Feldene*

Piroxicam

0.5% Topical Gel

Reference market: France

AfME Markets using same as LPD: Egypt

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

FELDENE 0.5%, gel for topical application

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Piroxicam ..... 0.5 g

For 100 g.

Excipient with known effect: This medicine contains 200 mg/g propylene glycol, 10 mg/g benzyl alcohol and 250 mg/g ethanol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gel for topical application.

Feldene 0.5% Topical gel is a clear pale yellow gel.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

- Symptomatic treatment of superficial tendinitis.
- Symptomatic treatment of benign trauma: sprains, bruises.

4.2. Posology and method of administration

Posology

2 to 4 applications per day.

Method of administration

For adults and children over 15 years of age.

EXTERNAL USE.

Cutaneous use.

Apply the gel by gently massaging the painful or inflamed area for some time.

Wash hands well after each application.

4.3. Contraindications

This medicinal product is contraindicated in the following situations:

- hypersensitivity to the active substance or to any of the excipients listed in section 6.1,
- pregnancy, from the start of the 6th month (beyond 24 weeks of amenorrhoea) (see section 4.6),
- history of allergy or asthma triggered by taking piroxicam or substances with similar activity, such as other NSAIDs, aspirin,
- broken skin, regardless of the type of wound: weeping dermatitis, eczema, infected wound, burn or cut.

4.4. Special warnings and precautions for use

Special warnings

Severe skin reactions, some of which may be fatal, including drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), Steven-Johnson syndrome and toxic epidermal necrolysis (Lyell's syndrome), have been reported during systemic treatment with piroxicam. Although these reactions have not been associated with topical applications of piroxicam, the possibility of such reactions with piroxicam in topical applications cannot be ruled out. 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.

Patients should be informed of the symptoms and be closely monitored for skin reactions. The risk of developing Steven-Johnson Syndrome or Lyell's syndrome is greater during the first few weeks of treatment.

Piroxicam should be discontinued as soon as any symptoms of Steven-Johnson syndrome or Lyell's syndrome appear, for example a progressive skin rash with blisters or mucosal lesions. Treatment with piroxicam should never be repeated in patients having previously developed symptoms of Steven-Johnson syndrome or Lyell's syndrome following administration of piroxicam.

The best results in the management of Steven-Johnson and Lyell's syndromes have been obtained by early diagnosis and immediate interruption of the treatment involved. Early discontinuation is associated with the best prognosis.

Patients presenting asthma associated with chronic rhinitis, chronic sinusitis and/or nasal polyposis have a higher risk than the general population of allergic events when they take aspirin and/or non-steroidal anti-inflammatories. Use of this medicine can trigger an asthma attack.

Do not apply on mucous membranes or the eyes. If applied accidentally, rinse well with water.

If a skin reaction appears after application of the gel, stop treatment immediately.

This medicine contains propylene glycol and can cause skin irritations.

NSAIDs, including piroxicam, may cause interstitial nephritis, nephrotic syndrome and renal impairment. Cases of interstitial nephritis, nephrotic syndrome and renal impairment have also been reported with piroxicam used in topical applications although the causal relationship between these conditions and piroxicam used in topical applications has not been established. The possibility that these events are related to the use of piroxicam in topical applications can therefore not be ruled out.

Precautions for use

Avoid applying under an occlusive bandage.

Gloves are recommended for health care professionals who use this medicine often.

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).

Propylene glycol may cause skin irritation. FELDENE 0.5%, gel for topical application 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

As only low levels of the gel pass into the system with normal use, the interactions with other medicines indicated for piroxicam taken orally are not probable.

4.6. Fertility, pregnancy and breastfeeding

Pregnancy

Inhibition of prostaglandin synthesis by NSAIDs may affect the course of pregnancy and/or the development of the embryo or foetus.

Risks related to the use during the 1st trimester

Data of epidemiological studies suggests an increase in the risk of miscarriage, heart malformations and gastroschisis, after treatment by a prostaglandin synthesis inhibitor at the start of pregnancy. The absolute risk of cardiovascular malformations went from less than 1% in general population to approximately 1.5% in people exposed to NSAIDs. The risk appears to increase with dose and treatment duration. In animals, it has been shown that the administration of a prostaglandin synthesis inhibitor causes an increased risk of pre- and post-implant loss and a rise in embryo-foetal fatality. Moreover, a higher incidence of certain malformations, including cardiovascular malformations, has been reported in animals who received a prostaglandin synthesis inhibitor during the organogenesis phase of gestation.

Risks related to the use from the 12th week of amenorrhoea and until birth:

- From the 12th week of amenorrhoea and until birth, all NSAIDs, by inhibition of prostaglandin synthesis, may expose the foetus to **renal function disorder:**
    - *in utero*, observed from 12 weeks of amenorrhoea (start of foetal diuresis): oligoamnios (usually reversible after discontinuation of treatment) or anamnios, especially after extended exposure.
    - at birth, renal impairment (reversible or irreversible) can persist, particularly in case of late, prolonged exposure (with a risk of severe delayed hyperkalaemia).

Risks related to the use from the 24th week of amenorrhoea and until birth:

From the 24th week of amenorrhea, NSAIDs may expose the foetus to **cardiopulmonary toxicity** (premature closure of the ductus arteriosus and pulmonary arterial hypertension). Constriction of the arterial canal may arise from the beginning of the 6th month (beyond the 24th week of amenorrhoea), and can lead to foetal or neonatal right heart failure or foetal death *in utero*. This risk is greater the closer administration is to delivery (less reversibility). This effect occurs even with occasional administration.

At the end of pregnancy, the mother and newborn may have:

- increased bleeding time due to an anti-aggregating action, which may arise even after the administration of very small doses of the medicinal product;
- an inhibition of uterine contractions, resulting in a delay in term or prolonged delivery.

Consequently:

Unless absolutely necessary, this medicinal product must not be prescribed in a woman considering pregnancy or during the first 5 months of pregnancy (first 24 weeks of amenorrhoea). If this medicinal product is administered to a woman intending to get pregnant or who is less than 6 months pregnant, the dose should be as low as possible and the duration of treatment as short as possible. Prolonged use is highly inadvisable.

From the beginning of the 6th month (after 24 weeks of amenorrhoea): any ongoing administration, however brief, is contraindicated. An inadvertent use from this date requires cardiac and renal monitoring of the foetus or neonate, depending on the date of exposure. The duration of this monitoring depends on the elimination half-life of the molecule.

Breastfeeding

Because NSAIDs pass into human breast milk, this medicinal product is not recommended for use by breastfeeding women.

Under no circumstances should this medication be applied to the breasts while breastfeeding.

Fertility

Like all NSAIDs, the use of this medicinal product may temporarily affect female fertility by acting on ovulation; it is therefore not recommended for women wishing to conceive a child. In women having difficulty conceiving or undergoing fertility tests, discontinuation of treatment should be considered.

4.7. Effects on ability to drive and use machines

Not applicable.

4.8. Side effects

Skin reactions:

- allergies such as rashes, pruritus, erythema, bullous cutaneous reactions, photosensitisation reactions, contact dermatitis, eczema.
- possibility of skin pigmentation.
- including drug reaction with eosinophilia and systemic symptoms (DRESS syndrome).
- frequency unknown: fixed drug eruption (see section 4.4)

Other systemic effects of NSAIDs: dependent upon the active ingredient that passes transdermal, and therefore the quantity of gel applied, the area treated, the degree of integrity of the skin, the duration of the treatment and the usage of a non-occlusive bandage (digestion, renal disorders).

Reporting of suspected side effects.

The reporting of side effects after marketing 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 side effects according to their local country requirements.

To report any side effect(s):
Egypt: Pharmacovigilance center, Pfizer Pharmaceutical Company: EGY.AEReporting@pfizer.com Egyptian Pharmacovigilance center (EPVC), EDA: pv.followup@edaegypt.gov.eg

4.9. Overdose

If over-applied, rinse well with water.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Topical non-steroidal anti-inflammatory drug, ATC code: M02AA07

Piroxicam is a non-steroidal anti-inflammatory agent (NSAID) in the oxicam group. In the form of a gel, it has anti-inflammatory, analgesic qualities

5.2. Pharmacokinetic properties

Absorption

Applied locally in the form of a gel, piroxicam is absorbed slowly through the skin. Its level of accumulation in the body is low. Compared to the oral forms of piroxicam, the passage into the system of the gel is along the lines of 5%.

Distribution

The elimination half-life is around 50 hours.

Binding to plasma proteins is significant: in the order of 99%.

Biotransformation/Elimination:

Piroxicam is eliminated slowly. It is almost completely metabolised.

A significant amount is eliminated in the urine in the form of hydroxy-5-metabolite.

5.3. Preclinical safety data

Subacute and chronic toxicity studies were conducted in rats, mice, dogs, and monkeys at oral doses ranging from 0.3 mg/kg/day to 25 mg/kg/day.

Non-clinical data show typical effects of non-COX-selective NSAIDs, including renal papillary necrosis and gastrointestinal lesions. In regard to this last point, monkeys proved relatively resistant to this effect, and dogs unusually sensitive.

In reproductive toxicity studies, piroxicam increased the incidence of dystocia and caused delayed parturition in animals when administration was pursued during gestation. It has also been shown that the administration of prostaglandin synthesis inhibitors results in increased losses before and after implantation. These observations were made following oral administration and, as mentioned in section 5.2, equilibrium plasma piroxicam concentrations obtained in patients taking the gel form reached only some 5% of those for the equivalent dose administered orally.

The acute toxicity, chronic toxicity and irritation of the product used topically have also been investigated.

In one acute toxicity study in albino rats administered a single topical application of 5 g/kg (200–300 times the recommended clinical application), no deaths, signs of toxicity or skin irritation were observed and no macroscopic changes were reported at autopsy.

A one-month study was conducted in albino rats. One group received a daily application of the gel on the dorsal skin at a dose of 1 g per rat, a second group was treated with the vehicle and a third, control, group was untreated. No skin irritation was reported at the sites of

application, and no treatment-related changes were observed in haematological, chemical, organ weight, autopsy or histopathological parameters.

The gel was also evaluated for primary skin irritation, ocular irritation and phototoxicity in rabbits and for its photo-allergy and skin sensitisation potential in guinea pigs, using established standard protocols.

No skin reaction was observed after application of the gel at 0.5% or after application of the vehicle to intact skin in rabbits. On abraded skin, piroxicam gel produced a slight erythema and a slightly more pronounced level of oedema than the vehicle alone.

The anti-inflammatory and analgesic effects of 0.5% piroxicam gel were studied in rats and guinea pigs using standard models of pain and inflammation, including carrageenan-induced paw oedema in rats, ultraviolet induced erythema in guinea pigs, traumatic oedema in rats, yeast-induced pain in rats, croton oil erythema on the guinea pig abdomen, granuloma formation induced by cotton wool pad in rats and adjuvant-induced arthritis in rats. Piroxicam gel at 0.5% was comparable to indomethacin gel at 1% in all these models and comparable to oral piroxicam on the inhibition of inflammation in the induced paw oedema model in rats.

Topical piroxicam is a non-steroidal anti-inflammatory (NSAID) that also has analgesic properties. Oedema, erythema, tissue proliferation, fever and pain can be inhibited in laboratory animals by the administration of piroxicam gel.

No teratogenic effects were observed when piroxicam was administered orally in animal tests. Piroxicam inhibits the synthesis and release of prostaglandin by reversible inhibition of the cyclooxygenase enzyme. This effect, as with other NSAIDs, is accompanied by increased incidence of dystocia and delayed parturition in pregnant animals when administration is continued into late pregnancy. NSAIDs are also known to cause closure of the ductus arteriosus in infants.

One preliminary study indicates that piroxicam is present in breast milk, following oral administration, at a concentration corresponding to approximately 1% of the plasma concentration achieved after oral administration.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Carbopol 940, propylene glycol (E1520), ethanol, benzyl alcohol (E1519), diisopropanolamine, hydroxyethylcellulose, purified water

6.2. Incompatibilities

Not applicable.

6.3. Shelf-life

Do not use Feldene 0.5% Topical Gel after the expiry date which is stated on the carton label after EXP:. The expiry date refers to the last day of that month.

6.4. Special precautions for storage

Store at a temperature not exceeding 30°C

6.5. Nature and contents of the outer packaging

carton box contains aluminium tube with HDPE plastic cap contains 15 g topical gel and an inner leaflet.

6.6. Special precautions for disposal and other handling

Keep out of sight and reach of children.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

7. FURTHER INFORMATION

MARKETING AUTHORISATION HOLDER

Pfizer Inc. USA.

MANUFACUTRED, PACKED & RELEASED BY:

Viatris Egypt

8. DATE OF REVISION OF TEXT

July 2021.

THIS IS A MEDICAMENT

- Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the Pharmacist who sold the medicament.
- The doctor and the Pharmacist are experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.

Keep all medicaments out of reach and sight of children

Council of Arab Health Ministers
Union of Arabic Pharmacists