LOPERAMIDE 2MG TABLETS
(Loperamide hydrochloride)
PL 33410/0064

UKPAR

TABLE OF CONTENTS

Lay Summary ........................................... Page 2
Scientific discussion ............................... Page 3
Steps taken for assessment ......................... Page 12
Steps taken after authorisation – summary ..... Page 13
Summary of Product Characteristics .......... Page 14
Product Information Leaflet ....................... Page 18
Labelling ............................................ Page 20
LOPERAMIDE 2MG TABLETS

PL 33410/0064

LAY SUMMARY

The MHRA granted APSLA Limited a Marketing Authorisation (licence) for the medicinal product Loperamide 2mg Tablets (PL 33410/0064) on 04 May 2011. This product is available as a prescription-only medicine (POM) and is used to treat sudden short-lived (acute) attacks of diarrhoea in adults and children aged 9 years and over and long-lasting (chronic) diarrhoea in adults.

Loperamide 2mg Tablets contain the active ingredient loperamide hydrochloride which belongs to a group of medicines called “antidiarrhoeals.” The tablets help reduce diarrhoea by slowing down an overactive bowel, which helps the body to absorb more water and salts from this organ, making the stools more solid and less frequent.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of taking Loperamide 2mg Tablets outweigh the risks, hence a Marketing Authorisation has been granted.
SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

Introduction .................................................. Page 4
Pharmaceutical assessment .......................... Page 5
Non-clinical assessment .............................. Page 8
Clinical assessment .................................. Page 9
Overall conclusions and risk benefit assessment ........................................ Page 11
INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted APSLA Limited, a Marketing Authorisation for the medicinal product Loperamide 2mg Tablets (PL 33410/0064) on 04 May 2011. This product is a prescription-only medicine (POM) indicated for the symptomatic treatment of acute diarrhoea of any aetiology including acute exacerbations of chronic diarrhoea for periods of up to 5 days in adults and children 9 years and over and also for the symptomatic treatment of chronic diarrhoea in adults.

This is a standard abridged application submitted under Article 10(1) of Directive 2001/83/EC, as amended claiming to be generic medicinal products of Imodium 2mg Capsules (Janssen-Cilag Ltd, UK), which was first authorised in March 1975.

These products contain the active ingredient loperamide hydrochloride which belongs to a pharmacotherapeutic group of drugs called ‘antipropulsives’ (ATC code: A07DA03).

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

No new non-clinical data have been submitted, which is acceptable given that the application was based on being a generic medicinal product of an originator product that has been in clinical use for over 10 years.

A single-dose, bioequivalence study was submitted to support this application, comparing the test product Loperamide 2mg Tablets (APSLA Limited, Ireland) and the reference product Imodium Tablets (Janssen-Cilag Ltd, Denmark). The bioequivalence study was carried out in accordance with Good Clinical Practice (GCP).

With the exception of the bioequivalence study, no new clinical studies were performed, which is acceptable given that the application was based on being a generic medicinal product of an originator product that has been in clinical use for over 10 years.

The MHRA considers that the Pharmacovigilance System as described by the applicant fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country. A suitable justification has been provided for the non-submission of a Risk Management Plan.

No new or unexpected safety concerns were raised during the assessment of this application and it was, therefore, judged that the benefits of taking Loperamide 2mg Tablets outweigh the risks; hence a Marketing Authorisation has been granted.
PHARMACEUTICAL ASSESSMENT

ACTIVE SUBSTANCE
INN: Loperamide hydrochloride
Chemical names: 4-[4-(4-Chlorophenyl)-4-hydroxypiperidin-1-yl]-N,N-dimethyl-2,2-diphenylbutanamide hydrochloride

Structure:

Molecular formula: C_{29}H_{33}ClN_2O_2 \cdot HCl
Molecular weight: 513.5
Description: White or almost white powder
Solubility: Slightly soluble in water, freely soluble in methanol, soluble in alcohol.

Loperamide hydrochloride is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance loperamide hydrochloride are covered by a European Directorate for the Quality of Medicines (EDQM) Certificate of Suitability.

Appropriate stability data have been generated to support a suitable retest period when stored in the proposed packaging.
MEDICINAL PRODUCT

Other ingredients

Other ingredients consist of pharmaceutical excipients, namely maize starch, lactose monohydrate, povidone (K-30), Brilliant Blue FCF (E133), Quinoline Yellow (E104), magnesium stearate, talc, colloidal anhydrous silica, sodium starch glycolate (Type A) and purified water.

Appropriate justification for the inclusion of each excipient has been provided.

All excipients used comply with their respective European Pharmacopoeia monograph with the exception of Brilliant Blue FCF (E133) and Quinoline Yellow (E104) which are compliant with suitable in-house specifications. In addition, the specifications for Brilliant Blue FCF (E133) and Quinoline Yellow (E104) are in compliance with Directive 78/25/EC (concerning use of colouring agents in foodstuff). Satisfactory Certificates of Analysis have been provided for all excipients.

With the exception of lactose monohydrate, none of the excipients are of animal or human origin. The supplier of lactose monohydrate has confirmed that it is sourced from healthy animals under the same conditions as milk for human consumption. No genetically modified organisms (GMO) have been used in the preparation of these excipients.

Pharmaceutical development

The aim of the development programme was to formulate a safe, efficacious, stable product that could be considered a generic medicinal product of Imodium Tablets (Janssen-Cilag Ltd, Denmark).

Suitable pharmaceutical development data have been provided for this application.

Comparable in vitro dissolution and impurity profiles have been provided for the proposed and originator product.

Manufacture

A description and flow-chart of the manufacturing method has been provided.

Satisfactory batch formulae have been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

Finished product specification

The finished product specification is satisfactory. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of Analysis have been provided for any working standards used.
Container Closure System
The product is packaged in clear polyvinylchloride /polyvinylidene chloride film-aluminium foil blisters in pack sizes of 12 and 30 tablets.

It has been stated that not all pack sizes may be marketed, however, the marketing authorisation holder has committed to submit the mock-ups to the relevant regulatory authorities for approval before marketing.

Stability
Finished product stability studies have been conducted in accordance with current guidelines and results were within the proposed specification limits. Based on the results, a shelf-life of 3 years with no special storage conditions is set and is acceptable.

Bioequivalence/Bioavailability
Satisfactory Certificates of Analysis have been provided for the test and reference batches used in the bioequivalence study.

Summary of Product Characteristics (SmPC), Patient Information Leaflets (PILs) and Labelling
The SmPC, PILs and labelling are pharmaceutically satisfactory.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC, as amended. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

MAA Form
The MAA form is pharmaceutically satisfactory.

Expert Report
A pharmaceutical expert report has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

Conclusion
It is recommended that a marketing authorisation is granted for this application.
NON-CLINICAL ASSESSMENT

PHARMACODYNAMICS, PHARMACOKINETICS AND TOXICOLOGY
No new non-clinical data were submitted, which is acceptable given that the proposed product is a generic medicinal product of an originator product that has been licensed for over 10 years.

NON-CLINICAL EXPERT REPORT
The non-clinical expert report has been written by an appropriately qualified person and is a suitable summary of the non-clinical aspects of the dossier.

ENVIRONMENTAL RISK ASSESSMENT
A suitable justification has been provided for non-submission of an Environmental Risk Assessment. As this product is intended for generic substitution with a product that is already marketed, no increase in environmental burden is anticipated. Thus, the justification for non-submission of an Environmental Risk Assessment is accepted.

CONCLUSION
It is recommended that a marketing authorisation is granted for this application.
CLINICAL ASSESSMENT

CLINICAL PHARMACOLOGY

The clinical pharmacology of loperamide hydrochloride is well-known. With the exception of the bioequivalence study, no pharmacokinetic or pharmacodynamic data were submitted for this application, and none were required for an application of this type.

The following bioequivalence study was submitted:

A balanced, analyst blind, randomised, two-treatment, two period, two sequence, single dose, crossover, study, comparing the pharmacokinetics of the test product Loperamide 2mg Tablets (APSLA Limited, UK) versus the reference product Imodium Tablets (Janssen Cilag Ltd, Denmark) in healthy adult male volunteers under fasting conditions.

Subjects were administered a single oral dose of 2mg loperamide hydrochloride of the test or the reference product with 240 ml of water after an overnight fast of at least 10 hours. Blood samples were collected pre- and up to 48 hours post dose. The two treatment periods were separated by a wash-out phase of at least 7 days.

The main pharmacokinetic results for loperamide hydrochloride are presented below (geometric means, ratio and confidence intervals [CI]):

<table>
<thead>
<tr>
<th>Pharmacokinetic Parameters</th>
<th>Geometric mean</th>
<th>* (%)T/R</th>
<th>90% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Test (T)</td>
<td>Reference (R)</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>25</td>
<td>25</td>
<td>-</td>
</tr>
<tr>
<td>C_max (ng/ml)</td>
<td>0.68</td>
<td>0.76</td>
<td>88.55</td>
</tr>
<tr>
<td>AUC_{0-t} (hr.ng/ml)</td>
<td>14.80</td>
<td>15.46</td>
<td>95.35</td>
</tr>
<tr>
<td>AUC_{0-∞} (hr.ng/ml)</td>
<td>17.46</td>
<td>17.90</td>
<td>97.21</td>
</tr>
</tbody>
</table>

AUC_{0-∞} area under the plasma concentration-time curve from time zero to infinity
AUC_{0-t} area under the plasma concentration-time curve from time zero to t hours
C_max maximum plasma concentration
90 % Confidence Interval calculated using ln-transformed data

The current Guidance on the Investigation of Bioequivalence (CPMP/EWP/QWP/1041/98 Rev 1) defines the confidence limits as 80% to 125% for C_max and AUC values. The 90% confidence intervals of the test/reference ratio for the ln-transformed parameters C_max AUC_{0-t} and AUC_{0-∞} lie within acceptable limits. Thus the data support the claim that the test product Loperamide 2mg Tablets (APSLA Limited, UK) is bioequivalent to the reference product Imodium Tablets (Janssen Cilag Ltd, Denmark).

EFFICACY

No new efficacy data have been submitted and none are required for an application of this type.

SAFETY

No new safety concerns were highlighted during the pharmacokinetic study.
EXPERT REPORT
A clinical expert report has been written by an appropriately qualified person and is a suitable summary of the clinical aspects of the dossier.

PRODUCT INFORMATION:
Summary of Product Characteristics (SmPC)
The SmPC is clinically satisfactory and consistent with that for the reference product.

Patient Information Leaflet (PIL)
The PIL is satisfactory and consistent with the SmPC.

Labelling
The labelling is satisfactory.

CONCLUSION
The applicant has demonstrated that this product and the reference product are bioequivalent. It is recommended that a marketing authorisation is granted for this application.
OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The important quality characteristics of Loperamide 2mg Tablets are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

NON-CLINICAL
No new non-clinical data were submitted. As the pharmacokinetics, pharmacodynamics and toxicology of loperamide hydrochloride are well-known, no additional data were required.

EFFICACY
Bioequivalence has been demonstrated between the applicant’s Loperamide 2mg Tablets (APSLA Limited, Ireland) and the respective reference product, Imodium Tablets (Janssen Cilag Ltd, Denmark).

No new or unexpected safety concerns arose from this application.

PRODUCT LITERATURE
The approved SmPC, PIL and labelling are satisfactory and consistent with those for the reference product.

BENEFIT-RISK ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant’s product and the innovator product are interchangeable. Extensive clinical experience with loperamide hydrochloride is considered to have demonstrated the therapeutic value of the compound. The benefit-risk is therefore considered to be positive.
LOPERAMIDE 2MG TABLETS

PL 33410/0064

STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the marketing authorisation application on 04 February 2010.

2 Following standard checks and communication with the applicant the MHRA considered the application valid on 19 February 2010.

3 Following assessment of the application the MHRA requested further information relating to the quality dossier on 30 April 2010 and the clinical dossier on 21 April 2010, 29 October 2010 and 02 December 2010.

4 The applicant responded to the MHRA’s requests, providing further information on the quality dossier on 12 November 2010 and the clinical dossier on 22 October 2010, 18 November 2010 and 21 February 2011.

5 The application was determined on 04 May 2011.
LOPERAMIDE 2MG TABLETS

PL 33410/0064

**STEPS TAKEN AFTER ASSESSMENT**

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
</tr>
</thead>
</table>
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Loperamide 2 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 2 mg Loperamide hydrochloride.
Excipients:
Lactose monohydrate. Each tablet contains 100 mg lactose monohydrate (see section 4.4).
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Tablet
Light green coloured capsule shaped, biconvex uncoated tablets with ‘2’ debossed on one side and
score line on other side.
The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
For the symptomatic treatment of acute diarrhoea of any aetiology including acute exacerbations of
chronic diarrhoea for periods of up to 5 days in adults and children 9 years and over. For the
symptomatic treatment of chronic diarrhoea in adults.

4.2 Posology and method of administration
Acute diarrhoea
Adults and children over 12 years
Two tablets initially, followed by one tablet after each loose stool. The usual dose is 3-4 tablets a
day. The total daily dose should not exceed 8 tablets.

Children 9 to 12 years
One tablet four times daily until diarrhoea is controlled (up to 5 days). This dose should not be
exceeded.
Further investigation into the cause of the diarrhoea should be considered if there is no improvement
within two days of starting treatment with Loperamide.

Chronic diarrhoea
Adults
Studies have shown that patients may need widely differing amounts of Loperamide. The starting
dose should be between two and four tablets per day in divided doses, depending on severity. If
required, this dose can be adjusted according to result up to a maximum of eight tablets daily.
Having established the patient's daily maintenance dose, the tablets may be administered on a twice
daily regimen. Tolerance has not been observed and therefore subsequent dosage adjustment should
be unnecessary.

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, Loperamide
should be used with caution in such patients because of reduced first pass metabolism (see section
4.4).

Paediatric population
Other pharmaceutical forms/strengths (e.g. syrup) are available for children aged 4 years and over.

Method of administration
Oral use.
4.3 Contraindications
Loperamide is contraindicated in:

- Patients with a known hypersensitivity to loperamide hydrochloride or to any of the excipients.
- Children less than 4 years of age.
- When inhibition of peristalsis is to be avoided due to the possible risk of significant sequelae including ileus, megacolon and toxic megacolon, in particular:
  - when ileus or constipation are present or when abdominal distension develops, particularly in severely dehydrated children,
  - 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.

Loperamide should not be used alone in acute dysentery, which is characterised by blood in stools and elevated body temperatures.

4.4 Special warnings and precautions for use
The priority in acute diarrhoea is the prevention or reversal of fluid and electrolyte depletion. This is particularly important in young children and in frail and elderly patients with acute diarrhoea. Use of Loperamide does not preclude the administration of appropriate fluid and electrolyte replacement therapy.

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

Loperamide must be used with caution when the hepatic function necessary for the drug's metabolism is defective (eg in cases of severe hepatic disturbance), as this might result in a relative overdose leading to CNS toxicity.

Patients with AIDS treated with Loperamide 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.

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

The results of one published pharmacokinetic study suggested that the concomitant administration of loperamide with oral desmopressin may result in a 3-fold increase of desmopressin plasma concentrations, although no clinical effects were reported.

4.6 Pregnancy and lactation
Fertility
There is no relevant data to demonstrate the effect of Loperamide on human fertility.

Pregnancy
Safety in human pregnancy has not been established although studies in animals have not demonstrated any teratogenic effects. As with other drugs, it is not advisable to administer Loperamide in pregnancy.
Lactation
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
Loss of consciousness, depressed level of consciousness, tiredness, dizziness, or drowsiness may occur when diarrhoea is treated with Loperamide. Therefore, it is advisable to use caution when driving a car or operating machinery (see section 4.8).

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. For clinical trials, the frequency is defined as follows: 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); very rare (<1/10,000), including isolated reports.

The following adverse events have been reported with use of loperamide hydrochloride:

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Very rare (&lt;1/10,000), not known (cannot be estimated from the available data)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organ system</td>
<td></td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>Isolated occurrences of allergic reactions, severe hypersensitivity reactions including anaphylactic shock and anaphylactoid reactions</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>Drowsiness</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Loss of consciousness, depressed level of consciousness, dizziness</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Abdominal pain, ileus, abdominal distension, nausea, constipation, vomiting, megacolon including toxic megacolon, flatulence and dyspepsia</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Rash, urticaria and pruritus, isolated occurrences of angioedema, and bullous eruptions including Stevens-Johnson Syndrome, erythema multiforme, and toxic epidermal necrolysis</td>
</tr>
<tr>
<td>Renal and urinary disorder</td>
<td>Isolated reports of urinary retention</td>
</tr>
</tbody>
</table>

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
In case of overdose the following effects may be observed: constipation, urinary retention, ileus and neurological symptoms (miosis, muscular hypertonia, somnolence and bradypnoea). If intoxication is suspected, naloxone may be given as an antidote. Since the duration of action of loperamide is longer than that of naloxone, the patient should be kept under constant observation for at least 48 hours in order to detect any possible depression of the central nervous system. Children, and patients with hepatic dysfunction, may be more sensitive to CNS effects. Gastric lavage, or induced emesis and or enema or laxatives may be recommended.

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 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 anti-diarrhoeal 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 9-14 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
Maize starch
Lactose monohydrate
Povidone (K-30)
Brilliant Blue FCF (E133)
Quinoline Yellow (E104)
Magnesium stearate
Talc
Colloidal anhydrous silica
Sodium starch glycolate (Type A)
Purified water

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years

6.4 Special precautions for storage
This medicinal product does not require any special temperature storage conditions.

6.5 Nature and contents of container
Clear PVC/PVdC film/Aluminium blister strips. The blister strips are packed in cartons to contain 12 or 30 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal
Not applicable

7 MARKETING AUTHORISATION HOLDER
APSLA Limited,
Bayview House,
49 North Strand Road,
Dublin 3, Ireland

8 MARKETING AUTHORISATION NUMBER(S)
PL 33410/0064

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
04/05/2011

10 DATE OF REVISION OF THE TEXT
04/05/2011
PACKAGE LEAFLET: INFORMATION FOR THE USER

Loperamide 2 mg Tablets
(Loperamide hydrochloride)

Read all of this leaflet carefully before you start taking this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Loperamide Tablets are and what they are used for
2. Before you take Loperamide
3. How to take Loperamide
4. Possible side effects
5. How to store Loperamide
6. Further information.

1. WHAT LOPERAMIDE TABLETS ARE AND WHAT THEY ARE USED FOR

The name of your medicine is Loperamide 2 mg Tablets. In the rest of this leaflet your medicine is called Loperamide. Loperamide hydrochloride is the active ingredient of Loperamide Tablets. The tablets are available in one strength.

Loperamide is one of a group of medicines called "antidiarrhoeals" which are used to treat diarrhoea.

Loperamide 2 mg tablets are used to treat sudden (short-lived) (acute) attacks of diarrhoea in adults and children aged 9 years and over and long-lasting (chronic) diarrhoea in adults. The tablets help reduce diarrhoea by slowing down an overactive bowel, which helps the body to absorb water and salts from this organ, making the stools more solid and less frequent.

2. BEFORE YOU TAKE LOPERAMIDE

DO NOT TAKE Loperamide
- if you are allergic (hypersensitive) to loperamide hydrochloride or any other ingredients of Loperamide Tablets
- if it is for a child under 9 years old (Other pharmacological forms/strengths e.g. syrup are available for children aged 4 years and over)
- if you have severe diarrhoea after taking antibiotics
- if you are having a flare up of an inflammatory bowel condition like ulcerative colitis
- if you are constipated or your stomach appears swollen (particularly in children with severe dehydration)
- if you have acute dysentery, the symptoms of which may include blood in your stools and a high temperature.

Do not use this medicine if any of the above applies to you.

If you are not sure, talk to your doctor or pharmacist before taking Loperamide tablets.

Take special care with Loperamide
If any of the following points apply to you now or in the past, talk to a doctor or pharmacist:
- if you have AIDS and your stomach becomes swollen, stop taking the tablets immediately and contact your doctor
- if you suffer from liver problems
- if you have acute dysentery, the symptoms of which may include blood in your stools and a high temperature. You will also need to be given other medicines to treat this.

If you have severe diarrhoea as your body loses more fluid, sugars and salts than normal.

If you are unsure about any of the medicines you are taking, show the bottle or pack to your pharmacist.

Special warnings:
- Loperamide only treats the symptoms of diarrhoea. When you have diarrhoea, your body can lose large amounts of fluids and salts. You will need to replace the fluid by drinking more liquid than usual. Ask your pharmacist about special drinks (known as oral rehydration therapy) which replace fluids and salts lost during diarrhoea. The prevention of fluid depletion (dehydration) is of particular importance in infants, children and frail and elderly people with some diarrhoea.

Taking other medicines
Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

In particular, tell your doctor or pharmacist if you are taking any of the following:
- ritonavir (used to treat HIV)
- quinidine (used to treat abnormal heart rhythms or malaria)
- oral docusate sodium (used to treat constipation)
- any other antidiarrhoeal preparations (except for oral rehydration therapy)

Pregnancy and breast-feeding
Ask your doctor for advice before taking any medicine if you are pregnant, think you might be pregnant or are planning to become pregnant.

Do not take Loperamide if you are breast-feeding as small amounts may get into your milk. Talk to your doctor about suitable treatment.

Driving and using machines
Do not drive if you feel dizzy, tired or sleepy after taking Loperamide. You may also lose consciousness, feel faint or lose sight. If affected do not drive or operate machinery.

Important information about some of the ingredients of Loperamide
This medicine contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. HOW TO TAKE LOPERAMIDE

Always take Loperamide exactly as your doctor has told you.
You should check with your doctor or pharmacist if you are not sure.

The dose of Loperamide that you will need will depend on whether your diarrhoea is a sudden, short lived attack (acute) or a long-lasting condition (chronic).
- Take this medicine by mouth.
- Swallow the correct number of tablets whole with a drink of water.

Short-lived (acute) diarrhoea
Adults and children over 12 years:
- Take two tablets to begin with and then one tablet after each episode of diarrhoea for up to 3 days.
- Never take more than 8 tablets in any 24 hour period.

Children aged 9-12 years:
- Take one tablet 4 times daily until diarrhoea is controlled or for up to 5 days.
- Never take more than this dose.

Children aged under 9 years old:
- Tablets are not recommended for children under 9 years old. Other pharmacological forms/strengths (e.g. syrup) are available for children aged 4 years and over.

If your symptoms are not getting better within 2 days of taking your first dose of Loperamide, you should see your doctor again, who may want to examine you to further check on the cause of the diarrhoea.

Long-lasting (chronic) diarrhoea
Adults only:
- Your doctor will tell you how much Loperamide tablets to take.
- The initial dose will probably be between two and four tablets per day taken in divided doses, but will depend on each individual’s needs. When your doctor is satisfied that.

MHRA PAR – Loperamide 2mg Tablets (PL 33410/0064) 18-
you are receiving the daily dose that best suits you, be or she will then probably suggest that you take your tablets twice a day.

- Never take more than 8 tablets in any 24 hour period.

Children:
NOT recommended.

If you take more Loperamide than you should
If you or anyone else takes too many Loperamide tablets, contact your doctor or go to the nearest accident and emergency department (casually) straight away taking this leaflet with you.

If you forget to take Loperamide
- You should only take this medicine as required following the dosage instructions above carefully.
- If you forget to take a dose, take a dose after the next loose stool (bowel movement).
- Do not take a double dose to make up for a forgotten dose.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Loperamide can cause side effects, although not everybody gets them.

Stop using Loperamide tablets and tell your doctor straight away if you notice or suspect any of the following.
You may need urgent medical treatment.

Very rare (affects less than 1 in 10,000 people)
- Sudden swelling of the face, lips, or throat.
- Hives (also known as urticaria or angioedema).
- Severe irritation, reddening or blistering of your skin.
- Blistering or peeling of your skin, mouth, eyes or genitals.
- Sudden pain or severe swollen stomach.
- Severe constipation.
- Loss of consciousness or reduced level of consciousness (feeling faint or less alert)

Tell your doctor if you notice any of the following side effects while using Loperamide tablets:

Very rare (affects less than 1 in 10,000 people)
- Itchy skin and rash.
- Difficulty passing water.

Other side effects which may occur:

Very rare (affects less than 1 in 10,000 people)
- Feeling sick (nausea), being sick (vomiting), indigestion (dyspepsia).
- Feeling drowsy or dizzy.
- Wind.

Other side effects that may be due to the medicine or diarrhoea:
- Feeling tired.
- Dry mouth.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE LOPERAMIDE

Keep out of the reach and sight of children.

Do not use Loperamide after the expiry date which is shown on the label or carton. The expiry date refers to the last day of that month.

Store in the original package.

If the tablets become discoloured or show any other signs of deterioration, consult your pharmacist who will tell you what to do.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Loperamide contains:
- The active substance is loperamide hydrochloride. Each tablet contains 2 mg loperamide hydrochloride.
- The other ingredients are microcrystalline cellulose, lactose monohydrate, povidone (K-30), Brilliant Blue FCF (E133), quinoline yellow (E104), magnesium stearate, talc, colloidal anhydrous silica and sodium starch glycolate and purified water.

What Loperamide looks like and contents of the pack:
Loperamide 2mg Tablets are light green coloured capsule shaped, biocoated uncoated tablets with ‘2’ debossed on one side and scoreline on other side.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

Loperamide is presented in a blister pack of 12 or 30 tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder:
APLSA Limited, Bayview House, 49 North Strand Road, Dublin 3, Ireland.

Manufacturer:
APC Pharmaceuticals & Chemicals (Europe) Limited, 9th Floor, CP House, 97-107 Uxbridge Road, Ealing, London W5 5TL.

Distributed By:
APC Pharmaceuticals & Chemicals (Europe) Limited, 9th Floor, CP House, 97-107 Uxbridge Road, Ealing, London W5 5TL.

This leaflet was last revised in 03/2011.
LABELLING

Carton:

Loperamide 2 mg Tablets
Loperamide hydrochloride
Oral use. Take as directed by the prescriber. Read the package leaflet before use.
Store in the original package.

Keep out of the reach and sight of children. Also contains lactose monohydrate. See leaflet for further information.

Blister:

Loperamide 2 mg Tablets
Loperamide hydrochloride
Each tablet contains 2 mg Loperamide hydrochloride.

PL Holder:
APSLA Limited,
Bayneor House, 49 North Strand Road,
Dublin 3, Ireland

Distributed By:
APC Pharmaceuticals & Chemicals (Europe) Ltd,
9th Floor, CP House, 97-107 Unbridge Road, Ealing, London W5 5TL.