SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Piroxicam Manx 0.5%w/w Gel
Reliviate Aches and Joint Pain Relief 0.5%w/w Gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Piroxicam gel 0.5% w/w

Excipients with known effect:
Propylene glycol 150 mg/g

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Topical Gel

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

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

4.2 Posology and method of administration

Posology

Adults: Apply 1 g of the gel (about 3 cms or $1^1/_4$ 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.

Occlusive dressings should not be used.

Children: Do not use on patients under 18 years of age.

Elderly: No special precautions are necessary.

Method of Administration

Topical

On first use, discard any small amount of liquid present when withdrawing product from the tube. The product can then be used normally.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. The potential exists for cross sensitivity to aspirin and other non-steroidal anti-inflammatory agents.

Piroxicam Manx Gel should not be used in patients in whom aspirin and other non-steroidal anti-inflammatory agents induce the symptoms of asthma, nasal polyps, angioneurotic oedema or urticaria.

Third trimester of pregnancy.

4.4. Special warnings and precautions for use

If local irritation develops discontinue use of the product.

Keep away from the eyes and mucosal surfaces. Do not apply to any sites affected by open skin lesions, dermatoses or infection.

Topical application of large amounts of piroxicam gel may result in increased systemic absorption of piroxicam with increased potential for systemic side effects.

Avoid excessive exposure to sunlight of the treated area to reduce the potential for development of photosensitivity reactions.

Piroxicam Manx Gel should be used with caution in patients who have a history of serious allergic drug reaction of any type, especially cutaneous reactions such as erythema multiforme, Stevens Johnson syndrome or toxic epidermal necrolysis.

Life-threatening cutaneous reactions, including drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with the systemic administration of piroxicam. These reactions have not been associated with topical piroxicam, but the possibility of occurring with topical piroxicam cannot be ruled out.

Patients should be advised of the signs and symptoms and monitored closely for skin reactions. The highest risk for occurrence of SJS or TEN is within the first weeks of treatment. If symptoms or signs of SJS or TEN (e.g. progressive skin rash often with blisters or mucosal lesions) are present, piroxicam treatment should be discontinued.

The best results in managing SJS and TEN come from early diagnosis and immediate discontinuation of any suspect drug. Early withdrawal is associated with a better prognosis.

If a patient has developed SJS or TEN with the use of piroxicam, piroxicam must not be restarted in this patient at any time.

Cases of fixed drug eruption (FDE) have been reported with piroxicam.

Piroxicam should not be reintroduced in patients with history of piroxicam-related FDE. Potential cross reactivity might occur with other oxicams.

Use with caution in patients with impaired hepatic function.

Use with caution in patients with renal impairment.

NSAIDs, including piroxicam, may cause interstitial nephritis, nephrotic syndrome and renal failure. There have also been reports of interstitial nephritis, nephrotic syndrome and renal failure with topical piroxicam, although the causal relationship to treatment with topical piroxicam has not been established. As a result, the possibility that these events may be related to the use of topical piroxicam cannot be ruled out.

The label will include the following warnings:

- Do not apply more of this medicine than the label tells you to
- Not recommended for patients aged under 18 years
- Use this medicine only on your skin
- Do not use if you are pregnant or breastfeeding
- Do not use if you are allergic to any of the ingredients or have experienced problems with aspirin, ibuprofen, piroxicam or related painkillers (including when taken by mouth)
- Do not use if you have ever had a severe skin reaction after applying or taking any other medicines
- Consult your doctor before use if you have asthma, active peptic ulcer or a history of liver or kidney problems
- If the symptoms do not get better after 7 days or if they worsen, consult your doctor

This medicine contains 150 mg propylene glycol in each 1 ¼ (3cm) application which is equivalent to 150 mg / 1 g of gel.

4.5. Interactions with other medicinal products and other forms of interaction

Non-steroidal anti-inflammatory drugs may interact with blood pressure lowering drugs, and may possibly enhance the effects of anticoagulants, although the chance of either of these occurring with a topically administered preparation is extremely remote. Where aspirin or other NSAID tablets are taken concurrently, it is important to bear in mind that these may increase the incidence of undesirable effects.

4.6. Fertility, pregnancy and lactation

Fertility

Based on the mechanism of action, the use of NSAIDs, including piroxicam may delay or prevent rupture of ovarian follicles, which has been associated with reversible infertility in some women. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of NSAIDs, including piroxicam should be considered.

Pregnancy

There are no clinical data from the use of piroxicam during pregnancy. Even if systemic exposure is lower compared with oral administration, it is not known if the systemic piroxicam exposure reached after topical administration can be harmful to an embryo/foetus. During the first and second trimester of pregnancy, piroxicam should not be used unless clearly necessary. If used, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, systemic use of prostaglandin synthetase inhibitors including piroxicam may induce cardiopulmonary and renal toxicity in the foetus. At the end of the pregnancy prolonged bleeding time in both mother and child may occur, and labour can be delayed. Studies in animals have shown reproductive toxicity with the systemic formulations (see section 5.3), but their relevance to the use of topical formulations in pregnant women is unknown. Inhibition of prostaglandin synthesis might adversely affect pregnancy. Data from epidemiological studies suggest an increased risk of spontaneous abortion after the use of prostaglandin synthesis inhibitors in early pregnancy. In animals, administration of prostaglandin synthesis inhibitors has been shown to result in increased pre- and postimplantation loss.
Therefore, piroxicam is contraindicated during the last trimester of pregnancy (see section 4.3).

Breast-feeding

Piroxicam 0.5%w/w Gel is not recommended for use in nursing mothers as clinical safety has not been established.

4.7 Effects on ability to drive and use machines

There should be no effect on the patient's ability to drive and use machinery.

4.8. Undesirable effects

Mild to moderate local irritation, erythema, pruritus and dermatitis may occur at the application site. Contact dermatitis, eczema and photosensitivity skin reactions have been reported. The systemic absorption of piroxicam gel is very low. In common with other topical NSAIDs, systemic reactions occur infrequently and have included minor gastro-intestinal side-effects such as nausea and dyspepsia. Cases of abdominal pain and gastritis have been reported rarely.

There have been isolated reports of bronchospasm and dyspnoea.

Severe cutaneous adverse reactions: Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported very rarely (see section 4.4).
Fixed drug eruption (see Section 4.4) has been reported with an unknown frequency.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Overdose is unlikely to occur with this topical preparation.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory preparations, non-steroids for topical use, ATC Code: M02A A07

Piroxicam is a non-steroidal anti-inflammatory agent useful in the treatment of inflammatory conditions. Although the mode of action for this agent is not precisely understood, 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.

5.2 Pharmacokinetic properties

Pharmacokinetic and tissue distribution studies have shown that the highest levels of piroxicam were achieved in tissues below the site of application with low levels in the plasma. A study in healthy human volunteers has shown that plasma concentrations following repeated topical application of a piroxicam 5% gel are about 5% of the level observed after equivalent doses of oral or intramuscular piroxicam.

The serum half-life of piroxicam is approximately 50 hours.

5.3 Preclinical safety data

In reproductive toxicity studies, piroxicam increases the incidence of dystocia and delayed parturition in animals, when drug administration is continued during pregnancy.

Administration of prostaglandin synthesis inhibitors has also been shown to result in increased pre-and post-implantation loss. These observations were made using parenteral dosing, and equilibrium plasma levels of piroxicam obtained in patients using the topical gel are only approximately 5% of those

achieved using an equivalent dose of parenteral product. In animal studies with the topical gel, there were no treatment-related adverse effects using 1 gram of gel daily for up to 30 days, nor was there evidence of photoallergy or skin sensitisation.

It is generally accepted that topical NSAID therapy provides a safer means of drug delivery than conventional routes. Clinical trials and post-marketing experience suggest that topical piroxicam is well-tolerated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol
isopropyl alcohol
macrogol 7 glyceryl cocoate
hypromellose, sodium hydroxide
sodium metabisulphite (E223)
potassium dihydrogen phosphate
purified water.

6.2 Incompatibilities

None known.

6.3 Shelf life

Three (3) years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5. Nature and contents of container

Aluminium tubes with a polypropylene cap containing 30 g.

6.6 Special precautions for disposal

Apply 1 g of the gel (about 3 cms or $1^{1}/_{4}$ inches) and rub into the affected area. Apply to three or four times a day. Occlusive dressings should not be used.

7 MARKETING AUTHORISATION HOLDER

Manx Healthcare Limited
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Warwick
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8 MARKETING AUTHORISATION NUMBER(S)

PL 14251/0028

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 DATE OF REVISION OF THE TEXT

14/03/2025