SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Piroxicam 0.5% Gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Piroxicam 0.5% w/w

Also contains:

Propylene Glycol 15 g / 100 g (or 15% w/w).

3 PHARMACEUTICAL FORM

Gel

Light yellow, transparent gel.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Piroxicam gel is a non-steroidal anti-inflammatory agent indicated for a variety of conditions characterised by pain and inflammation, or stiffness. It is effective in the treatment of osteoarthritis of superficial joints such as the knee, acute musculoskeletal injuries, periarthritis, epicondylitis, tendinitis, and tenosynovitis.

4.2 Posology and method of administration

Posology

Adults

No occlusive dressings should be employed.

Apply 1g of gel, corresponding to 3cm, and rub into the affected site three to four times daily leaving no residual material on the skin. Therapy should be reviewed after 4 weeks.

Paediatric population
Dosage recommendations and indications for use of Piroxicam Gel in children have not been established.

Elderly
No special precautions are required.

Method of administration
Piroxicam Gel is for external use only.

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 Gel should not be given to 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

Piroxicam 0.5% Gel is not suitable for use in children under 12 years of age.

The gel should not be used for any condition other than those specified.

Skin reactions

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 use of systemic administration of piroxicam. These reactions have not been associated with topical piroxicam, but the possibility of occurring with topical piroxicam cannot be excluded.

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 signs or symptoms 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 the patient has developed SJS or TEN with the use of piroxicam, piroxicam must not be re-started 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.

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

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.

Instruct patients not to smoke or go near naked flames - risk of severe burns. Fabric (clothing, bedding, dressings etc) that has been in contact with this product burns more easily and is a serious fire hazard. Washing clothing and bedding may reduce product build-up but not totally remove it.

This medicinal product contains 150mg propylene glycol per gram and may cause skin irritation. If local irritation develops, the use of the gel should be discontinued and appropriate therapy instituted as necessary. Because this medicine contains propylene glycol, Piroxicam Gel should not be used on open wounds or large areas of broken or damaged skin (such as burns).

4.5 Interaction with other medicinal products and other forms of interaction

Dose-dependent percutaneous absorption of piroxicam has been demonstrated in rabbits and there is theoretical possibility of systemic interactions / effects.

For example, oral piroxicam has been reported to potentiate the anticoagulant effect of dicumarol because of its effect on platelets. It can cause sodium, potassium and fluid retention and may interfere with the natriuretic action of diuretic agents and thus aggravate or precipitate heart failure.

Under conditions of solar or UV-irradiation of Piroxicam 0.5 % Gel – treated exposed skin, phototoxic products may evolve which may induce cross-sensitivity reactions to Thimerosal (sodium ethylmercurithiosalicylate) or thiosalicylic acid in the case of relevant allergy. Sodium bisulphite (excipient) when used as a food additive, reduces the content of thiamine.

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 topical 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. Therefore, piroxicam is contraindicated during the last trimester of pregnancy (see section 4.3).

Breast-feeding
Piroxicam 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

Not relevant.

4.8 Undesirable effects

Piroxicam Gel is well tolerated.

Mild to moderate local irritation, erythema, pruritus, and dermatitis may occur at the application site.

The systemic absorption of Piroxicam 0.5% Gel is very low. In common with other topical NSAIDs, systemic reactions occur infrequently.
Gastrointestinal: nausea, dyspepsia, abdominal pain and gastritis have been reported.

Respiratory, thoracic and mediastinal disorders: There have been isolated reports of bronchospasm and dyspnoea (see also section 4.3).

Skin and subcutaneous tissue disorders:
Severe cutaneous adverse reactions (SCARs): 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.

Contact dermatitis, eczema and photosensitivity skin reaction have also been observed from post-marketing experience.

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 M02AA07.

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 inhibits prostaglandin synthesis and release through a reversible inhibition of the cyclo-oxygenase enzyme. New data are presented on the anti-inflammatory and analgesic effects of piroxicam gel compared with its vehicle and indometacin 1% Gel in rats and guinea pigs. Using established animal models of pain and inflammation, piroxicam gel was as effective as oral piroxicam and indometacin 1% Gel and significantly more effective than its vehicle.

5.2 Pharmacokinetic properties

A study in man examining skin biopsies following piroxicam gel administration concluded that piroxicam rapidly permeates through the stratum corneum into the epidermis/dermis after application of the gel with plasma levels being low.

A separate study in man demonstrated mean plasma concentrations of piroxicam gel to be approximately 5% of those observed after equivalent doses of oral or intramuscular piroxicam. In healthy subjects or patients following the administration of a single oral dose, the pharmacokinetics of Piroxicam are linear, with maximum plasma concentration usually being obtained in about 2 h, but this can vary from 1-6 h in different subjects. It has a low clearance rate of approximately 45 h, but the half-life can vary from 30-60 h. After repeated doses of 20 mg daily, steady – state concentrations are generally achieved in 7-12 days; with a peak plasma concentration ranging from 4.5-2.2 mg/l.

In humans it penetrates into the synovial fluid of patients with rheumatoid arthritis, osteoarthritis, and reactive synovitis where mean concentrations are approximately 40% of those in plasma; it is also demonstrable in synovial tissues. Concentrations of piroxicam in breast milk are about 1% of those in the maternal plasma at the same time. Overall, piroxicam is 99% bound to plasma protein. Pharmacokinetics of the drug do not appear to be age related, and renal function has only a limited influence on its elimination, but plasma concentrations are increased in patients with severe liver dysfunction.

Piroxicam is eliminated by biotransformation in the liver. The major route is by hydroxylation, with the resultant products being excreted alone or as a glucuronide in urine and faeces. The metabolites of piroxicam have little or no anti-inflammatory activity in animal models. Approximately 10% of an oral dose is excreted as unchanged drug in 10 days.

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 as noted in section 5.2,

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 photo-allergy or skin sensitisation.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol

Isopropyl alcohol

Macrogol 7 glyceryl cocoate

Hypromellose

Sodium hydroxide

Sodium metabisulfite

Potassium dihydrogen phosphate

Purified water

6.2 Incompatibilities

The metabolism of Piroxicam is inhibited by cimetidine and it itself can inhibit antipyrine metabolism.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 25°C. Keep the tube tightly closed.

6.5 Nature and contents of container

Aluminium tubes with inner protective lacquer and polypropylene screw caps. Each tube contains 60g or 112g of Piroxicam gel.

6.6 Special precautions for disposal

Pierce the tube by reversing the cap and screwing down to break the seal on the tube. Apply 3cm (1¼" approximately) of the gel on the affected area. Rub the gel into the skin until the gel disappears. Do this three or four times a day. For muscle sprains and strains, you should start to feel better within one week. If the pain has not got any less after a week, tell your pharmacist or doctor. Replace the cap after use.

Wash hands after each application unless it is the hand that is being treated.

7 MARKETING AUTHORISATION HOLDER

Accord Healthcare Limited
Sage House
319 Pinner Road
North Harrow
Middlesex
HA1 4HF
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 20075/0704

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16 March 2001

10 DATE OF REVISION OF THE TEXT

14/01/2025