PROFESSIONAL INFORMATION

SCHEDULING STATUS: **S2**

1. Name of the medicine

ADCO LOPERAMIDE 1 mg, syrup

2. Qualitative and quantitative composition

Each 5 ml contains:

Loperamide hydrochloride	1 mg

Preservatives:

Methyl hydroxybenzoate	0,07 % *m/v*
Propyl hydroxybenzoate	0,008 % *m/v*

Contains sweetener:

Sodium saccharin	11,58 mg

Sugar free

3. Pharmaceutical form

Syrup

Clear, red syrup with a fruity raspberry flavour.

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

Do not administer **ADCO LOPERAMIDE** syrup to infants under 2 years of age.

Shake the bottle before use.

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

For children 2 to 5 years:	One medicine measureful (5 ml) per 12,5 kg body mass eight hourly**.**

Acute diarrhoea:

For adults and children 6 years and older:	One medicine measureful (5 ml) per 12,5 kg body mass followed by ½ a medicine measureful (2,5 ml) per 12,5 kg after each subsequent loose stool. Daily dosage should not exceed three medicine measuresful (15 ml)/12,5 kg body mass.

In acute diarrhoea, if clinical improvement is not observed within forty-eight hours of administration of **ADCO LOPERAMIDE** syrup this medication should be discontinued and a doctor should be consulted.

Chronic diarrhoea:

If constipation occurs, treatment should be discontinued.

For adults and children 6 years and older:	With individually adjusted dosage it is usually possible to obtain a virtually normal bowel movement. The initial dose is one medicine measureful (5 ml)/12,5 kg body mass daily for children. The initial dose should be adjusted until one to two solid stools per day are obtained. This is usually achieved on a maintenance dose of ½ to 2 medicine measuresful (2,5 ml to 10 ml) daily.

4.3 Contraindications

ADCO LOPERAMIDE syrup is contraindicated

- In patients with a known hypersensitivity to loperamide hydrochloride or any of the excipients in the product. (See **section 6.1**)
- In patients with acute ulcerative colitis.
- In patients with pseudomembranous colitis and associated with the use of broad-spectrum antibiotics.
- **ADCO LOPERAMIDE** syrup 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 **Section 4.4**). **ADCO LOPERAMIDE** syrup must be discontinued promptly when constipation, abdominal distension or ileus develop.

- In patients with bacterial enterocolitis caused by invasive organisms including *Salmonella, Shigella ,* and *Campylobacter.*
- Do not use as primary therapy in acute dysentery, which is characterised by blood in the stools and high fever.
- **ADCO LOPERAMIDE** syrup is contraindicated in children under 2 years of age.

4.4 Special warnings and precautions for use

- Treatment of diarrhoea with **ADCO LOPERAMIDE** syrup is only symptomatic. Whenever an underlying etiology can be determined, specific treatment should be given as appropriate (or as indicated).
- **ADCO LOPERAMIDE** syrup 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.
- No pharmacokinetic data is available in patients with hepatic impairment**. ADCO LOPERAMIDE** syrup 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.
- Patients with inflammatory bowel disease should be carefully observed for signs of toxic megacolon as Loperamide may precipitate this condition in these patients (**see Section 4.3**).
- In patients with diarrhoea, especially in children, fluid and electrolyte depletion may occur. In such cases administration of appropriate fluid and electrolyte replacement is essential.
- **ADCO LOPERAMIDE** syrup is not recommended for routine use in acute or chronic diarrhoea in children under the age of 6 years.

- **ADCO LOPERAMIDE** syrup should not be given to children less than 6 years of age, without medical prescription and supervision.
- 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 with AIDS treated with **ADCO LOPERAMIDE** syrup 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.
- **ADCO LOPERAMIDE** syrup should not be used for prolonged periods. Since persistent diarrhoea can be an indicator of potentially more serious conditions, the underlying cause of the prolonged diarrhoea should be 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.
- Gemfibrozil is an inhibitor of CYP2C8 and the metabolism of loperamide to N-desmethylloperamide. Gemfibrozil significantly increases 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 pharmacodynamics 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

Safety in fertility, pregnancy and lactation has not been established.

Small amounts of loperamide may appear in human breast milk. Therefore, **ADCO LOPERAMIDE** syrup is not recommended during breastfeeding.

Women who are breastfeeding infants should 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, fatigue, dizziness, or drowsiness may occur when diarrhoea is treated with **ADCO LOPERAMIDE** syrup**.** Therefore, it is advisable to use caution when driving a car or operating machinery. (See **section 4.8**)

4.8 Undesirable Effects

Headache, dizziness, flatulence, constipation, nausea and flatulence are frequently occurring undesirable effects.

System Organ class	**Frequency**	**Undesirable effects**
Immune System Disorders	Frequency Unknown	Hypersensitivity reaction; Anaphylactic reaction (including Anaphylactic shock); Anaphylactoid reaction; Fluid and electrolyte depletion in patients with diarrhoea.
Nervous System Disorders	Frequent	Headache; Dizziness.
	Less Frequent	Somnolence.
	Frequency Unknown	Loss of consciousness; Stupor; Depressed level of consciousness; Hypertonia and coordination abnormality.
Eye Disorders	Frequency Unknown	Miosis.
Gastrointestinal Disorders	Frequent	Constipation; Nausea; Flatulence.
	Less Frequent	Upper abdominal pain; Abdominal discomfort; Dry mouth; Acute pancreatitis; Vomiting;

		Dyspepsia.
	Frequency Unknown	Ileus (including paralytic ileus); Megacolon (including toxic megacolon); Abdominal distension.
Skin and Subcutaneous Tissue Disorders	Less Frequent	Skin Rash.
	Frequency Unknown	Bullous eruption (including Stevens-Johnson syndrome, Toxic epidermal necrolysis and Erythema multiforme); Angioedema; Urticaria; Pruritus.
Renal and Urinary Disorders	Frequency Unknown	Urinary retention.
General Disorders and Administration Site Conditions	Frequency Unknown	Fatigue.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 overdosage (including relative overdose due to hepatic dysfunction), constipation and depression of the central nervous system(CNS) depression (stupor, coordination abnormality, somnolence, miosis, muscular hypertonia, and respiratory depression), urinary retention, constipation and paralytic ileus may occur. Children and patients with hepatic dysfunction may be more sensitive to the central nervous system effects than adults.
- Convulsions have been reported in children under the age of two years.
- Excessive inhibition of peristalsis with nausea and dryness of the mouth may occur.
- 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.
- **Treatment:**

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

  Naloxone can be given as antidote. Since the duration of action of **ADCO-LOPERAMIDE** syrup 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.
- Treatment is symptomatic and supportive.

5. Pharmacological properties

5.1 Pharmacodynamics properties

A 11.9 Medicines acting on gastrointestinal tract. Antidiarrhoeals

Mechanism of action

ADCO-LOPERAMIDE inhibits gastrointestinal motility by direct action on the circular and longitudinal muscles of the intestine. Part of its antidiarrhoeal effect may be due to a reduction of gastrointestinal secretion produced by actions at opioid receptors in the intestinal mucosa.

ADCO-LOPERAMIDE normalises the stool in both acute and chronic diarrhoea.

5.2 Pharmacokinetics 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

Glycerin

Propylene glycol

Sodium saccharin

Red dye

Raspberry flavour

Citric acid monohydrate

Sodium hydroxide

Purified water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 ºC and keep tightly closed.

6.5 Nature and contents of container

Round amber glass bottles containing 50 ml and 500 ml of syrup.

Not all pack sizes may necessarily be marketed.

6.6 Special precautions for disposal

No special requirements

7. Holder of the certificate of registration

Adcock Ingram Limited

1 New Road,

Erand Gardens

Midrand, 1685

Customer Care: 0860 ADCOCK / 232625

8. Registration number

28/11.9/0003

9. Date of first authorisation/renewal of authorisation

12 November 1993

Date of approval: 26 April 2023

10. Date of revision of the text

26 April 2023

Namibia: NS1 04/11.9/1560

Botswana: S2 BOT1803284

Date of approval: 26 April 2023