SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Feldene Gel®

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains 5mg piroxicam (0.5% w/w).

Excipients with known effect:

Feldene Gel contains 200mg/g propylene glycol
10mg/g benzyl alcohol and 250 mg/g ethanol 96%.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gel for topical application.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Feldene Gel is indicated for a variety of conditions characterized by pain and inflammation such as osteoarthritis of superficial joints, acute musculoskeletal injuries, periarthritis, tendinitis and tenosynovitis.

4.2 Posology and method of administration

Posology

Adults
No occlusive dressings should be employed. Apply 1g of Gel, corresponding to 5mg of piroxicam, 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 the use of Feldene Gel in children have not been established.

Elderly

No special precautions are required.

Method of administration

Feldene 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 (NSAIDs). Feldene 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.

4.4 Special warnings and precautions for use

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 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 week 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.

Excipient Information

This medicinal product contains ethanol, propylene glycol and benzyl alcohol (see section 2).

The ethanol may cause a burning sensation on damaged skin. In neonates (pre-term and term newborn infants), high concentrations of ethanol may cause severe local reactions and systemic toxicity due to significant absorption through immature skin (especially under occlusion).

Propylen glycol may cause skin irritation. If local irritation develops, the use of the Feldene Gel should be discontinued and appropriate therapy instituted as necessary. Feldene Gel should not be used in neonates with open wounds or large areas of broken or damaged skin (such as burns).

Benzyl alcohol may cause mild local irritation and may also cause allergic reactions.

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 topical piroxicam should be considered.

Pregnancy:

There are no studies of the use of topical piroxicam in pregnant women. 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. As a precautionary measure, it is preferable to avoid the use of topical piroxicam in pregnant women.

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 post-implantation loss.
Therefore, the use of Feldene Gel during pregnancy is not recommended.

Breast-feeding

Feldene 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**

Feldene Gel is well tolerated. Mild to moderate local irritation, erythema, pruritus and dermatitis may occur at the application site.
The systemic absorption of Feldene Gel is very low. In common with other topical non-steroidal anti-inflammatory agents, 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 (see also section 4.3).

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) at 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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/

4.9 **Overdose**

Overdosage is unlikely to occur with this topical preparation.

5. **PHARMACOLOGICAL PROPERTIES**

5.1 **Pharmacodynamic properties**

Pharmacotherapeutic group: 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 Feldene Gel compared with its vehicle and indometacin 1% Gel in rats and guinea pigs. Using established animal models of pain

and inflammation, Feldene Gel was as effective as oral Feldene and indometacin 1% Gel and significantly more effective than its vehicle.

5.2 Pharmacokinetic properties

On the basis of various pharmacokinetic and tissue distribution studies in animals, with piroxicam gel 0.5%, the highest concentrations of piroxicam were achieved in the tissues below the site of application with low concentrations being reached in the plasma. Piroxicam gel 0.5% was continuously and gradually released from the skin to underlying tissues, equilibrium between skin, and muscle or synovial fluid appeared to be reached rapidly, within a few hours of application.

From a pharmacokinetic study in man, 2g of the Gel was applied to the shoulders of normal volunteers twice daily (corresponding to 20mg piroxicam/day) for 14 days, plasma levels of piroxicam rose slowly, reaching steady state after about 11 days. The plasma levels at this time were between 300-400 ng/ml, or one-twentieth of those observed in subjects receiving 20mg orally

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 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

Purified Water, Ethanol 96%, Propylene Glycol, Diisopropanol Amine, Benzyl Alcohol, Carbopol 980, Hydroxyethyl Cellulose..

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials

6.4 Special precautions for storage

Store below 25˚C.
After first opening the preparation can be used within 6 months, no later than the expiration date.

6.5 Nature and contents of container

Aluminium tube containing 25g, 50g or 100g of Feldene Gel.

6.6 Special precautions for disposal and other handling

No special requirements.

7. LICENSE HOLDER

Pfizer PFE Pharmaceuticals Israel Ltd. 9 Shenkar St ,Hertzliya Pituach 46725.

8. LICENSE NUMBER

113-55-26646

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