IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PPA1151/060/001
Case No: 2073853

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Imbat Limited

Unit L2, **North Ring Business Park**, **Santry**, **Dublin 9**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Imodium 2mg Capsules

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **23/11/2009**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Imodium 2mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 2 mg of loperamide hydrochloride.
Excipients: lactose
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, hard.
Product imported from the UK
Gelatin capsules with an opaque green cap marked with ‘Imodium’ and an opaque dark grey body marked with ‘JANSSEN’, containing white powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Adults
As an adjunct in the management of acute diarrhoea, together with appropriate fluid and electrolyte replacement.
In the symptomatic control of diarrhoea associated with chronic inflammatory bowel disease, eg Crohn's disease and ulcerative colitis, as an adjunct to specific measures such as corticosteroids and sulphasalazine. Use in these conditions should be under specialist supervision.
In the adjunctive short-term, control of post-surgical diarrhoea, including ileostomy.

Children
For the occasional use in the control of intractable diarrhoea under specialist supervision.
Since persistent diarrhoea can be an indicator of potentially serious conditions, the underlying cause must always be investigated.

4.2 Posology and method of administration

For oral administration.
i) As an adjunct in the management of acute diarrhoea

Adults and children 9-12 years:
2 to 4 mg is the usual initial dose, followed by 2 mg three times daily. The maximum daily dose should not exceed 10 mg.

Children 4-8 years:
A total maximum daily dose of 4 mg in divided doses.

Under 4 years:
Not recommended.

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

ii) For the symptomatic treatment of diarrhoea associated with chronic bowel disorders

Adults only:
Studies have shown that patients may need differing amounts of loperamide. The starting dosage should be between 4 to 8 mg (2 to 4 capsules) per day in divided doses depending on severity. If required, this dose can be adjusted according to response. Having established the patient's daily maintenance dose, the capsules may be administered on a twice daily regimen.

4.3 Contraindications

• Imodium is contraindicated in patients under 4 years of age
• Imodium is 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:
o In patients with acute dysentery, which is characterised by blood in the stools and high fever
o In patients with acute ulcerative colitis
o In patients with bacterial enterocolitis caused by invasive organisms including Salmonella, Shigella, and Campylobacter
o In patients with pseudomembranous colitis associated with the use of broad spectrum antibiotics.
In general, 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

The necessity for specific therapy, such as anti-infectives, should be borne in mind, particularly should treatment be required for a period longer than three days.
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 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.
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.

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 ritinovir, 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
(2 mg, up to 16 mg maximum daily dose), is unknown.

4.6 Pregnancy and lactation

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

In clinical trials constipation and dizziness have been reported with greater frequency in loperamide hydrochloride treated patients than placebo treated patients.
The following adverse events have also been reported with use of loperamide hydrochloride:

Skin and subcutaneous tissue disorders
Very rare: rash, urticaria and pruritus. Isolated occurrences of angioedema, and bullous eruptions including Stevens-Johnson Syndrome, erythema multiforme, and toxic epidermal necrolysis.

Immune system disorders
Very rare: isolated occurrences of allergic reactions and in some cases severe hypersensitivity reactions including anaphylactic shock and anaphylactoid reactions.

Gastrointestinal System Disorders
Very rare: abdominal pain, ileus, abdominal distension, nausea, constipation, vomiting, megacolon including toxic megacolon, flatulence, and dyspepsia.

Renal and urinary disorders
Very rare: isolated reports of urinary retention.

Psychiatric system disorders
Very rare: drowsiness

Nervous system disorders
Very rare: loss of consciousness, depressed level of consciousness, dizziness .

A number of the adverse events reported during the clinical investigations and post-marketing experience with loperamide are frequent symptoms of the underlying diarrhoeal syndrome (abdominal pain/discomfort, nausea, vomiting, dry mouth, tiredness, drowsiness, dizziness, constipation, and flatulence). These symptoms are often difficult to distinguish from undesirable drug effects.

4.9 Overdose

Overdose (relative or absolute) may lead to constipation, urinary retention, ileus and central nervous system depression (myosis, 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 receptor in the gut wall, reducing propulsive peristalsis, increasing intestinal transit time and enhancing resorption of water and electrolytes. Loperamide increases the tone of the anal sphincter.

5.2 Pharmacokinetic properties

The half-life of loperamide in man is 10.8 hours with a range of 9-14 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. Excretion occurs mainly through the faeces.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Maize starch
Talc
Magnesium stearate
Titanium dioxide (E171)
Yellow ferric oxide (E172)
Indigotindisulphonate sodium (E132)
Black ferrous oxide (E172)
Erythrosine (E127)
Gelatin

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

The shelf life expiry date of this product shall be the date shown on the container and outer package of the product on the market in the country of origin.

6.4 Special precautions for storage

Do not store above 25°C.
Store in the original package.

6.5 Nature and contents of container

Cardboard outer containing blister strips. Pack size 30 capsules.

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

8 Parallel Product Authorisation Number

PPA 1151/60/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 1st February 2008

10 DATE OF REVISION OF THE TEXT

November 2009