PIROXICAM
FELDENE
5 mg/g (0.5%) Gel

1.0 THERAPEUTIC CATEGORY

Non- Steroidal Anti-Inflammatory

2.0 DESCRIPTION

Piroxicam (Feldene) is 4-Hydroxy-2-methyl-N-2-pyridinyl-2H-1,2-benzothiazine-3-carboxamide 1,1-dioxide, an oxicam. Members of the oxicam family are not carboxylic acids, but they are acidic by virtue of the enolic 4-hydroxy substituent. Piroxicam occurs as a white crystalline solid, sparingly soluble in water, dilute acid and most organic solvents. It is slightly soluble in alcohols and in aqueous alkaline solution. It exhibits a weakly acidic 4-hydroxy proton (pKa 5.1) and a weakly basic pyridyl nitrogen (pKa 1.8).

Molecular Formula: C\textsubscript{15}H\textsubscript{13}N\textsubscript{3}O\textsubscript{4}S
Molecular Weight: 331.35

3.0 FORMULATION

Piroxicam (Feldene) 0.5% Gel: Each gram contains 5 mg of piroxicam.

4.0 CLINICAL PARTICULARS

4.1. Therapeutic Indications

Piroxicam (Feldene) topical is indicated for a variety of conditions characterized by pain, and inflammation such as osteoarthritis (arthrosis, degenerative joint disease), post traumatic or acute musculoskeletal disorders including tendinitis, tenosynovitis, periarthritis, sprains, strains and low back pain.

4.2 Dosage and Method of Administration

This product is intended for external use only. A 1 gram dose of the 0.5% gel (corresponding to 5 mg of piroxicam) should be applied to the affected site three or four times per day. No occlusive dressing should be employed. Rub in the gel, leaving no residual material on the skin.

Use in Children – Dosage recommendations and indications for use in children have not been established.

4.3 Contraindications

1. Piroxicam (Feldene) topical should not be used in those patients who have previously shown a hypersensitivity to the gel or piroxicam in any of its dosage forms. The potential exists for cross sensitivity to aspirin and other Non-Steroidal Anti-Inflammatory Drugs (NSAIDs).
2. Piroxicam (Feldene) topical should not be given to patients in whom aspirin and other NSAIDs induce the symptoms of asthma, rhinitis, angioedema or urticaria.

4.4 Special Warnings and Special Precautions for Use

Life-threatening cutaneous reactions 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 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 the patient has developed SJS or TEN with the use of piroxicam, piroxicam must not be re-started in this patient at any time.

If local irritation develops, the use of piroxicam (Feldene) topical should be discontinued and appropriate therapy instituted as necessary. Do not apply to the eyes, mucosa or to open skin lesions, or skin conditions affecting the site of application.

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.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

None known.

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
The safety of piroxicam use during pregnancy or during lactation has not yet been established.

Inhibition of prostaglandin synthesis might adversely affect pregnancy. Data from epidemiological studies suggest an increased risk of spontaneous abortion after use of prostaglandin synthesis inhibitors in early pregnancy. In animals, administration of prostaglandin synthesis inhibitors has been shown to result in increased pre- and post-implantation loss.
Lactation
Piroxicam (Feldene) topical is not recommended for use in nursing mothers as the clinical safety has not been established.

4.7 Effects on Ability to Drive and Use Machines
None known

4.8 Undesirable Effects
Side effects possibly related to treatment have been infrequently reported. In clinical trials the vast majority of side effects involved mild or moderate local irritation, erythema, rash, pityroid desquamation, pruritus, and reactions at the application site.

In post-marketing experience, the following additional dermatological effects have been reported: contact dermatitis, eczema and photosensitivity skin reaction.

Mild but transient skin discoloration and staining of clothing have been noted when the gel is not rubbed in completely.

4.9 Overdosage
Overdosage is unlikely to occur with this topical preparation.

5.0 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties
Piroxicam (Feldene) 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 cyclooxygenase enzyme.

5.2 Pharmacokinetic Properties
On the basis of various pharmacokinetic and tissue distribution studies in rats and dogs, piroxicam 0.5% gel is continuously and gradually released from the skin to underlying muscle or synovial fluid. In addition, equilibrium between skin and muscle or synovial fluid appears to be reached rapidly, within a few hours after application.

A multiple dose study of twice daily application of piroxicam 0.5% gel (total daily dose equivalent to 20 mg per day, piroxicam) for 14 days found that plasma levels rose slowly over the course of the treatment period and reached a value of over 200 ng/ml on the 4th day. On average, steady state plasma levels were between 300 and 400 ng/ml and mean values remained below 400 ng/ml even on the fourteenth day of treatment. These piroxicam levels observed at equilibrium were approximately 5% of those observed in subjects receiving similar oral dosing (20 mg daily). Elimination half-life in this study was calculated to be approximately 79 hours. In humans, the gel was well tolerated in skin sensitive volunteers.

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

5.3 Preclinical Safety Data
Acute and chronic toxicity and irritation studies have been carried out in animals. In an acute study, albino rats were given a single dermal application of 5 g/kg (200-300 times the recommended clinical application). No deaths, toxic signs or skin irritation were observed and no gross changes were found at autopsy. A one month study was conducted in albino rats. One group received a daily application of gel to dorsal skin of 1 g per rat, another was treated with the vehicle and the third group served as untreated controls. No skin irritation was noted at the treatment sites, and no drug-related changes were observed in hematology, laboratory chemistries, organ weight, autopsy findings or histopathology. The gel was also evaluated for primary skin irritation, eye irritation, and phototoxicity in rabbits and for photoallergy and skin sensitization potential in guinea pigs, all according to standard established protocols. No skin reactions were found after application of 0.5% gel or the vehicle to intact rabbit skin. On abraded skin, piroxicam (Feldene) gel produced slight erythema and edema which was slightly greater than that following vehicle.

The anti-inflammatory and analgesic effects of piroxicam (Feldene) 0.5% gel were studied in rats and guinea pigs using such standard models of pain and inflammation as carrageenin induced rat paw edema, ultraviolet erythema in guinea pigs, traumatic edema in rats, yeast induced pain in rats, croton oil induced erythema on guinea pig abdomens, cotton pellet induced granuloma formation in rats and adjuvant induced arthritis in rats. Piroxicam (Feldene) 0.5% gel was comparable to indomethacin 1% gel in all of these models and was comparable to orally administered piroxicam in inhibiting inflammation in the rat paw edema model.

Piroxicam (Feldene) topical is a nonsteroidal anti-inflammatory (NSAID) agent which also possesses analgesic properties. Edema, erythema, tissue proliferation, fever and pain can all be inhibited in laboratory animals by the administration of piroxicam gel.

No teratogenic effects were seen when piroxicam was orally administered in animal testing. Piroxicam inhibits prostaglandin synthesis and release through a reversible inhibition of the cyclooxygenase enzyme. This effect, as with other NSAIDs has been associated with an increased incidence of dystocia and delayed parturition in pregnant animals when drug administration was continued into late pregnancy. NSAIDs are also known to induce closure of the ductus arteriosus in infants.

A preliminary study indicates that following oral administration piroxicam exists in maternal milk in a concentration of approximately 1% of that reached in plasma after oral administration.

6.0 PHARMACEUTICAL PARTICULARS

6.1 Shelf Life

See outer package for the expiry date of the product.

6.2 Storage

Store at temperatures not exceeding 30°C.

6.3 Availability

Piroxicam (Feldene) 0.5% Gel is available as clear pale yellow gel. Available in aluminum tubes containing 10 g of piroxicam (Feldene) gel.

CAUTION: Foods, Drugs, Devices and Cosmetics Act prohibit dispensing without a prescription.
Keep out of reach of children.

Manufactured by:
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