PT Pfizer Indonesia
Local Product Document

Generic Name: Piroxicam
Trade Name: Feldene
CDS Effective Date: September 02, 2021
Supersedes: November 01, 2019

TRADE NAME

FELDENE

QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: anhydrous piroxicam

PHARMACEUTICAL FORM

Gel: 0.5% (5 mg per gram of gel) by weight anhydrous piroxicam

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Piroxicam is a non-steroid 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.

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 the underlying muscle or synovial fluid. In addition, equilibrium between the 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 fourth day. On an average, steady state plasma levels were between 300 ng/ml 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.

Preclinical Safety Data
Subacute and chronic toxicity studies have been carried out in rats, mice, dogs, and monkeys, using oral doses which ranged from 0.3 mg/kg/day to 25 mg/kg/day.

Non-clinical data show effects typical of a non-cox-selective NSAID; namely, renal papillary necrosis and gastrointestinal lesions. With regard to the latter, the monkey proved to be quite resistant to this effect and the dog unusually sensitive. 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 oral dosing, and as noted in section **Pharmacokinetic Properties**, equilibrium plasma levels of piroxicam obtained in patients using the topical gel are only approximately 5% of those achieved using an equivalent dose of oral product.

Acute and chronic toxicity and irritation has additionally been studied using the dermal product. 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 the application of 0.5% gel or the vehicle to intact rabbit skin. One abraded skin, piroxicam gel produced slight erythema and edema was slightly greater than that following vehicle.

The anti-inflammatory and analgesic effects of piroxicam 0.5% Gel were studied in rats and guinea pigs using standard models of pain and inflammation, such as carrageenan induced rat paw edema, ultraviolet erythema on guinea pigs, traumatic edema in rats, yeast induced pain in rats, croton oil induced erythema on guinea pigs abdomens, cotton pellet induced granuloma formation in rats and adjuvant induced arthritis in rats. Piroxicam 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 topical is a non-steroidal 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 non-steroidal anti-inflammatory agents has been associated with an increased incidence of dystocia and delayed parturition in pregnant animals when drug administration is continued into late pregnancy. Non-steroidal anti-inflammatory drugs are also known to induce closure of the ductus arteriosus in infants.

INDICATIONS

Piroxicam 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.

CONTRAINDICATIONS

1. Piroxicam 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 acetyl salicylic acid and other non-steroidal anti-inflammatory drugs (NSAIDs).
2. Piroxicam topical should not be given to patients in whom acetyl salicylic acid and other non-steroidal anti-inflammatory drugs induce the symptoms of asthma, rhinitis, angioedema or urticaria.

SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE

Life-threatening cutaneous reactions, 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 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 (see section **UNDESIRABLE EFFECTS**).

If local irritation develops, the use of piroxicam 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.

Interactions with Other Medicaments and Other Forms of Interactions
None known.

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

There are no studies of the use of topical piroxicam in pregnant women. Studies in animals have shown reproductive toxicity with systemic formulations (see section **Preclinical Safety Data**), 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 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
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. Piroxicam topical is not recommended for use in nursing mothers as the clinical safety has not been established.

Effects on Ability to Drive and Use Machines
None known.

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: fixed drug eruption, contact dermatitis, eczema and photosensitivity skin reactions.

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

OVERDOSAGE

Overdosage is unlikely to occur with this topical preparation.

POSOLOGY 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.

SUPPLY

FELDENE 0.5% Gel is available in tubes of 15 g and 25 g, Reg. No. DKL8819801828A1

FOR EXTERNAL USE ONLY

HARUS DENGAN RESEP DOKTER

STORE IN DRY PLACE AT TEMPERATURE BELOW 30°C.

Shelf-life: 5 years.

Manufactured by:
PT. Pfizer Indonesia
Jakarta, Indonesia

Leaflet kemasan: Informasi bagi pengguna

FELDENE 0,5% Gel

Piroksikam

Baca semua bagian leaflet ini dengan cermat sebelum mulai menggunakan obat ini karena berisi informasi penting untuk Anda.
- Simpan leaflet ini. Anda mungkin perlu membacanya kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, apoteker, atau perawat Anda.
- Obat ini telah diresepkan hanya untuk Anda. Jangan berikan kepada orang lain. Obat ini dapat membahayakan mereka, sekali pun gejala-gejala penyakit mereka sama dengan Anda.
- Jika Anda mengalami efek samping apa pun, berkonsultasilah dengan dokter, apoteker, atau perawat Anda. Ini termasuk segala kemungkinan efek samping yang tidak tercantum di dalam leaflet ini. Lihat bagian 8.

Isi leaflet ini:

1. Nama produk

FELDENE

2. Deskripsi produk

FELDENE adalah zat antiinflamasi nonsteroid yang juga memiliki khasiat analgesik dan antipiretik.

3. Apa kandungan obat ini?

Bahan aktif: piroksikam anhidrat

4. Kekuatan obat

Gel: 0,5% (5 mg per gram gel) berdasarkan berat piroksikam anhidrat

5. Apa kegunaan obat ini?

FELDENE topikal diindikasikan untuk berbagai kondisi yang ditandai oleh rasa nyeri dan peradangan, seperti osteoartritis (artrosis, penyakit sendi degeneratif), gangguan muskuloskeletal pascatrauma atau akut, termasuk tendinitis, tenosinovitis, periartritis, keseleo, cedera otot, dan nyeri punggung bawah.

6. Berapa banyak dan seberapa sering Anda seharusnya menggunakan obat ini?

Gunakan obat ini tepat sesuai anjuran dokter atau apoteker Anda. Tanyakan kepada dokter atau apoteker jika Anda merasa tidak yakin.

Feldene Gel hanya untuk penggunaan eksternal pada kulit.

Tusuk tube menggunakan tutupnya dalam posisi dibalik kemudian menekannya untuk melubangi segel tube.

Oleskan 1 gram Gel pada bagian yang sakit. Gosok Gel hingga meresap ke dalam kulit. Lakukan hal ini tiga atau empat kali sehari. Jika gejala tidak mereda, beri tahu dokter Anda. Jika gel tidak digosok hingga benar-benar meresap, maka dapat menimbulkan noda ringan yang bersifat sementara pada kulit dan pakaian.

Jangan menggosokkan obat pada kulit yang bermasalah, misalnya pada kulit yang luka, tergores, infeksi, atau dermatitis. Jangan oleskan di dekat mata, hidung, mulut, alat kelamin, atau area anus. Jika Gel mengenai area tersebut di atas, segera bilas dengan air.

Jangan menutupi bagian tubuh yang sudah digosok dengan Feldene Gel menggunakan perban atau pembalut.

Pasang kembali tutupnya dan cuci tangan Anda selalu setelah menggunakan FELDENE Gel.

7. Kapan seharusnya Anda tidak menggunakan obat ini?

FELDENE tidak diindikasikan untuk pasien yang mengalami kondisi berikut ini:
- Hipersensitivitas yang diketahui terhadap piroksikam atau komponen apa pun yang ada dalam obat.
- Jika sebelumnya Anda menunjukkan gejala-gejala asma, rinitis, angioedema, atau urtikaria yang disebabkan oleh aspirin dan obat-obatan antiinflamasi nonsteroid lainnya.

8. Efek yang tidak diinginkan

Seperti semua obat-obatan yang ada, obat ini bisa menimbulkan efek samping, meskipun tidak semua orang mengalaminya.

Segera beri tahu dokter Anda dan hentikan penggunaan Feldene Gel jika Anda mengalami gejala-gejala berikut setelah mengoleskan obat ini.

- Ruam kulit yang berpotensi mengancam jiwa (reaksi obat dengan gejala eosinofilia dan sistemik (Sindrom DRESS), sindrom Stevens-Johnson, nekrolisis epidermal toksik).
- Kulit memerah, ruam, dan/atau gatal-gatal pada bagian tempat Anda menggosokkan Feldene Gel (misalnya eksim, dermatitis kontak).
- Erupsi obat menetap (dapat terlihat seperti bercak bulat atau lonjong yang memerah dan membengkak pada kulit).
- Kulit bereaksi terhadap matahari.
- Perubahan warna kulit sementara dan noda pada pakaian.

Efek ini akan mereda jika Anda berhenti menggunakan Feldene Gel. Jika ketidaknyamanan berlanjut, beri tahu dokter atau apoteker Anda.

Melaporkan efek samping

Jika Anda mengalami efek samping apa pun, berkonsultasilah dengan dokter, apoteker, atau perawat Anda. Ini termasuk segala kemungkinan efek samping yang tidak tercantum di dalam leaflet ini. Dengan melaporkan efek samping, Anda dapat membantu memberikan lebih banyak informasi perihal keamanan obat ini.

9. Apa saja obat lain atau makanan yang harus dihindari selama menggunakan obat ini?

Beri tahu dokter, apoteker, atau perawat jika Anda sedang menggunakan atau baru-baru ini menggunakan obat lain, termasuk obat yang diperoleh tanpa resep dokter. Jika Anda menerima pengobatan dari dokter, perawat, atau petugas kesehatan yang berkualifikasi, pastikan mereka mengetahui bahwa Anda sedang menggunakan FELDENE.

10. Apa yang harus dilakukan jika ada dosis terlewat?

Jika Anda lupa menggunakan Feldene Gel, gunakan segera saat Anda teringat kecuali jika sudah masuk jadwal untuk pengolesan berikutnya. Jangan menggandakan jumlahnya untuk menggantikan jadwal pengolesan yang terlewat.

11. Bagaimana cara menyimpan obat ini?

- Jauhkan dari jangkauan dan penglihatan anak-anak.
- Simpan di tempat kering di bawah suhu 30 °C.
- Jangan gunakan FELDENE Gel setelah tanggal kadaluwarsa.
- Dilarang membuang obat-obatan melalui saluran air limbah atau bersama sampah rumah tangga. Tanyakan kepada apoteker cara membuang obat yang sudah tidak dibutuhkan. Langkah-langkah ini akan membantu melindungi lingkungan.

12. Tanda-tanda dan Gejala-gejala overdosis

Efek samping mana pun yang disebutkan di atas mungkin terjadi.

13. Apa yang harus dilakukan jika Anda menggunakan lebih dari dosis yang dianjurkan?

Beri tahu dokter, apoteker, atau perawat jika Anda mengalami kelebihan dosis.

Jika tanpa sengaja obat tertelan dalam jumlah yang banyak, segera beri tahu dokter Anda, atau hubungi unit gawat darurat di rumah sakit terdekat.

14. Apa saja yang perlu diperhatikan saat menggunakan obat ini?

Ruam kulit yang berpotensi mengancam jiwa (reaksi obat dengan gejala eosinofilia dan sistemik (Sindrom DRESS), sindrom Stevens-Johnson, nekrolisis epidermal toksik) telah dilaporkan berkenaan dengan penggunaan piroksikam, yang awalnya terlihat seperti bintik-bintik kemerahan menyerupai sasaran tembak atau bercak-bercak lingkaran kemerahan yang sering kali dengan lepuh di bagian tengah pada badan.

Tanda-tanda tambahan yang perlu diperhatikan meliputi ulkus di mulut, tenggorokan, hidung, alat kelamin, dan konjungtivitis (mata merah dan bengkak).

Ruam kulit yang berpotensi mengancam jiwa ini sering kali disertai dengan gejala menyerupai flu. Ruam dapat berkembang menjadi lepuh yang menyebar luas atau pengelupasan kulit.

Risiko tertinggi terjadinya reaksi kulit serius adalah dalam minggu-minggu pertama pengobatan.

Jika Anda pernah mengalami sindrom Stevens-Johnson atau nekrolisis epidermal toksik saat menggunakan piroksikam, berarti Anda sama sekali tidak boleh menggunakan piroksikam kembali.

Jika Anda mengalami ruam atau gejala kulit ini, Anda harus segera berhenti menggunakan Feldene Gel, segera minta saran dari dokter dan beri tahu mereka bahwa Anda sedang menggunakan obat ini.

OAINS, termasuk Feldene Gel, dapat menyebabkan kerusakan ginjal atau gagal ginjal.

Jika Anda sedang hamil atau menyusui, atau berencana untuk hamil, konsultasikan dengan dokter Anda sebelum menggunakan FELDENE.

15. Kapan sebaiknya Anda berkonsultasi dengan dokter?

Jika Anda memiliki pertanyaan lebih lanjut atau Anda mengalami kondisi yang sama seperti yang tercantum dalam brosur ini, konsultasikan dengan dokter, apoteker, atau perawat Anda.

16. Nama/logo produsen/importir/Pemegang Hak Pemasaran

Diproduksi oleh:
PT Pfizer Indonesia, Jakarta

HANYA UNTUK PEMAKAIAN LUAR

HARUS DENGAN RESEP DOKTER

FELDENE 0,5% Gel tersedia dalam kemasan tube 15 g dan 25 g, No. Reg. DKL8819801828A1

17. Tanggal revisi PIL

09/2021