

## COLODIUM

VICOL14-2 (MY)

### DESCRIPTION

Green opaque and grey opaque capsule with "HD" printed on one end and "CD 2" on the other end of the capsule.

### COMPOSITION

Loperamide Hydrochloride 2 mg per capsule.

### PHARMACODYNAMICS

Loperamide is a synthetic derivative of pethidine that inhibits gut motility and may also reduce gastrointestinal secretions. Loperamide binds to the opiate receptor in the gut wall. Consequently, it inhibits the release of acetylcholine and prostaglandins, thereby reducing propulsive peristalsis, and increasing intestinal transit time. Loperamide increases viscosity, increases bulk density, reduces daily fecal volume, and diminishes loss of fluids and electrolytes. Loperamide increases the tone of the anal sphincter, thereby reducing incontinence and urgency. Additionally, loperamide will prolong mouth-to-cecum transit time without affecting gastric emptying.

Loperamide has an antidiarrhoeal effect. It slows gastrointestinal motility by effects on the circular and longitudinal muscles of the intestine. It binds to opioid receptors in brain homogenates and intestinal strips. Its constipating action is probably due, at least in part, to actions at these receptors.

### PHARMACOKINETICS

#### Absorption

Loperamide is not well absorbed from the gastrointestinal tract. Most ingested loperamide is absorbed from the gut, but as result of significant first pass metabolism, systemic bioavailability is only approximately 0.3%.

#### Blood Concentration

Concentrations of loperamide in plasma peak about 4 hours after ingestion of large doses.

#### Half-life

The elimination half-life of loperamide is about 10 hours.

#### Distribution

Loperamide does not penetrate well into the brain. Little intact drug reaches the systemic circulation. Gastrointestinal Tract: 85%, Liver: 5%, Tissues: 0.04 to 0.2%. The plasma protein binding of loperamide is 95%, mainly to albumin.

#### Protein Binding

About 97% is bound to plasma protein.

#### Metabolism

Loperamide undergoes first-pass metabolism in the liver. Loperamide undergoes significant first pass metabolism in the liver. Oxidative N-demethylation is the main metabolic pathway for loperamide, and is mediated mainly through CYP3A4 and CYP2C8. Oxidative N-dealkylation may be another pathway. Due to this very high first pass effect, plasma concentrations of unchanged drug remain extremely low.

#### Excretion

Excreted predominantly in the faeces. The half-life of loperamide in man is 10.8 hours with a range of 9-14 hours. Approximately 50% of an orally administered dose is excreted unchanged, primarily in the faeces, there is slight urinary excretion.

### INDICATIONS

For the relief of acute nonspecific diarrhoea and of chronic diarrhoea associated with inflammatory bowel disease, as well as to reduce the volume of discharge from ileostomies.

### CONTRAINDICATIONS

Infants and patients with severe colitis or diarrhoea associated with pseudomembranous colitis resulting from treatment with broad spectrum antibiotics.

### WARNINGS AND PRECAUTIONS

#### NOT RECOMMENDED FOR CHILDREN UNDER 6 YEARS OF AGE

- Loperamide is not recommended for children under 6 years of age. Its use has been associated with fatal episodes of paralytic ileus in infants and young children.
- Appropriate fluid and electrolyte therapy should be given to protect against dehydration in all cases of diarrhoea. Oral rehydration therapy - which is the use of appropriate fluids including oral rehydration salts, remains the most effective

treatment for dehydration due to diarrhoea. The intake of as much of these fluids as possible is therefore imperative.

- Drug-induced inhibition of peristalsis may result in fluid retention in the intestine, which may aggravate and mask dehydration and depletion of electrolytes. If severe dehydration or electrolyte imbalance is present, loperamide should be withheld until appropriate corrective therapy has been initiated.
- Safety for use in pregnancy and lactation has not been established.
- Use of this medication should be carefully considered when the following medical problems exist: Conditions where constipation must be avoided, dehydration, diarrhoea caused by infectious organisms, hepatic function impairment.
- The use of higher than the recommended doses for control of the diarrhea may cause abnormal heart rhythms and serious cardiac events leading to death. However, in adult patients receiving the recommended dosage of loperamide, cases of syncope and ventricular tachycardia have been reported. Some of these patients were taking other drugs or had other risk factors that may have increased their risk of cardiac adverse reactions. Abuse and misuse of loperamide, as an opioid substitute, have been described in individuals with opioid addiction (see Overdose).

#### Pregnancy and Lactation

Safety for use in pregnancy and lactation has not been established.

### MAIN SIDE/ADVERSE EFFECTS

- Abdominal pain and other gastrointestinal disturbances including toxic megacolon.
- Dry mouth.
- Dizziness, fatigue, CNS depression.
- Nausea, vomiting and loss of appetite.
- Skin rashes.
- Constipation.
- Cardiac Disorders: QT/ QTc interval prolongation, Torsades de pointes, other ventricular arrhythmias, cardiac arrest, syncope, and death (see Warnings and Precautions)

### OVERDOSAGE

**Clinical features:** Nausea, epigastric discomfort, constipation, dizziness, drowsiness, stupor and coma.

In individuals who have intentionally ingested overdoses (reported in doses from 40 mg to 792 mg per day) of loperamide HCl, prolongation of the QT/QTc interval Torsade de Pointes, other ventricular arrhythmias and cardiac arrest, have been observed (see Warnings and Precautions). Fatal cases have also been reported.

Abuse, misuse and/or overdose with excessively large doses of loperamide, may unmask Brugada syndrome.

**Treatment:** Emesis or gastric lavage is unnecessary unless a very substantial overdose has been ingested.

Naloxone 0.4 to 1.2 mg IV may antagonize the clinical features described above.

### DOSAGE AND ADMINISTRATION

#### Usual adult dose:

Oral, 6 to 8 mg per day up to a maximum of 16 mg per day.

#### Usual paediatric dose:

Below 6 years - Not recommended.  
6 to 8 years - Oral, 4.0 mg per day in divided doses.  
9 to 12 years - Oral, 6.0 mg per day in divided doses.

**Note:** In general, dietary treatment of diarrhoea in children is preferred whenever possible.

The information given here is limited. For further information, consult your doctor or pharmacist.

**Storage:** Store below 30°C. Protect from moisture.

**Presentation/Packing:** Capsule of 500's, blister of 10 x 10's. (not all presentations may be available locally).

**Product Registration Holder:** HOVID Bhd.  
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**Revision date:** April 2020



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