Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

Public Assessment Report

UK PAR

Loperamide 2mg Tablets

(Loperamide hydrochloride)

UK Licence No: PL 20117/0304

Morningside Healthcare Limited

LAY SUMMARY

Loperamide 2mg Tablets

(Loperamide hydrochloride)

This is a summary of the Public Assessment Report (PAR) for Loperamide 2mg Tablets (PL 20117/0304). It explains how the application for Loperamide 2mg Tablets was assessed and its authorisation recommended, as well as the conditions of use. It is not intended to provide practical advice on how to use Loperamide 2mg Tablets.

For practical information about using Loperamide 2mg Tablets, patients should read the package leaflet or contact their doctor or pharmacist.

For ease of reading, Loperamide 2mg Tablets (PL 20117/0304). may be referred to as 'Loperamide Tablets' in this Lay Summary.

What are Loperamide Tablets and what are they used for?

This medicine is the same as Loperamide 2mg Tablets (PL 20117/0087; Morningside Healthcare Limited), which are already authorised in the UK. The licence holder (Morningside Healthcare Limited) for Loperamide 2mg Tablets (PL 201117/0087) has agreed that its own scientific data can be used as a basis for the grant of an identical licence for Loperamide 2mg Tablets (PL 20117/0304).

Loperamide Tablets are used to treat two types of diarrhoea. The two types have different age limits:

1. **Short-term diarrhoea**
   - for adults and children aged 12 and over
   - to treat attacks that last up to 48 hours
   - if the patient's attack lasts longer than 48 hours, the patient should talk to his/her doctor.

2. **Irritable Bowel Syndrome (IBS) diarrhoea**
   - for adults and young people aged 18 and over who have been diagnosed with IBS
   - to treat attacks that last up to 48 hours
   - this medicine can be taken for up to 2 weeks for repeated attacks, but if any one attack lasts continuously for longer than 48 hours the patient should talk to his/her doctor.

How do Loperamide Tablets work?

Loperamide Tablets contain the active substance, loperamide hydrochloride, which helps reduce diarrhoea by slowing down an overactive bowel. This allows water and salts that are usually lost in diarrhoea to be absorbed by the body.

How are Loperamide Tablets used?

Loperamide Tablets are taken by mouth.

The patient should always take this medicine exactly as described in the package leaflet or as his/her doctor or pharmacist has advised. The patient should check with his/her doctor or pharmacist if not sure.

Loperamide Tablets can be obtained without a prescription.

Please read section 3 of the package leaflet for detailed information on dosing recommendations and the duration of treatment.

What benefits of Loperamide Tablets have been shown in studies?

The application for Loperamide Tablets (PL 20117/0304) is considered to be identical to the previously authorised licence for Loperamide 2mg Tablets (PL 20117/0087; Morningside Healthcare Limited), with the same benefits and risks. So, no new studies have been provided for Loperamide Tablets (PL 20117/0304). However, reference is made to the studies for Loperamide 2 mg Tablets (PL 20117/0087; Morningside Healthcare Limited).

What are the possible side effects of Loperamide Tablets?

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

For the full list of all side effects reported with Loperamide Tablets, see section 4 of the package leaflet.

For the full list of restrictions, see the package leaflet.

Why are Loperamide Tablets approved?

No new or unexpected safety concerns arose from this application. The MHRA, therefore, considered that the benefits of Loperamide Tablets outweigh their risks; and the grant of Marketing Authorisation was recommended.

What measures are being taken to ensure the safe and effective use of Loperamide Tablets?

A Risk Management Plan has been developed to ensure that Loperamide Tablets are used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics and the package leaflet for Loperamide Tablets, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored/reviewed continuously.

Other information about Loperamide Tablets

A Marketing Authorisation was granted in the UK to Morningside Healthcare Limited on 30 April 2018.

The full PAR for Loperamide Tablets follows this summary.

For more information about treatment with Loperamide Tablets read the package leaflet or contact your doctor or pharmacist.

This summary was last updated in June 2018.

Loperamide 2mg Tablets

(Loperamide hydrochloride)

PL 20117/0304

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

I. INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Morningside Healthcare Limited a Marketing Authorisation for the medicinal product Loperamide 2mg Tablets (PL 20117/0304) on 30 April 2018. The product is indicated only for the symptomatic treatment of acute:

- diarrhoea in adults and children aged 12 years and over.
- episodes of diarrhoea associated with Irritable Bowel Syndrome in adults aged 18 years and over following initial diagnosis by a doctor.

The application was submitted as a simple abridged (informed consent) application according to Article 10c of Directive 2001/83/EC, as amended. The application for Loperamide 2mg Tablets (PL 20117/0304) cross-refers to Loperamide 2mg Tablets (PL 20117/0087; Morningside Healthcare), which was granted in the UK on 25 February 2011 as a generic application cross-referring to Imodium 2 mg Capsules (PL 00242/0028; Janssen-Cilag Limited).

The active substance is loperamide (as loperamide hydrochloride). 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, which helps reduce faecal incontinence and urgency.

No new data were submitted nor were they required for this application, as the product is identical to that of the previously granted cross-reference product.

II. QUALITY ASPECTS

II.1 INTRODUCTION

This is an informed consent application for Loperamide 2mg Tablets (PL 20117/0304) submitted under Article 10c of Directive 2001/83/EC, as amended.

The application for Loperamide 2mg Tablets (PL 20117/0304) cross-refers to Loperamide 2mg Tablets (PL 20117/0087; Morningside Healthcare Limited), which was granted in the UK on 25 February 2011 as a generic application cross-referencing Imodium Capsules (PL 00242/0028; Janssen-Cilag Limited). The application is considered valid.

II.2 Drug substance

The proposed drug substance specification is consistent with the details registered for the cross-reference product.

II.3 Medicinal Product

Name

The proposed name of the product is Loperamide 2mg Tablets. The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes

Each tablet contains 2 mg of loperamide hydrochloride, as the active substance. The tablets are taken orally (by mouth).

The product is packaged in polyvinylchloride/polyvinylidene chloride/aluminium blisters, in a pack size of 8 tablets.

The proposed shelf life for the product is 3 years, with no special storage conditions.

The packaging, proposed shelf life and storage conditions are consistent with the details registered for the cross-reference product.

Legal status

The product is available as a Prescription Only Medicine (POM).

Marketing Authorisation Holder/Contact Persons/Company

Morningside Healthcare Limited, 115 Narborough Road, Leicester, LE3 0PA, United Kingdom.

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory CV has been provided.

Manufacturers

The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

Qualitative and quantitative composition

The proposed composition is consistent with the details registered for the cross-reference product.

Manufacturing process

The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

Finished product/shelf-life specification

The proposed finished product specification is consistent with the details registered for the cross-reference product.

TSE Compliance

With the exception of lactose monohydrate, none of the excipients contain materials of animal or human origin.

The supplier of lactose monohydrate has confirmed that the milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that intended for human consumption. In addition, the supplier has confirmed that no ruminant material, other than calf rennet, is used during the production of lactose monohydrate. This is consistent with the cross-reference product.

Bioequivalence

No bioequivalence data are required to support this simple abridged application because the proposed product is manufactured to the same formula and utilises the same processes as the reference product Loperamide 2mg Tablets (PL 20017/0087; Morningside Healthcare Limited).

Product Name and Appearance

See Section II.3 ‘Medicinal Product, Name’ for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

Summary of Product Characteristics (SmPC)

The proposed SmPC is consistent with the details registered for the cross-reference product.

Patient Information Leaflet (PIL) and Labelling

PIL

The PIL has been prepared in line with the details registered for the cross-reference product.

Carton and label

The proposed artwork is consistent with the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation, the applicant has also included the name of the product in Braille on the outer packaging.

II.4 Discussion on chemical, pharmaceutical and biological aspects

The data submitted with the application are acceptable. The grant of a Marketing Authorisation is recommended.

III. NON-CLINICAL ASPECTS

Introduction

As this is an informed consent application submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

Ecotoxicity/Environmental Risk Assessment (ERA)

Suitable justification has been provided for non-submission of an Environmental Risk Assessment. Since Loperamide 2 mg Tablets are intended for generic substitution, this will not lead to an increase of the environmental exposure. An environmental risk assessment is therefore not deemed necessary.

Discussion on the non-clinical aspects

The grant of a Marketing Authorisation is recommended.

IV. CLINICAL ASPECTS

Introduction

As this informed consent application submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

Pharmacovigilance and Risk Management Plan (RMP)

The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that they have the services of a qualified person responsible for pharmacovigilance, and have the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

An acceptable Risk Management Plan (RMP) has been submitted. A summary of safety concerns is listed in the following table.

Table 1: Summary of safety concerns

Summary of safety concerns (for Pharmacy and GSL use medicine)	
Important identified risks	• Severe hypersensitivity reactions, including anaphylaxis • Severe skin reactions, including Stevens Johnson syndrome, toxic epidermal necrolysis and erythema multiforme • Ileus (including paralytic ileus) • Megacolon (including toxic megacolon)
Important potential risks	• Cardiac events (QT prolongation and/or serious ventricular arrhythmias including Torsades de Pointes) • Prolonged use masking an underlying condition requiring medical attention • Central nervous system (CNS) toxicity due to relative overdose in patients with hepatic impairment • Use during lactation
Missing information	• Use during pregnancy

Routine pharmacovigilance and routine risk minimisation activities are proposed for all safety concerns.

Discussion on the clinical aspects
The grant of a Marketing Authorisation is recommended.

V. USER CONSULTATION

A user consultation with target patient groups on the PIL has been performed on the basis of a bridging report making reference to the PIL for Loperamide 2mg Tablets (PL 20117/0087; Morningside Healthcare Limited). The bridging report is acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

QUALITY

The data for this application are consistent with those previously assessed for the cross-reference product and as such have been judged to be satisfactory.

NON-CLINICAL

No new non-clinical data were submitted, and none are required for this type of application.

EFFICACY

No new efficacy data were supplied or required for this application. Loperamide hydrochloride has a well-established efficacy profile. The product is identical to the previously granted licence for Loperamide 2mg Tablets (PL 20117/0087; Morningside Healthcare Limited).

SAFETY

No new safety data were supplied or required for this application. Loperamide hydrochloride has a well-established safety profile. This product is identical to the previously authorised Loperamide 2mg Tablets (PL 20117/0087; Morningside Healthcare Limited).

PRODUCT LITERATURE

The SmPC and PIL are satisfactory, and consistent with those for the respective cross-reference product. The labelling text complies with statutory requirements and is satisfactory.

BENEFIT/RISK ASSESSMENT

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product. Extensive clinical experience with loperamide hydrochloride is considered to have demonstrated the therapeutic value of the compound. The benefit/risk assessment is, therefore, considered to be positive.

The SmPC, PIL and labelling text are satisfactory and in line with current guidance.

The Marketing Authorisation Holder has submitted the text version only and has committed to submitting mock-up livery to the regulatory authorities for approval before packs are marketed.

In accordance with Directive 2010/84/EU, the current version of the SmPC and PIL is available on the MHRA website. The current labelling is presented below:

PARTICULARS TO APPEAR ON THE <OUTER PACKAGING> <AND> <THE IMMEDIATE PACKAGING>

{NATURE/TYPE} P Pack

1. NAME OF THE MEDICINAL PRODUCT

Loperamide 2mg Tablets
Loperamide hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 2mg of loperamide hydrochloride

3. LIST OF EXCIPIENTS

Contains lactose monohydrate

4. PHARMACEUTICAL FORM AND CONTENTS

Tablets

8

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Loperamide Tablets work by slowing down your bowel and returning it to normal rhythm. This helps you to restore the absorption of more fluids into your body.

CAN RELIEVE DIARRHOEA IN ONE DOSE

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Not recommended for children under 12 years

8. EXPIRY DATE

Expiry
EXP
Exp

9. SPECIAL STORAGE CONDITIONS

This medicine does not require any special storage conditions.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Morningside Healthcare Limited

115 Narborough Road

Leicester, LE3 0PA

U.K.

12. MARKETING AUTHORISATION NUMBER(S)

PL 20117/0304

13. BATCH NUMBER

Batch No
BN
Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Prescription Only Medicine

15. INSTRUCTIONS ON USE

One dose of Loperamide 2mg Tablets can relieve diarrhoea quickly and effectively.

Loperamide tablets help reduce diarrhoea by slowing down an overactive bowel. It also helps the body to absorb more water and salts from the bowel.

Dosage: For oral use only.

Short term diarrhoea:
Adults and children over 12 years; Take 2 (two) tablets to start treatment. Take 1 (one) tablet after each loose bowel movement, up to a maximum of 6 tablets per day. If your diarrhoea lasts for more than 48 hours, consult your doctor.

IBS Diarrhoea, previously diagnosed by a doctor:
Adults and over 18 years; Take 2 (two) tablets to start treatment. Take 1 (one) tablet after each loose bowel movement, or as previously advised by a doctor, up to a maximum of 6 tablets per day. You can use this medicine for up to 2 weeks for repeated attacks, but do not take for any one attack lasting longer than 48 hours. If your symptoms change or worsen or are not improved after 2 weeks, consult your doctor.

Loperamide 2mg Tablets are for the symptomatic relief of diarrhoea only and are not a substitute for rehydration therapy.

16. INFORMATION IN BRAILLE

Loperamide 2mg Tablets

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

{NATURE/TYPE}

1. NAME OF THE MEDICINAL PRODUCT

Loperamide 2mg Tablets
Loperamide hydrochloride

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Morningside Healthcare Limited

3. EXPIRY DATE

Expiry
EXP
Exp

4. BATCH NUMBER

Batch No.
BN
Lot

5. OTHER

Loperamide 2mg Tablets

(Loperamide hydrochloride)

PL 20117/0304

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome