



Public Assessment Report

Prescription only medicine to Pharmacy Reclassification

Piroxicam 0.5%w/w Gel

PL 14251/0028 - 0006

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The Medicines and Healthcare products Regulatory Agency (MHRA) is the UK government agency responsible for regulating medicines and medical devices. We continually review the safety of medicines and vaccines in the UK, and inform healthcare professionals and the public of the latest updates through several means, including public reclassification reports. Suspected side-effects to any drug or vaccine can be reported to MHRA by both healthcare professionals and members of the public via the Yellow Card Scheme (<http://www.mhra.gov.uk/yellowcard>).

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1. Background on deciding where medicines are available

The role of MHRA

MHRA regulates medicines and medical devices in the UK, on behalf of the UK Licensing Authority. This means that MHRA decides whether medicines are available:

- on prescription only - 'prescription only medicine' (POM)
- bought from pharmacies - 'pharmacy medicine' (P)
- bought from other shops - 'general sales list medicine' (GSL)

What is re-classification of a medicine?

Making a change on where a medicine is available is called 're-classification'. This is sometimes referred to as 'switching'. To decide on this change, MHRA may:

- take advice from the Commission on Human Medicines and its Expert Advisory Groups¹
- take advice from a group ('stakeholder group') of health professionals and representatives of people affected by the classification change
- run a public consultation

To be reclassified from POM to P, a medicine must:

- be unlikely to be a direct or indirect danger to human health when used without the supervision of a doctor, even if used correctly
- be generally used correctly (ie not frequently or to a wide extent used correctly)
- not contain substances or preparations of substances where the activity of the product or its side effects require further investigation
- not normally be prescribed by a doctor for injection (parenteral administration)

What evidence is needed?

A company or organisation can ask MHRA for a medicine to be available as a pharmacy medicine or a general sale medicine. To do this, they need to get together evidence to show that the medicine

- a) is likely to be used appropriately, and
- b) with relatively little danger to the public.

This evidence needs to focus on the risk to the public. This includes evidence on the possible abuse or misuse of the medicine. The evidence may include:

- clinical studies
- evidence showing acceptable level of side effects
- advice of experts
- views of relevant health professionals and their professional bodies
- views of relevant public associations and individuals with an interest in the medicine under consideration.

Who makes the final decision?

The final decision on whether to approve a change is made by the MHRA, on behalf of the UK Licensing Authority.

2. About Piroxicam Gel

Piroxicam Gel is a gel containing 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 inflammation (swelling) and relieve pain.

Piroxicam works by blocking the production of chemicals (prostaglandins), which the body produces in response to injury or certain diseases. These prostaglandins would otherwise go on to

¹ The Commission on Human Medicines (CHM) is an advisory non-departmental public body, sponsored by the Department of Health. The CHM advises ministers on the safety, efficacy and quality of medicines. The CHM is supported in its work by Expert Advisory Groups (EAGs), covering various areas of medicine. The CHM's views are sought on reclassifications when more complex or new reclassifications of medicines are being proposed.

cause swelling and pain. Piroxicam can be used to treat joint pain caused by mild, non-serious arthritis and pain or swelling from a sprain, back strain, or bruise in adults aged 18 years and over.

The full name of the medicine is Piroxicam 0.5% w/w Gel – in this document, we will call it ‘Piroxicam Gel’.

This report outlines the evidence that the MHRA reviewed which led to the decision to approve this application.

What is piroxicam used for?

Piroxicam is an NSAID. It is currently available from several companies as capsules, tablets, and gel as a prescription only medicine. This application was to make Piroxicam Gel (authorised by Manx Healthcare Limited) available as a Pharmacy medicine.

Who has made the proposal?

The licence-holder² for Piroxicam Gel (Manx Healthcare Limited) applied to make this product available through Pharmacies.

3. Proposed terms of reclassification

Piroxicam Gel will be made available through Pharmacy outlets under the following conditions:

- Pharmaceutical form: topical gel
- Composition: 0.5% w/w piroxicam
- Indication: For the local symptomatic relief of pain and stiffness accompanying non-serious arthritic conditions; and pain or swelling accompanying sprains, strains and sports injuries
- Dose: Adults: Apply 1 g of the gel (about 3 cms or 1¹/₄ inches) and rub into the affected area until the gel completely disappears. Wash hands immediately after use. Apply three times a day. Individual doses should be administered at least 4 hours apart. If the symptoms do not improve by day 7, or if they worsen in the first 7 days, a consultation with a doctor is recommended. Do not use for more than 14 days unless recommended by a doctor. Do not use on patients under 18 years of age.
- Maximum pack size: 30g

4. How the proposal was assessed

To be reclassified from POM to P, a medicine must:

- be unlikely to be a direct or indirect danger to human health when used without the supervision of a doctor, even if used correctly
- be generally used correctly (ie not frequently or to a wide extent used correctly)
- not contain substances or preparations of substances where the activity of the product or its side effects require further investigation
- not normally be prescribed by a doctor for injection (parenteral administration)

These criteria are set out in the Human Medicines Regulations 2012, regulation 62(3).

Assessment of suitability for Pharmacy availability

The MHRA assessed the application against these criteria for reclassification:

Direct danger

A direct danger may be present if the product causes adverse reactions that are important because of their seriousness, severity, or frequency, or because the reaction is one for which there is no suitable preventative action such as the exclusion of a clearly identifiable risk

² A License Holder or Marketing Authorisation Holder is the company with legal authorisation to make the medicine available to patients

group. Direct danger may arise from drug interactions with commonly used medicines and how these may be prevented.

Piroxicam has been in use in oral form (capsules and tablets) for more than 30 years, and in topical form (gel) for more than 25 years. As with all NSAIDs such as ibuprofen, the major adverse reactions are gastrointestinal (stomach and intestines) toxicity (with ulceration and bleeding being the most serious of these), and or skin reactions. These side effects seem to be more common with oral piroxicam (taken by mouth) than many other oral NSAID preparations but are very rare and no more common with formulations of piroxicam that are applied to the skin than with any other NSAID gel.

Piroxicam gel formulations in other respects are generally well tolerated. Mild to moderate local irritation, erythema (redness), pruritus (itching), and dermatitis (inflammation) on the skin may occur with any product applied to the skin. The absorption into the blood of piroxicam from the gel is very low giving blood levels of approximately 5% of those seen following oral ingestion (of a similar amount applied to the skin) over 5 to 10 days. In common with other topical NSAIDs, systemic reactions occur infrequently and have included minor gastrointestinal side effects such as nausea and dyspepsia. Cases of abdominal pain and gastritis have been reported rarely. There have been isolated reports of bronchospasm (tightening of the airways), serious skin reactions, sensitivity to light, liver reactions, kidney dysfunction, and difficulty breathing.

Although drug to drug interactions (interactions between piroxicam and other drugs taken at the same time) have been identified, people who are known to be using any of the drugs known to interact with piroxicam gel are instructed to not use this medicine and, as a P medicine the pharmacist or pharmacy staff will still be available to give this advice. Therefore, the danger of drug to drug interactions leading to adverse reactions is low for this product.

Indirect danger

Indirect danger to human health, even when the product is used correctly, could occur when a treatment might mask or hide an underlying condition requiring medical attention and supervision. Use of a medicine might delay diagnosis and definitive treatment and jeopardise the chance of more successful therapy. Therefore, it is important that the condition or symptoms for which a medicinal product not subject to a medical prescription is indicated, can be correctly assessed by an individual, without medical advice and, if needed with the help of a pharmacist.

The indicated conditions are well established as both pharmacy and general sale licence products for other similar medicines – ibuprofen and diclofenac gels – so it is not considered that there is an unacceptable risk of misdiagnosis or a delay in patients receiving treatment for an underlying condition.

The duration of treatment (up to 14 days) is consistent with other topical pain relief gels, and it not considered to be an indirect danger to health through delaying diagnosis of a more serious condition. The 30 g pack size provides a maximum of 10 days continuous treatment and is considered to be acceptable.

Incorrect use – frequently and to a very wide extent

There is no evidence that piroxicam gel is frequently and to a very wide extent used incorrectly.

Activity and/or adverse reactions require further investigation

This product has been used as a prescription product for over 25 years and the activity and adverse reactions are well established. Therefore, this criterion does not apply.

Is normally prescribed as an injection

This product is for topical use only, so this criterion does not apply.

5. Further details on the application

Risk Management Plan

The application contains a risk management plan (RMP). RMPs are documents that contain information on a medicine's safety profile and one or more of the following:

- how any risks identified in the safety profile will be prevented or minimised in patients
- plans for studies and other activities to gain more knowledge about the safety and efficacy of the medicine
- risk factors for side effects
- measuring the effectiveness of measures taken to prevent or minimise risks.

The RMP for this product identified the main risks associated with the product and proposed how these will be managed in the product information (Summary of Product Characteristics³, label, and patient information leaflet⁴). Also, since the product will be classified as a Pharmacy medicine, additional advice on correct use will be available from the pharmacy staff.

6. Reasons for not seeking advice from the Commission on Human Medicines

Overall, no new issues of concern have been raised in relation to Pharmacy availability of Piroxicam Gel. The indications are well established for Pharmacy medicines therefore the risk of misdiagnosis is low. There is not considered to be significant direct danger from the side effect profile when the medicine is used as instructed, and there is no evidence that piroxicam gel is frequently and to a wide extent used incorrectly. The patient information leaflet text and design submitted to support this reclassification application have been revised, improved, and user-tested to ensure that patients can make an informed decision about this medicine.

7. Conclusion

The MHRA has taken the decision to approve Pharmacy legal status for Piroxicam Gel under the following conditions:

- Pharmaceutical form: topical gel
- Composition: 0.5% w/w piroxicam
- Indication: For the local symptomatic relief of pain and stiffness accompanying non-serious arthritic conditions; and pain or swelling accompanying sprains, strains and sports injuries
- Dose: Adults: Apply 1 g of the gel (about 3 cms or 1¹/₄ inches) and rub into the affected area until the gel completely disappears. Wash hands immediately after use. Apply three times a day. Individual doses should be administered at least 4 hours apart. If the symptoms do not improve by day 7, or if they worsen in the first 7 days, a consultation with a doctor is recommended. Do not use for more than 14 days unless recommended by a doctor. Do not use on patients under 18 years of age.
- Maximum pack size: 30g

³ The Summary of Product Characteristics (SmPC) is a legal document describing a medicine's properties and how it can be used. SmPCs are available [online](#) via the MHRA.

⁴ The label and leaflet (patient information leaflet) provide information to patients about the medicine, including information about how to use it