usually achieved on a maintenance dose of one to six tablets.

If constipation occurs, treatment should be stopped.

Method of administration

Oral.

4.3 Contraindications:

- **ADCO LOPERAMIDE** is contraindicated in patients with a known hypersensitivity to loperamide hydrochloride or any of the excipients in the product (see Section 6.1).
- **ADCO LOPERAMIDE** is contraindicated in children under 2 years of age.
- **ADCO LOPERAMIDE** is contraindicated in acute ulcerative colitis.
- **ADCO LOPERAMIDE** is contraindicated in diarrhoea associated with pseudomembranous colitis with the use of broad-spectrum antibiotics.
- The safety of use during pregnancy has not been established.
- **ADCO LOPERAMIDE** should not be used in patients with acute dysentery, which is characterised by blood in stools and high fever.
- In patients with bacterial enterocolitis caused by invasive organisms including Salmonella, Shigella, and Campylobacter.

- **ADCO LOPERAMIDE** should 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 (see **Special warnings and precautions for use**). **ADCO LOPERAMIDE** must be discontinued promptly when constipation, abdominal distension or ileus develop.
- Contains lactose. Patients with the rare hereditary conditions of galactose intolerance e.g., galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take **ADCO LOPERAMIDE.**

4.4 Special warnings and precautions for use:

Treatment of diarrhoea with **ADCO LOPERAMIDE** is only symptomatic. Whenever an underlying etiology can be determined, specific treatment should be given when appropriate (or when indicated).

ADCO LOPERAMIDE should be used with caution in conditions where constipation must be avoided and in patients with hepatic dysfunction, because of its considerable first-pass metabolism in the liver.

Patients with inflammatory bowel disease should be carefully observed for signs of toxic megacolon as loperamide may precipitate this condition in these patients (See **CONTRAINDICATIONS**).

In patients with diarrhoea, especially in infants, frail and elderly patients, fluid and electrolyte depletion may occur. In such cases administration of appropriate fluid and electrolyte replacement (oral rehydration therapy [ORT]) is the most important measure.

ADCO LOPERAMIDE is not recommended for routine use in acute and chronic diarrhoea in children under the age of 6 years.

ADCO LOPERAMIDE should not be given to children less than 6 years of age, without medical prescription and supervision.

Contains lactose. Patients with the rare hereditary conditions of galactose intolerance e.g., galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take **ADCO LOPERAMIDE.**

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.

Patients should not exceed the recommended dose and/or the recommended duration of treatment.

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

Although no pharmacokinetic data are available in patients with hepatic impairment, **ADCO LOPERAMIDE** should be used with caution in such patients because of reduced first pass metabolism. **ADCO LOPERAMIDE** must be used with caution in patients with hepatic impairment as it may result in a relative overdose leading to central nervous system (CNS) toxicity.

ADCO LOPERAMIDE should not be used for prolonged periods. Since persistent diarrhoea can be an indicator of potentially more serious conditions, **ADCO LOPERAMIDE** should not be used for prolonged periods until the underlying cause of the diarrhoea has been investigated.

For acute diarrhoea:

If symptoms persist for more than 48 hours, consult a doctor.

4.5 Interaction with other medicines and other forms of interaction

Non-clinical data have shown that loperamide is a P-glycoprotein substrate. Quinidine and ritonavir are both glycoprotein inhibitors. Concomitant administration of loperamide with quinidine or ritonavir result in increased loperamide plasma levels.

Itraconazole is an inhibitor of CYP3A4 and P-glycoprotein. The concomitant administration of loperamide (4 mg single dose) and itraconazole significantly increase peak plasma concentration of loperamide and prolongs the half-life of loperamide.

The combination of itraconazole and gemfibrozil results in an increase in peak plasma levels of loperamide.

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. The increase was not associated with increased pharmacodynamic effects as measured by pupillometry.

Concomitant treatment of loperamide with oral desmopressin may result in increased desmopressin plasma concentration, presumably due to slower gastrointestinal motility.

It is expected that medicines with similar pharmacological properties may potentiate loperamide's effect and that medicines that accelerate gastrointestinal transit may decrease loperamide’s effect.

4.6 Fertility, pregnancy and lactation

Pregnancy:
The safety of this medicine in pregnant women has not yet been established, **(see Section 4.3, Contraindications).**
As with other drugs, it is not advisable to administer this medicine in pregnancy, especially during the first trimester.

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

Fertility:
The effect on human fertility has not been established.

4.7 Effects on ability to drive and use machines
Loss of consciousness, depressed level of consciousness, fatigue, dizziness, or drowsiness may occur when diarrhoea is treated with **ADCO LOPERAMIDE**. Therefore, it is advisable to use caution when driving a car or operating machinery (**see Section 4.8, Undesirable effects).**

4.8 Undesirable effects

The most frequently reported undesirable effect are headache, flatulence, nausea and constipation.

System organ class	**Frequency**	**Undesirable effects**
	Frequent	• Headache

Nervous System Disorders	Less frequent	• Dizziness • Somnolence • Loss of consciousness • Stupor • Depressed level of consciousness • Hypertonia • Coordination abnormality
Eye Disorders	Less frequent	• Miosis
Immune System Disorders	Frequency Unknown	• Hypersensitivity reaction • Anaphylactic reaction (including anaphylactic shock) • Anaphylactoid reaction
Gastrointestinal Disorders	Frequent	• Flatulence • Nausea • Constipation
	Less frequent	• Abdominal discomfort • Ileus (including paralytic ileus) • Megacolon (including toxic megacolon) • Abdominal pain • Dry mouth
	Frequency Unknown	• Abdominal distension • Dyspepsia • Vomiting • Acute pancreatitis
Skin and Subcutaneous Tissue Disorders	Less frequent	• Rash
	Frequency Unknown	• Bullous eruption (Including Stevens-Johnson syndrome, toxic epidermal necrolysis and erythema multiforme) • Angioedema • Urticaria

		• Pruritus
Renal and Urinary Disorders	Less frequent	• Urinary retention
General Disorders and Administration Site Conditions	Less frequent	• Fatigue

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Drug Reactions Reporting Form",** found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.
Adverse reactions can also be reported to the Adcock Ingram Pharmacovigilance department by e-mail to Adcock.Aereports@adcock.com, fax to +27 86 553 0128 or call 011 635 0134

4.9 Overdose:

In case of overdose (including relative overdose due to hepatic dysfunction), central nervous system (CNS) depression (stupor, coordination abnormality, somnolence, miosis, muscular hypertonia, and respiratory depression), urinary retention, constipation and paralytic ileus may occur. Children may be more sensitive to the central nervous system effects than adults. Excessive inhibition of peristalsis with nausea and dryness of the mouth may occur.

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. Fatal cases have also been reported.

Treatment:

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

Treatment is symptomatic and supportive.

Naloxone can be given as antidote. Since the duration of action of **ADCO LOPERAMIDE** is longer than that of naloxone (1 to 3 hours) repeated treatment of naloxone may be indicated.

Therefore, the patient should be monitored closely for at least 48 hours in order to detect possible central nervous system depression.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 11.9 Medicines acting on gastrointestinal tract. Antidiarrhoeals

Mechanism of action

ADCO LOPERAMIDE inhibits gastrointestinal motility by effects on the circular and longitudinal muscles of the intestine. Part of its antidiarrheal effect may be due to a reduction of gastro intestinal secretion produced by actions at opioid receptors in the intestinal mucosa.
ADCO LOPERAMIDE normalises the stool in both acute and chronic diarrhoea.

5.2 Pharmacokinetic properties

ADCO LOPERAMIDE is incompletely absorbed after oral administration. It undergoes considerable first-pass metabolism in the liver and is excreted mainly in the faeces. Elimination half-life is about ten hours.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Lactose,

Gelatin,

Magnesium stearate,

Maize starch,

Purified water,

Sodium lauryl sulphate,

Sodium starch glycolate.

6.2. Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store in well closed containers, at or below 25 ºC.

Keep in original packaging until required for use.

6.5 Nature and contents of container

White, round tablet.
Cartons containing PVC/Aluminium foil blister strips of 6.

White cylindrical HPDE securitainers containing 60 and 300 tablets sealed with a LDPE screw caps.
Not all pack sizes may be necessarily marketed.

6.6 Special precautions for disposal and other handling

No special requirements

7. HOLDER OF CERTIFICATE OF REGISTRATION:

Adcock Ingram Limited
1 New Road

Erand Gardens

Midrand, 1685,

Customer Care: 0860 ADCOCK / 232625

8. REGISTRATION NUMBER:

Y/11.9/5

Date of approval: 26 April 2023

Namibia: NS1 04/11.9/1561

Botswana: S3 BOT1402531A

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION.

14 March 1990

10. DATE OF REVISION OF THE TEXT

26 April 2023