Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Imodium Instants 2mg Orodispersible Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 2mg loperamide hydrochloride.
Excipient: aspartame (E951), mannitol (E421)
For a full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Orodispersible tablet.
Product imported from the UK:
Imodium Instants are white to off-white, circular, freeze-dried tablets.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

As an adjunct in the management of diarrhoea together with fluid and electrolyte replacement.

4.2 Posology and method of administration

The orodispersible tablet should be placed on the tongue. The tablet will dissolve and is to be swallowed with saliva. No liquid intake is needed for the orodispersible tablet.

Adults and children over 12 years only
The usual dose is 2 tablets initially, followed by 1 tablet after each further episode of diarrhoea up to a maximum of 5 in 24 hours.

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, Imodium Instants should be used with caution in such patients because of reduced first pass metabolism (see 4.4 Special warnings and precautions for use).

Method of administration
Oral.

4.3 Contraindications

- Imodium use is contraindicated in patients under 12 years of age.
- Imodium Instants are contraindicated in patients with a known hypersensitivity to loperamide hydrochloride or to any of the excipients.

- Imodium should not be used as the primary therapy:

- 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.

o Imodium should not be used when the inhibition of peristalsis is to be avoided due to the possible risk of significant sequelae including ileus, megacolon and toxic megacolon. Imodium must be discontinued promptly when constipation, abdominal distension or ileus develop.

4.4 Special warnings and precautions for use

Treatment of diarrhoea with loperamide HCl is only symptomatic. Whenever an underlying etiology can be determined, specific treatment should be given when appropriate.

Imodium is not a substitute for rehydration therapy. In addition to taking Imodium, the patient should be advised to drink plenty of fluids such as water, clear soup and squash.

Patients should be advised to consult their doctor if diarrhoea persists for more than 24 hours.

Loperamide should be used with caution when hepatic function, necessary for the drug's metabolism, is defective as this may result in relative overdose leading to CNS toxicity.

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

Antimotility agents such as loperamide may precipitate ileus and toxic megacolon in patients with ulcerative colitis, and should be avoided in severe acute attacks. It may be used cautiously in mild or less severe attacks as an adjunct to other measures, but should be discontinued promptly should abdominal distension or other untoward symptoms occur.

The stated dose should not be exceeded.

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-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 (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 Fertility, pregnancy and lactation

The safety of loperamide in human pregnancy has not been established.
Small amounts of loperamide may appear in human breast milk. Therefore, loperamide 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

Tiredness, dizziness, or drowsiness may occur when diarrhoea is treated with Imodium. Therefore, it is advisable to use caution when driving a car or operating machinery. *See section 4.8 Undesirable effects.*

4.8 Undesirable effects

Adults and children aged ≥ 12 years
The safety of loperamide HCl was evaluated in 2755 adults and children aged ≥ 12 years who participated in 26 controlled and uncontrolled clinical trials of loperamide HCl used for the treatment of acute diarrhoea.

The most commonly reported (i.e. ≥ 1% incidence) adverse drug reactions (ADRs) in clinical trials with loperamide HCl 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 HCl 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); and 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[a] Stupor[a] Depressed level of consciousness[a] Hypertonia[a]

			Coordination abnormality[a]
Eye Disorders			Miosis[a]
Gastrointestinal Disorders	Constipation Nausea Flatulence	Abdominal pain Abdominal discomfort Dry mouth Abdominal pain upper Vomiting Dyspepsia[a]	Ileus[a] (including paralytic ileus) Megacolon[a] (including toxic megacolon[b]) Abdominal distension
Skin and Subcutaneous Tissue Disorders		Rash	Bullous eruption[a] (including Stevens−Johnson syndrome, Toxic epidermal necrolysis and Erythema multiforme) Angioedema[a] Urticaria[a] Pruritus[a]
Renal and Urinary Disorders			Urinary retention[a]
General Disorders and Administration Site Conditions			Fatigue[a]

a: Inclusion of this term is based on post−marketing reports for loperamide HCl. 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 HCl (acute and chronic), including trials in children ≤ 12 years (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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Overdose (relative or absolute) may lead to constipation, urinary retention, ileus and central nervous system depression (miosis, muscular hypertonia, somnolence and bradypnoea). Naloxone may be given as an antidote, repeated as necessary over an observation period of at least 48 hours.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Antipropulsives; ATC code A07DA03

Loperamide binds to the opiate receptors in the gut wall, reducing propulsive peristalsis and increasing intestinal transit time. Loperamide increases the tone of the anal sphincter.

In a double blind randomised clinical trial in 56 patients with acute diarrhoea receiving loperamide, onset of antidiarrhoeal 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

The half-life of loperamide in man is 10.8 hours with a range of 9 to 14 hours. Studies on distribution in rats show high affinity for the gut wall with preference for binding to the receptors in the longitudinal muscle layer. Loperamide is well absorbed from the gut, but is almost completely extracted and metabolised by the liver where it is conjugated and excreted via the bile. Due to its high affinity for the gut wall and its high first pass metabolism, very little loperamide reaches the systemic circulation.

5.3 Preclinical safety data

No relevant information additional to that contained elsewhere in the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gelatin
Mannitol (E421)
Aspartame (E951)
Sodium hydrogen carbonate
Mint flavour

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf-life expiry date of this product shall be the date shown on the blister strips and the outer carton of the product as marked in the country of origin.

6.4 Special precautions for storage

Store in the original container.

6.5 Nature and contents of container

Cardboard outer carton containing aluminium blisters.

Pack size: 12

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 PARALLEL PRODUCT AUTHORISATION HOLDER

Imbat Limited
Unit L2, North Ring Business Park
Santry
Dublin 9
Ireland

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA1151/060/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st August 2014

10 DATE OF REVISION OF THE TEXT