Public Assessment Report

UKPAR

PIROXICAM MANX 0.5% W/W GEL

(Piroxicam)

UK Licence No: PL 14251/0028

Manx Healthcare Limited.
This is a summary of the public assessment report (PAR) for Piroxicam Manx 0.5% w/w Gel (PL 14251/0028). It explains how Piroxicam Manx 0.5% w/w Gel was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use Piroxicam Manx 0.5% w/w Gel.

For practical information about using Piroxicam Manx 0.5% w/w Gel, patients should read the package leaflet or contact their doctor or pharmacist.

What is Piroxicam Manx 0.5% w/w Gel and what is it used for?

Piroxicam Manx 0.5% w/w Gel contains the active substance piroxicam. Piroxicam Manx 0.5% w/w Gel is prescribed to help relieve inflammation (swelling), pain and stiffness. Piroxicam can be used to treat:

- joint pain caused by rheumatism or injury
- joint pain caused by mild, non-serious arthritis
- pain or swelling from a sprain, back strain or bruise

This medicine is identical to Piroxicam 0.5% w/w Gel (PL 14251/0001), which was authorised in the UK to Manx Healthcare Limited on 8 December 2000. The Marketing Authorisation Holder for Piroxicam Manx 0.5% w/w Gel and Piroxicam 0.5% w/w Gel is the same (Manx Healthcare Limited), therefore the scientific data presented for Piroxicam 0.5% w/w Gel (PL 14251/0001) can be used for this application for Piroxicam Manx 0.5% w/w Gel.

How is Piroxicam Manx 0.5% w/w Gel used?

Piroxicam Manx 0.5% w/w Gel can only be obtained from a pharmacy with a prescription. The gel can be applied three to four times a day as required, by massaging it gently onto the skin around the injury. Piroxicam Manx 0.5% w/w Gel should not be used for more than four weeks. The gel contains an ingredient known as propylene glycol, which can cause allergic reactions in some people.

How does Piroxicam Manx 0.5% w/w Gel work?

Piroxicam Manx 0.5% w/w Gel contains the active ingredient piroxicam. Piroxicam belongs to a group of medicines called topical non-steroidal anti-inflammatory drugs (often shortened to NSAIDs) which are applied to the skin to reduce swelling and pain. Piroxicam works by blocking the production of chemicals (prostaglandins) which the body produces in response to injury or certain diseases. These chemicals would otherwise cause swelling and pain.

How has Piroxicam Manx 0.5% w/w Gel been studied?

This application is identical to the previously granted application for Piroxicam 0.5% w/w Gel (PL 14251/0001; Manx Healthcare Limited). The Marketing Authorisation
Holder is the same for this application and the previously authorised application for Piroxicam 0.5% w/w Gel. Manx Healthcare referred to the data provided for Piroxicam 0.5% w/w Gel as a basis for the grant of an identical licence for Piroxicam Manx 0.5% w/w Gel.

**What are the benefits and risks of Piroxicam Manx 0.5% w/w Gel?**

Piroxicam Manx 0.5% w/w Gel is considered identical to Piroxicam 0.5% w/w Gel, therefore the risks and benefits are considered the same.

**Why is Piroxicam Manx 0.5% w/w Gel approved?**

No new or unexpected safety concerns arose from this application. It was, therefore, considered that the benefits of Piroxicam Manx 0.5% w/w Gel outweigh the risks; and the grant of a Marketing Authorisation was recommended.

**What measures are being taken to ensure the safe and effective use of Piroxicam Manx 0.5% w/w Gel?**

A risk management plan has been developed to ensure that Piroxicam Manx 0.5% w/w Gel is 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 Piroxicam Manx 0.5% w/w Gel, including the appropriate precautions to be followed by healthcare professionals and patients.

**Other information about Piroxicam Manx 0.5% w/w Gel**

A Marketing Authorisation was granted in the UK on 21 March 2014. For more information about treatment with Piroxicam Manx 0.5% w/w Gel, read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in November 2016.

The full PAR for Piroxicam Manx 0.5% w/w Gel follows this summary.
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I INTRODUCTION
Based on the review of the data on quality, safety and efficacy, the UK granted a Marketing Authorisation for the medicinal product Piroxicam Manx 0.5% w/w Gel (PL 14251/0028) on 21 March 2014 to Manx Healthcare Limited.

This application for Piroxicam Manx 0.5% w/w Gel was submitted as an abridged simple application according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to Piroxicam 0.5% w/w Gel, which was licenced to Manx Healthcare Limited on 08 October 2000 (PL 14251/0001).

This medicine can only be obtained with a prescription (legal status POM). Piroxicam Manx 0.5% w/w Gel is used for the local symptomatic relief of pain and stiffness accompanying non-serious arthritic conditions; and pain or swelling accompanying sprains, strains and sports injuries.

The product contains the active substance piroxicam. Piroxicam is a cyclo-oxygenase (COX) inhibitor which has anti-inflammatory effects, in addition to having anti-pyretic and analgesic effects. Piroxicam’s main mechanism of action is by inhibition of the enzyme cyclo-oxygenase in the arachidonic acid metabolism pathway, resulting in reduced prostaglandin synthesis. Piroxicam inhibits prostaglandin (thromboxane) synthesis in the platelet, and thus inhibits the secondary phase of platelet aggregation.
II  QUALITY ASPECTS

II.1  Introduction

This is a simple, abridged application for Piroxicam Manx 0.5% w/w Gel submitted under Article 10c of Directive 2001/83/EC, as amended. The proposed MA holder is Manx Healthcare Limited, Taylor Group House, Wedgnock Lane, Warwick, CV34 5YA United Kingdom.

The application cross-refers to Piroxicam 0.5% w/w Gel (PL 14251/0001), which was licenced to Manx Healthcare Limited on 08 December 2000.

The current application is considered valid.

II.2.  Drug Substance

Drug substance specifications

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 Piroxicam Manx 0.5% w/w Gel. The product has been named in line with current requirements.

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

Piroxicam Manx 0.5% w/w Gel is available in aluminium tubes with a polypropylene cap containing 30g, 60g or 112g of the finished product.

The marketing authorisation holder has stated that not all pack sizes are intended for marketing. However, they have committed to providing the relevant licensing authority with the mock-ups for any pack size before marketing it in that country.

The proposed shelf-life (36 months) and the storage conditions for the gel (Do not store above 25 °C) are consistent with the details registered for the cross-reference product.
Legal status

On approval, the product can only be obtained with a medical prescription (legal status POM).

Marketing authorisation holder/Contact Persons/Company

Manx Healthcare Limited, Taylor Group House, Wedgnock Lane, Warwick, CV34 5YA United Kingdom.

The QP responsible for pharmacovigilance is stated and his CV is included.

Manufacturers

The proposed manufacturing site is consistent with that 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 sizes are stated.

Finished product/shelf-life specification

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

TSE Compliance

No materials of animal or human origin are included in this product. This is consistent with the cross-reference product.

Expert Report

The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts’ CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

Product name and appearance

See Section II.3 ‘Medicinal Product; Name’ for details of the proposed product names. 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)/carton and label

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

Carton and label
The proposed artwork is comparable to 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 and has included sufficient space for a standard UK pharmacy dispensing label.

II.4 Discussion on chemical, pharmaceutical and biological aspects

The data submitted with this application are acceptable. From a quality perspective, a Marketing Authorisation should be granted.

III NON-CLINICAL ASPECTS
No new non-clinical data have been supplied with this application and none are required for applications of this type.

IV CLINICAL ASPECTS
No new clinical data have been supplied with this application and none are required for applications of this type.

Pharmacovigilance System and Risk Management Plan

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 risk management plan has been developed to ensure that Piroxicam Manx 0.5% w/w Gel is 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 Piroxicam Manx 0.5% w/w Gel, including the appropriate precautions to be followed by healthcare professionals and patients.

Discussion on the clinical aspects
The grant of Marketing Authorisations is recommended.
V  User consultation
A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to the product for Piroxicam 0.5% w/w Gel (PL 14251/0001). The bridging report submitted by the applicant is acceptable.

VI  Overall conclusion, benefit/risk assessment and recommendation

QUALITY

The important quality characteristics of Piroxicam Manx 0.5% w/w Gel are identical to those of the already granted reference product. 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 and none are required for applications of this type.

CLINICAL PHARMACOLOGY/EFFICACY

No new clinical pharmacology/efficacy data have been submitted with this application and none are required for applications of this type.

SAFETY

No new safety data have been submitted with this application and none are required for applications of this type.

No new or unexpected safety concerns arise from this application.

The SmPC, PIL and labels are satisfactory.

BENEFIT-RISK ASSESSMENT

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with Piroxicam Manx 0.5% w/w Gel is considered to have demonstrated the therapeutic value of the product. The benefit/risk is, therefore, considered to be positive.
Summary of Product Characteristics and Patient Information Leaflet

The current approved UK versions of the Summary of Product Characteristics (SmPC) and Patient Information Leaflet (PIL) for this product are available on the MHRA website.

The approved labelling for this medicine is presented below:
Piroxicam Manx
0.5% w/w Gel

Each gram contains 5mg piroxicam. Also contains propylene glycol, isopropyl alcohol, macrogel 7 glyceryl coclate, hydroxyethyl, sodium hydrosolide, sodium metabsulphite, potassium dihydrogen phosphiate and purified water.

Use as directed by your doctor. If symptoms persist, consult your doctor.

Please read the enclosed leaflet before use. Keep out of the reach and sight of children.

Do not store above 25°C.

PL. Holder: Manx Healthcare Ltd.
Prepared & Packaged by: Manx Pharma Ltd.

Address: Taylor Group House, Whitbrook Lane, Wrexham LL12 8PR, United Kingdom

FOR EXTERNAL USE ONLY

PL 14251/0028

MANX
Pharma

112g
Piroxicam Manx 0.5% w/w Gel

Use as instructed by your doctor. If symptoms persist, consult your doctor.
Please read the enclosed leaflet before use.
Keep out of the reach and sight of children.
Do not store above 30°C.
Table of content of the PAR update

Steps taken after the initial procedure with an influence on the Public Assessment Report (Type II variations, PSURs, commitments)

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<td>30/06/2016</td>
<td>Medical Type II</td>
<td>To update section 4.1 of the SmPC to change a therapeutic indication by modifying an already approved one. Consequentially the PIL has been updated.</td>
<td>Approved on 02/11/2016- see Annex 1.</td>
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ANNEX 1

Our Reference: PL 14251/0028-0009

Product: Piroxicam Manx 0.5% w/w Gel

Marketing Authorisation Holder: Manx Healthcare Limited
Active Ingredient(s): Piroxicam

Type of Procedure: National
Submission Type: Variation
Submission Category: Type II
Submission Complexity: Standard
EU Procedure Number (if applicable): Not applicable

Reason:
To update section 4.1 of the SmPC to change a therapeutic indication by modifying an already approved one.

Consequentially the PIL has been updated.

Supporting Evidence
Clinical overview, revised SmPC fragment and PIL.

Background
Piroxicam is a nonsteroidal anti-inflammatory agent with analgesic and antipyretic properties. Piroxicam gel is applied three or four time a day to the affected area for a maximum of 4 weeks.

Evaluation
The proposed indication is narrower than the present indication, as it claims symptomatic relief rather than treatment, and lists fewer conditions. The indication is supported by the evidence submitted with the initial marketing authorisation application (MAA). The clinical overview includes an adequate review of the relevant literature, including a recent review of the role of topical NSAIDs in acute musculoskeletal pain.

The proposed indication wording of:
For the local symptomatic relief of pain and stiffness accompanying non-serious arthritic conditions; and pain or swelling accompanying sprains, strains and sports injuries.

Is acceptable and supported by the submitted evidence.

Package leaflet
Section 1 of the patient information leaflet (PIL) has also been updated as follows:
Piroxicam can be used to treat:

• joint pain caused by rheumatism or injury
• *joint pain caused by mild, non-serious arthritis*
• *pain or swelling from a sprain, back strain or bruise*

The wording is in line with the agreed indication, and is acceptable.

**Conclusion**
The proposed changes to the SmPC and PIL are satisfactory. The updated SmPC fragment and PIL have been incorporated into the Marketing Authorisation.

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPC) and Patient Information Leaflets (PIL) for products granted Marketing Authorisations at a national level are available on the MHRA website.

**Decision** - Approved on 02 November 2016.