Prescribing Information

1. NAME OF THE MEDICINAL PRODUCT

EXIPAN 0.5 %W/W Gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Piroxicam 0.5% W/W
Each 1 g gel contains 5 mg Piroxicam.

Excipient with known effect:
Exipan contains 180.83mg/g Alcohol 95%, 0.28 mg/g Methyl Parahydroxybenzoate and 0.14 mg/g Propyl Parahydroxybenzoate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

3.1. Preparations

Clear -Yellowish Gel for topical application

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Exipan Gel is a non-steroidal anti-inflammatory agent.
For local treatment of inflammatory conditions accompanied by pain.

4.2. Posology and Method of Administration

Posology:

- Adults

No occlusive dressings should be applied.
Apply 1 g 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 the use of Exipan Gel in children have not been established.

- Elderly

No special precautions are required.

Method of administration

Exipan 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). Exipan Gel should not be given to patients in whom aspirin and other nonsteroidal 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 restarted in this patient at any time.

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.

This medicinal product contains180.83 mg/g equivalent to 18.1 %w/w Alcohol 95% It may cause burning sensation on damaged skin.

This medicinal product contains Methyl Parahydroxybenzoate and Propyl Parahydroxybenzoate that may cause allergic reactions (possibly delayed).

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 postimplantation loss. Therefore, the use of Exipan Gel during pregnancy is not recommended.

NSAIDs use after 20th week of pregnancy may rarely cause fetal renal dysfunction leading to reduction in amniotic fluid (Oligohydramnios) . These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Oligohydramnios is often, but not always, reversible with treatment discontinuation.
If NSAID treatment is deemed necessary after 20th week of pregnancy, limit use to the lowest effective dose and shortest duration possible.
Consider ultrasound monitoring of amniotic fluid if NSAID treatment extends beyond 5 days. Discontinue the NSAID if oligohydramnios.

Breast-feeding

Exipan 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

Exipan Gel is well tolerated. Mild to moderate local irritation, erythema, pruritus and dermatitis may occur at the application site. The systemic absorption of Exipan 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 .

Severe cutaneous adverse reactions (SCARs): Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported very rarely (see section 4.4).

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 authorization 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 at https://sideeffects.health.gov.il
In addition, you can report to Padagis via the following address: Padagis.co.il

4.9.Overdose

Overdosage is unlikely to occur with this topical product.

5. PHARMACOLOGICAL PROPERTIES

5.1.Pharmacodynamic Properties

Pharmacotherapeutic group: non-steroidal anti-inflammatory agent

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 cyclooxygenase enzyme.
New data are presented on the anti-inflammatory and analgesic effects of
piroxicam gel 0.5 % compared with its vehicle and indometacin 1% gel in rats and guinea pigs.

Using established animal models of pain and inflammation, piroxicam gel 0.5 % was as effective as oral piroxicam 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 20 mg 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 20 mg 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 photoallergy or skin sensitisation.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Purified Water, Alcohol 95%, Diethylene Glycol Monoethylether (Transcutol), Cetiol HE, Hydroxyethyl Cellulose (Natrosol), Poloxyl-(23)-Lauryl Ether (BRIJ 35), Trolamine, Arlacel 186, Methyl Parahydroxybenzoate (Methyl Paraben), Propyl Parahydroxybenzoate (Propyl Paraben)

6.2. Incompatibilities

Not applicable

6.3. Shelf Life

The expiry date of the product is indicated on the packaging materials
After first opening: 6 months.

6.4. Special Precautions for Storage

Store below 25°C.

Caution! Inflammable material; keep away from fire.

6.5. Nature and Contents of Container

ROLL-ON HDPE 90 ML

TUBE ALUMINIUM 50 G

6.6. Special Precautions for Disposal and Other Handling

Caution! Inflammable - Keep away from fire!
Do not light a cigarette or come into contact with fire until the product is fully dry.

7. MANUFACTURER AND MARKETING AUTHORISATION HOLDER

Padagis Israel Pharmaceuticals LTD Israel, 1Rakefet st, Shoham, Israel

8. MARKETING AUTHORISATION NUMBER

065-11-27132-00

Prepared according to the guidelines of the Ministry of Health in December 2023

12/2023