LOPERAMIDE 2MG TABLETS
(Loperamide hydrochloride)
PL 20117/0087

UKPAR

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LOPERAMIDE 2MG TABLETS

PL 20117/0087

LAY SUMMARY

The MHRA granted Morningside Healthcare Limited a Marketing Authorisation (licence) for the medicinal product Loperamide 2mg Tablets (PL 20117/0087) on 25 February 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 which helps reduce diarrhoea by slowing down an overactive bowel. It also helps the body to absorb more water and salts from the bowel.

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.
LOPERAMIDE 2MG TABLETS

PL 20117/0087

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Morningside Healthcare Limited, a Marketing Authorisation for the medicinal product Loperamide 2mg Tablets (PL 20117/0087) on 25 February 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 a generic medicinal product of Imodium 2mg Capsules (Janssen-Cilag Ltd, UK), which was first authorised in March 1975.

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

Loperamide hydrochloride inhibits the peristaltic activity of longitudinal and circular smooth muscle in the intestine by interacting with cholinergic and non-cholinergic neuronal mechanisms responsible for producing the peristaltic reflux. Loperamide hydrochloride binds to the opiate receptor in gut wall, reducing propulsive peristalsis and increasing intestinal transit time. Loperamide hydrochloride increases the tone of anal sphincter. Loperamide hydrochloride also inhibits electrolyte and fluid secretion in intestine.

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 (Morningside Healthcare Limited, UK) 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:

\[
\begin{align*}
\text{Cl} & \quad \text{OH} \\
& \quad \text{N} \\
& \quad \text{CH}_3 \\
\end{align*}
\]

Molecular formula: \( \text{C}_{29}\text{H}_{33}\text{ClN}_2\text{O}_2 \cdot \text{HCl} \)
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 lactose monohydrate, maize starch, talc, magnesium stearate, povidone, Brilliant Blue (E133), Quinoline Yellow (E104), colloidal anhydrous silica and sodium starch glycolate.

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 (E133) and Quinoline Yellow (E104) which are compliant with suitable in-house specifications. In addition, the specifications for Brilliant Blue (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 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 polyvinylchloride/polyvinylidene chloride film-aluminium foil blisters in pack sizes of 30 tablets.

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 SPC, 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 (Morningside Healthcare 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 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>90% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Test (T)</td>
<td>Reference (R)</td>
</tr>
<tr>
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<td>25</td>
<td>25</td>
</tr>
<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt; (ng/ml)</td>
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<tr>
<td>AUC&lt;sub&gt;0-4&lt;/sub&gt; (hr.ng/ml)</td>
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<td>15.46</td>
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<tr>
<td>AUC&lt;sub&gt;0-∞&lt;/sub&gt; (hr.ng/ml)</td>
<td>17.46</td>
<td>17.90</td>
</tr>
</tbody>
</table>

AUC<sub>0-∞</sub> area under the plasma concentration-time curve from time zero to infinity
AUC<sub>0-4</sub> area under the plasma concentration-time curve from time zero to 4 hours
C<sub>max</sub> 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<sub>max</sub> and AUC values. The 90% confidence intervals of the test/reference ratio for the ln-transformed parameters C<sub>max</sub>, AUC<sub>0-4</sub> and AUC<sub>0-∞</sub> lie within acceptable limits. Thus the data support the claim that the test product Loperamide 2mg Tablets (Morningside Healthcare 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 is consistent with that for the reference product.

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

Labelling
The labelling is satisfactory.

CONCLUSION
The applicant has demonstrated that this product and its 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 pre-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 (Morningside Healthcare Limited, UK) 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 20117/00087

STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the marketing authorisation application on 13 May 2010

2 Following standard checks and communication with the applicant the MHRA considered the application valid on 08 June 2010

3 Following assessment of the application the MHRA requested further information relating to the quality dossier on 25 August 2010 and 18 January 2011 the clinical dossier on 10 September 2010.

4 The applicant responded to the MHRA’s requests, providing further information on the quality dossier on 20 December 2010 and 10 February 2011 and the clinical dossier on 20 December 2010

5 The application was determined on 25 February 2011.
LOPERAMIDE 2MG TABLETS

PL 20117/00087

STEPS TAKEN AFTER ASSESSMENT

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

1 NAME OF THE MEDICINAL PRODUCT
Loperamide 2mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 2mg loperamide hydrochloride.
Excipients: each tablet contains 100mg of lactose monohydrate.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Light green coloured capsule shaped, biconvex uncoated tablets, plain 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 over 8 years. For the symptomatic treatment of chronic diarrhoea in adults.

4.2 Posology and method of administration
ACUTE DIARRHOEA
Adults and children over 12:
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 9-12 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 2mg Tablets 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 use.

4.3 Contraindications
Loperamide 2mg Tablets are contraindicated in:
- patients with a known hypersensitivity to loperamide hydrochloride or to any of the excipients.
- children less than 9 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 2mg Tablets 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 2mg Tablets 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 2mg Tablets should not be used for prolonged periods until the underlying cause of the diarrhoea has been investigated.

Loperamide 2mg Tablets 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 2mg Tablets 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

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 administer Loperamide 2mg Tablets in pregnancy.

Small amounts of loperamide may appear in human breast milk. Therefore, Loperamide 2mg Tablets 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 Loperamide 2mg Tablets. 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:
Frequencies are 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),

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

Psychiatric system disorders
Very rare: drowsiness

Nervous System disorders
Very rare: Loss of consciousness, depressed level of consciousness, dizziness

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

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.

Renal and urinary disorders
Very rare: isolated reports of urinary retention.
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 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
Lactose monohydrate
Maize starch
Talc
Magnesium stearate
Povidone
Brilliant Blue (E133)
Quinoline Yellow (E104)
Colloidal anhydrous silica
Sodium starch glycolate

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years

6.4 Special precautions for storage
This medicine product does not require any special storage instructions.

6.5 Nature and contents of container
Blisters composed of PVC/PVDC film, which is clear, non-toxic, transparent and thermoformable and of aluminium foil.

Pack size: 30 tablets.
Not all pack sizes may be marketed

6.6 Special precautions for disposal
No special requirements.
Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER
Marketing Authorisation Holder:
Morningside Healthcare Limited
115 Narborough Road
Leicester, LE3 0PA
United Kingdom.

8 MARKETING AUTHORISATION NUMBER(S)
PL 20117/0087

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
25/02/2011

10 DATE OF REVISION OF THE TEXT
25/02/2011
PACKAGE LEAFLET: INFORMATION FOR THE USER

Loperamide 2 mg Tablets
Loperamide Hydrochloride

Read all of this leaflet carefully because it contains important information for you:

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if your symptoms worsen or do not improve after 2 (two) days.
- 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 Tablets
3. How to take Loperamide Tablets
4. Possible side effects
5. How to store Loperamide Tablets
6. Further information

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

The name of your medicine is Loperamide 2mg Tablets (called Loperamide Tablets in this leaflet). The active ingredient is loperamide hydrochloride. It belongs to a group of medicines which help reduce diarrhoea by slowing down an overactive bowel. It also helps the body to absorb more water and salts from the bowel.

Loperamide Tablets are used to treat sudden short-lived (acute) attacks of diarrhoea in adults and children over 9 years of age and for the treatment of long-lasting (chronic) diarrhoea in adults.

2. BEFORE YOU TAKE LOPERAMIDE TABLETS

Do not take Loperamide Tablets:

- If you have had any allergic reaction to loperamide or to any of the other ingredients in this product.
- If you have severe diarrhoea after taking antibiotics.
- If you are having a flare up of ulcerative colitis.
- If you have acute dysentery, the symptoms of which may include blood in your stools and a high temperature.
- If you are constipated or your stomach appears swollen (particularly in children with severe dehydration).
- If your child is less than 9 years old.

Take special care with Loperamide Tablets:

Check with your doctor before using Loperamide Tablets if:

- You suffer from liver problems.
- You have AIDS and your stomach becomes swollen. Stop taking the tablets immediately and contact your doctor.
- You have an intolerance to some sugars.

You may still be able to use Loperamide Tablets, but you should discuss this with your doctor first.

Replacing fluid and salts

Loperamide Tablets only treat the symptoms of diarrhoea. When you have diarrhoea, your body loses large amounts of fluid and salts. You should therefore replace this lost fluid by drinking more than normal. This is especially important for children.

Your doctor may also give you a special powder containing sugar and salts (known as oral rehydration therapy) to help your body replace the fluid and salts lost during diarrhoea.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This includes medicines that you buy without a prescription or herbal medicines.

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 desmopressin (used to treat excessive urination)

Taking Loperamide Tablets with food and drink

Take Loperamide Tablets with or without food.

Drinking extra fluids is recommended while you have diarrhoea.

Alcohol should be avoided as loperamide may cause drowsiness or dizziness and alcohol may intensify these effects.

Pregnancy and breast-feeding

Tell your doctor before taking Loperamide Tablets if you are pregnant, think you may be pregnant or might become pregnant.

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

Ask your doctor or pharmacist for advice before taking any medicine if you are pregnant or breast-feeding.

Driving and using machines

This medicine may make you feel dizzy, tired or sleepy. If affected do not drive or operate machinery.

Important information about some of the ingredients of Loperamide Tablets

Loperamide Tablets contain lactose. If your doctor has told you that you are intolerant of some sugars, discuss it with them before taking this medicine.

3. HOW TO TAKE LOPERAMIDE TABLETS

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

Take this medicine by mouth. Swallow the correct number of tablets with a drink of water. The break line is to facilitate breaking for ease of swallowing.
Short-lived (acute) diarrhoea
Adults: Take 2 (two) tablets straight away. From then on take 1 (one) tablet after each episode of diarrhoea. You can take this medicine for up to 5 days. Never take more than 8 tablets in any 24 hour period.
Children aged 9-12 years old: Take 1 (one) tablet 4 (four) times a day until diarrhoea is controlled. You can take this medicine for up to 5 days.
Children under 9 years old: Loperamide Tablets are not recommended for children under 9 years old. If you are not getting better within 2 days of taking your first dose of Loperamide Tablets, go back to your doctor. He or she may want you to examine you to check on why you have diarrhoea.

Long-lasting (chronic) diarrhoea
Adults: Your doctor will tell you how many Loperamide Tablets to take. This will depend on how serious your condition is. You will probably start with a dose of 2 (two) and 4 (four) tablets spread out over a day. Your doctor will find the dose that suits you best. He or she may then suggest you take the tablets twice a day. Never take more than 8 tablets in any 24 hour period.
Children: Loperamide Tablets are not recommended for long-lasting (chronic) diarrhoea.

If you take more Loperamide Tablets than you should
If you take more Loperamide Tablets than you were told to by someone who has taken any, talk to a doctor or go to the nearest hospital casualty department straight away.
If you have any further questions on the use of this product, ask your doctor or pharmacist.

If you forget to take Loperamide Tablets
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 stop taking Loperamide Tablets
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 Tablets 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. (anaphylaxis)
- Hives (also known as nettle rash or urticaria), severe irritation, reddening or blistering of your skin. These may be signs of a severe allergic reaction
- Blistering of your skin, mouth, eyes and genitals
- Stomach pain or severe swollen stomach
- Severe constipation

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)
- Wind
- Feeling drowsy or dizzy

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 other side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE LOPERAMIDE TABLETS

Keep out of the reach and sight of children. This medicine does not require any special storage conditions. If the tablets become discoloured or show any other signs of deterioration, consult your pharmacist who will tell you what to do.

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

Disposal: Medicines should not be disposed of via wastewater or household waste. These measures will help protect the environment. Return any leftover Loperamide Tablets to your pharmacist.

6. FURTHER INFORMATION

What Loperamide Tablets contain
The active substance is loperamide. Each tablet contains 2 mg loperamide as loperamide hydrochloride.

The other ingredients are lactose monohydrate, maize starch, talc, magnesium stearate, povidone, brilliant blue (E133), quinoline yellow (E104), colloidal anhydrous silica and sodium starch glycolate.

What Loperamide Tablets look like and contents of the pack
Light green coloured capsule shaped, biconvex uncoated tablets, plain 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.

Loperamide Tablets are available in blister packs of 30 tablets.

Marketing Authorisation Holder:
Morningside Healthcare Ltd.
115 Narborough Road, Leicester, LE3 0PA, UK

Site responsible for batch release:
Morningside Pharmaceuticals Ltd.
5 Pavilion Way, Loughborough, UK.

This leaflet was last approved in 05/2011.
Each tablet contains 2mg of loperamide hydrochloride
Contains lactose monohydrate

Dosage: For oral use.
Take as directed by your doctor.
Read the package leaflet before use.
Keep out of the reach and sight of children.