PT. PFIZER INDONESIA
Local Product Document

Generic Name: Piroxicam
Trade Name: FELDENE
CDS Effective Date: February 17, 2022
Supersedes: November 01, 2019

FDDF

Cardiovascular Risk

- NSAIDs may cause an increased risk of serious cardiovascular (CV) thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with CV disease or risk factors for CV disease may be at greater risk (see section **SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

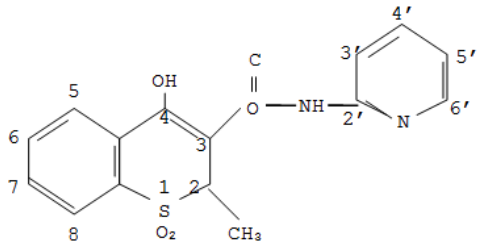
- FELDENE is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery (see section **SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

Gastrointestinal Risk

- NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events (see section **SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

DESCRIPTION

FELDENE, brand of piroxicam, is a member of the chemical class of non-steroidal anti-inflammatory agents, N-heterocyclic carboxamides of 1,2-benzothiazine-1,1-dioxide. Piroxicam is an amphoteric compound. It exhibits a weakly acidic 4-hydroxy proton (pKa 5.1) and a weakly basic pyridiyl nitrogen (pKa 1.8) as determined by ultraviolet absorption spectrophotometry in methanol-water (2.5/97.5, v/v) solvent medium. It occurs as a white to off-white crystalline solid, poorly soluble in water, dilute acid and most organic solvents. It is slightly soluble in alcohols and in aqueous alkaline solution.



FELDENE is available as:
Fast dissolving dosage form (FDDF), containing 20 mg of piroxicam with the following inert ingredients: aspartame, citric acid, gelatin, and mannitol.

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMIC PROPERTIES

FELDENE is a non-steroidal anti-inflammatory agent, which also possesses analgesic and antipyretic properties. Edema, erythema, tissue proliferation, fever, and pain can all be inhibited in laboratory animals by the administration of FELDENE. It is effective regardless of the etiology of the inflammation. While its mode of action is not fully understood, independent studies *in vitro* as well as *in vivo* have shown that piroxicam interacts at several steps in the immune and inflammation responses through:

* Inhibition of prostanoid synthesis, including prostaglandins, through a reversible inhibition of the cyclooxygenase enzyme.
* Inhibition of neutrophil aggregation.
* Inhibition of polymorphonuclear cell and monocyte migration to the area of inflammation.
* Inhibition of lysosomal enzyme release from stimulated leucocytes.
* Inhibition of superoxide anion generation by the neutrophil.
* Reduction of both systemic and synovial fluid rheumatoid factor production in patients with seropositive rheumatoid arthritis.

It is established that piroxicam does not act by pituitary-adrenal axis stimulation. *In vitro* studies have not revealed any negative effects on cartilage metabolism.

PHARMACOKINETIC PROPERTIES

Absorption

FELDENE is well absorbed following oral administration. With food, there is a slight delay in the rate but not the extent of absorption following oral administration. Stable plasma concentrations are maintained throughout the day on once-daily dosage. Continuous treatment

with 20 mg/day for periods of 1 year produces similar blood levels to those seen once steady state first is achieved.

Drug plasma concentrations are proportional for 20 mg doses and generally peak within three to five hours after administration. A single 20 mg dose generally produces peak piroxicam plasma levels of 1.5 to 2 mcg/ml while maximum drug plasma concentrations, after repeated daily ingestion of 20 mg piroxicam, usually stabilize at 3 to 8 mcg/ml. Most patients approximate steady state plasma levels within 7 to 12 days.

Treatment with a loading dose regimen of 40 mg daily for the first two days followed by 20 mg daily thereafter allows a high percentage (approximately 76%) of steady state levels to be achieved immediately following the second dose. Steady state levels, area under the curves and elimination half-life are similar to that following a 20 mg daily dose regimen.

Elimination/Biotransformation

FELDENE is extensively metabolized and less than 5% of the daily dose is excreted unchanged in urine and feces. Piroxicam metabolism is predominantly mediated via cytochrome P450 CYP-2C9 in the liver. One important metabolic pathway is hydroxylation of the pyridyl ring of the FELDENE side chain, followed by conjugation with glucuronic acid and urinary elimination. The plasma half-life is approximately 50 hours in man.

Patients who are known or suspected to be poor CYP2C9 metabolizers based on previous history/experience with other CYP2C9 substrates should be administered piroxicam with caution as they may have abnormally high plasma levels due to reduced metabolic clearance (see section **SPECIAL WARNINGS AND PRECAUTIONS FOR USE**, **Poor Metabolizers of CYP2C9 Substrates**).

Pharmacogenetics

CYP2C9 activity is reduced in individuals with genetic polymorphisms, such as the CYP2C9*2 and CYP2C9*3 polymorphisms. Limited data from two published reports showed that subjects with heterozygous CYP2C9*1/*2 (n=9), heterozygous CYP2C9*1/*3 (n=9), and homozygous CYP2C9*3/*3 (n=1) genotypes showed 1.7-, 1.7-, and 5.3-fold higher piroxicam systemic levels, respectively, than the subjects with CYP2C9*1/*1 (n=17, normal metabolizer genotype) following administration of an oral single dose. The mean elimination half-life values of piroxicam for subjects with CYP2C9*1/*3 (n=9) and CYP2C9*3/*3 (n=1) genotypes were 1.7- and 8.8-fold higher than subjects with CYP2C9*1/*1 (n=17). It is estimated that the frequency of the homozygous*3/*3 genotype is 0% to 5.7% in various ethnic groups.

Preclinical Safety Data

Subacute and chronic toxicity studies have been carried out in rats, mice, dogs, and monkeys, using doses which ranged from 0.3 mg/kg/day to 25 mg/kg/day. The latter dose is approximately 90 times the recommended human dose level. The only pathology seen was that characteristically associated with the animal toxicology of non-steroidal anti-inflammatory agents; 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.

THERAPEUTIC INDICATIONS

FELDENE is a non-steroidal anti-inflammatory drug indicated for a variety of conditions requiring anti-inflammatory activity, such as rheumatoid arthritis, osteoarthritis (arthrosis, degenerative joint disease), ankylosing spondylitis, acute musculoskeletal disorders and acute gout.

Dosage recommendations for use in children have not been established.

CONTRAINDICATIONS

Piroxicam is contraindicated in:

Patients with a history of gastrointestinal ulceration, bleeding or perforation.

Patients with active peptic ulcerations or a history of recurrent ulceration.

Patients with known hypersensitivity to piroxicam or to any of the excipients. The potential exists for cross sensitivity to aspirin and other non-steroidal anti-inflammatory drugs. FELDENE should not be given to patients in whom aspirin and other non-steroidal anti-inflammatory drugs induce the symptoms of asthma, nasal polyps, angioedema or urticaria.

Treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.

Patients with severe renal and hepatic failure.

Patients with severe heart failure.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

The use of piroxicam with concomitant systemic non-aspirin NSAIDs including cyclooxygenase 2 (COX-2) inhibitors should be avoided. Concomitant use of a systemic NSAID and another systemic NSAID may increase frequency of gastrointestinal ulcers and bleeding.

Cardiovascular Effects
NSAIDs may cause an increased risk of serious CV thrombotic events, myocardial infarction, and stroke, which can be fatal. All NSAIDs, both COX-2 selective and non-selective, may have a similar risk. This risk may increase with duration of use. The relative increase of this risk appears to be similar in those with or without known CV disease or CV risk factors. However, patients with known CV disease or CV risk factors may be at greater risk in terms of absolute incidence, due to their increased rate at baseline. To minimize the potential risk for an adverse CV event in patients treated with piroxicam, the lowest effective dose should be used for the shortest duration possible.

Physicians and patients should remain alert for the development of such events, even in the absence of previous CV symptoms. Patients should be informed about the signs and/or symptoms of serious CV toxicity and the steps to take if they occur (see section **CONTRAINDICATIONS**).

There is no consistent evidence that concurrent use of acetyl salicylic acid mitigates the increased risk of serious CV thrombotic events associated with NSAID use. The concurrent use of acetyl salicylic acid and an NSAID does increase the risk of serious GI events (see section **SPECIAL WARNINGS AND PRECAUTIONS FOR USE, Gastrointestinal (GI) Effects - Risk of GI Ulceration, Bleeding, and Perforation**).

Two large, controlled, clinical trials of a COX-2 selective NSAID for the treatment of pain in the first 10-14 days following CABG surgery found an increased incidence of myocardial infarction and stroke (see section **CONTRAINDICATIONS).**

Fluid Retention and Edema
As with other drugs known to inhibit prostaglandin synthesis, fluid retention and edema have been observed in some patients taking NSAIDs, including piroxicam. Therefore, piroxicam should be used with caution in patients with compromised cardiac function and other conditions pre-disposing to, or worsened by, fluid retention. Patients with pre-existing congestive heart failure or hypertension should be closely monitored.

Hypertension
NSAIDs, including FELDENE can lead to onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of CV events. Patients taking thiazides or loop diuretics may have impaired response to these therapies when taking NSAIDs. NSAIDs, including FELDENE, should be used with

caution in patients with hypertension. Blood pressure (BP) should be monitored closely during the initiation of NSAID treatment with FELDENE and throughout the course of therapy.

Gastrointestinal (GI) Effects - Risk of GI Ulceration, Bleeding, and Perforation
NSAIDs, including piroxicam, can cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the stomach, small intestine, or large intestine, which can be fatal. Administration of doses of greater than 20 mg per day carries an increased risk of gastrointestinal side effects. Evidence from observational studies suggests that piroxicam may be associated with a high risk of serious gastrointestinal toxicity, relative to other NSAIDs.

These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with NSAIDs. Only one in five patients, who develop a serious upper GI adverse event on NSAID therapy, is symptomatic. Upper GI ulcers, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3-6 months, and in about 2%-4% of patients treated for one year. These trends with longer duration of use, increasing the likelihood of developing a serious GI event at some time during the course of therapy. However, even short-term therapy is not without risk.

NSAIDs should be prescribed with extreme caution in patients ingesting alcohol or patients with a prior history of ulcer disease or gastrointestinal bleeding. Patients with a prior history of ulcer disease and/or gastrointestinal bleeding and who use NSAIDs, have a greater than 10-fold higher risk for developing a GI bleed compared to patients with neither of these risk factors. Other factors that increase the risk for GI bleeding in patients treated with NSAIDs include concomitant use of corticosteroids, antiplatelet drugs (such as aspirin), selective serotonin reuptake inhibitors or anticoagulants, longer duration of NSAID therapy, smoking, use of alcohol, older age, and poor general health status. Most spontaneous reports of fatal GI events are in the elderly or debilitated patients, and therefore, special care should be taken in treating this population.

To minimize the potential risk for an adverse GI event, in patients treated with NSAIDs, the lowest effective dose should be used for the shortest possible duration. Patients and physicians should remain alert for signs and symptoms of GI ulceration and bleeding during NSAID therapy and promptly initiate additional evaluation and treatment if a serious GI adverse event is suspected. This should include discontinuation of the NSAID until a serious GI adverse event is ruled out. For high-risk patients, alternate therapies that do not involve NSAIDs should be considered.

FELDENE should be withdrawn if peptic ulceration or gastrointestinal bleeding occurs.

Renal Effects

In rare cases, NSAIDS may cause interstitial nephritis, glomerulitis, papillary necrosis and the nephrotic syndrome. NSAIDS inhibit the synthesis of renal prostaglandin which plays a supportive role in the maintenance of renal perfusion in patients whose renal blood flow and blood volume are decreased. In these patients, administration of an NSAID may precipitate overt renal decompensation which is typically followed by recovery to pre-treatment state upon discontinuation of NSAID therapy. Patients at greatest risk of such a reaction are those with congestive heart failure, liver cirrhosis, nephrotic syndrome and overt renal disease. Such patients should be carefully monitored while receiving non-steroidal anti-inflammatory drug therapy.

Caution should be used when initiating treatment with piroxicam in patients with severe dehydration. Caution is also recommended in patients with kidney disease (see section **CONTRAINDICATIONS**).

Because of extensive renal excretion of piroxicam and its biotransformation products, lower doses of piroxicam should be considered in patients with impaired renal function, and they should be carefully monitored (see section **CONTRAINDICATIONS** and section ***PHARMACOKINETIC PROPERTIES***).

Hepatic Effects
Piroxicam can cause fatal hepatitis and jaundice. Although such reactions are rare, if abnormal liver function tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), piroxicam should be discontinued.

Skin Reactions
Serious skin reactions, some of them fatal, including drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs, including piroxicam. Patients appear to be at highest risk for these events early in the course of therapy, the onset of the event occurring in the majority of cases within the first month of treatment. Piroxicam should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

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**).

Ophthalmologic Effects
Because of reports of adverse eye findings with non-steroidal anti-inflammatory drugs, it is recommended that patients who develop visual complaints during treatment with FELDENE have an ophthalmic evaluation.

Poor Metabolizers of CYP2C9 Substrates
Patients who are known or suspected to be poor CYP2C9 metabolizers based on previous history/experience with other CYP2C9 substrates should be administered piroxicam with caution as they may have abnormally high plasma levels due to reduced metabolic clearance (see section ***PHARMACOKINETIC PROPERTIES***, *Pharmacogenetics*).

Use with Oral Anticoagulants
The concomitant use of NSAIDs, including piroxicam, with oral anticoagulants increases the risk of GI and non-GI bleeding and should be given with caution. Oral anticoagulants include warfarin/coumarin-type and novel oral anticoagulants (e.g., apixaban, dabigatran, rivaroxaban). Anticoagulation/INR should be monitored in patients taking a warfarin/coumarin-type anticoagulant (see section **INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION**).

General
For patients with phenylketonuria: because of its aspartame content, FELDENE FDDF contains phenylalanine 0.070 mg and 0.140 mg per 10 mg dose and 20 mg dose, respectively.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Non-steroidal anti-inflammatory drugs may cause sodium, potassium and fluid retention, and may interfere with the natriuretic action of diuretic agents. These properties should be kept in mind when treating patients with compromised cardiac function or hypertension since they may be responsible for a worsening of those conditions.

Cardiac glycosides (digoxin and digitoxin):
NSAIDs may exacerbate cardiac failure, reduce glomerular filtration rate (GFR) and increase plasma glycoside levels. Concomitant administration of digoxin or digitoxin had no effect on the plasma levels of piroxicam or either drug.

Bleeding has been reported rarely when FELDENE has been administered to patients on coumarin type anticoagulants. Patients should be monitored closely if FELDENE and oral anticoagulants are administered together.

FELDENE, like other non-steroidal anti-inflammatory drugs, decreases platelet aggregation and prolongs bleeding time. This effect should be kept in mind when bleeding times are determined.

As with other non-steroidal anti-inflammatory drugs, the use of FELDENE in conjunction with acetylsalicylic acid or the concomitant use of two NSAIDs is not recommended because

data are inadequate to demonstrate that the combination produces greater improvement than that achieved with the drug alone and the potential for adverse reactions is increased.

Studies in man have shown that the concomitant administration of FELDENE and acetylsalicylic acid resulted in a reduction of plasma levels of piroxicam to about 80% of the normal values. Concomitant administration of antacids had no effect on piroxicam plasma levels. Neither did concurrent therapy with FELDENE and digoxin or FELDENE and digitoxin affect the plasma levels of either drug.

Piroxicam interferes with the antiplatelet effect of low-dose aspirin, and thus may interfere with aspirin's prophylactic treatment of CV disease.

Anti-hypertensives including diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II antagonists (AIIA and beta-blockers):
NSAIDs can reduce the efficacy of diuretics and other anti-hypertensive drugs including ACE inhibitors, AIIA and beta-blockers. In patients with impaired renal function (e.g., dehydrated patients or elderly patients with the renal function compromised), the co-administration of an ACE inhibitor or an AIIA and/or diuretics with a cyclo-oxygenase inhibitor can increase the deterioration of the renal function, including the possibility of acute renal failure, which is usually reversible.

The occurrence of these interactions should be considered in patients taking piroxicam with an ACE inhibitor or an AIIA and/or diuretics. Therefore, the concomitant administration of these drugs should be done with caution, especially in elderly patients. Patients should be adequately hydrated and the need to monitor the renal function should be assessed in the beginning of the concomitant treatment and periodically thereafter.

Cholestyramine:
Cholestyramine has been shown to enhance the oral clearance and decrease the half-life of piroxicam. To minimize this interaction, it is prudent to administer piroxicam at least 2 hours before or 6 hours after cholestyramine.

Corticosteroids:
Increased risk of gastrointestinal ulceration or bleeding.

Cyclosporine:
Increased risk of nephrotoxicity.

Methotrexate:
When methotrexate is administered concurrently with NSAIDs, including piroxicam, NSAIDs may decrease elimination of methotrexate resulting in increased plasma levels of

methotrexate. Caution is advised, especially in patients receiving high doses of methotrexate.

Tacrolimus:
Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

Lithium and other protein-bound agents:
FELDENE is highly protein-bound, and therefore, might be expected to displace other protein-bound drugs. The physician should closely monitor patients for change in dosage requirements when administering FELDENE to patients on highly protein-bound drugs. NSAIDs, including FELDENE, have been reported to increase steady-state plasma lithium levels. It is recommended that these levels are monitored when initiating, adjusting and discontinuing FELDENE.

Cimetidine:
Results of two separate studies indicate a slight increase in absorption of piroxicam following cimetidine administration but no significant changes in elimination parameters. Cimetidine increases the area under the curve ($AUC_{0\text{-}120\ hours}$) and C_{max} of piroxicam by approximately 13% to 15%. Elimination rate constants and half-life show no significant differences. The small but significant increase in absorption is unlikely to be clinically significant.

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
Although no teratogenic effects were seen in animal testing, the use of FELDENE during pregnancy is not recommended. FELDENE 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 was continued into late pregnancy. Non-steroidal anti-inflammatory drugs are also known to induce premature closure of the ductus arteriosus in infants. Therefore, piroxicam should be avoided during the third trimester of pregnancy.

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.

If used during second or third trimester of pregnancy, NSAIDs may cause fetal renal dysfunction which may result in reduction of amniotic fluid volume or oligohydramnios in severe cases. Such effects may occur shortly after treatment initiation and are usually reversible upon discontinuation. Pregnant women on piroxicam should be closely monitored for amniotic fluid volume.

Lactation
The presence of piroxicam in breast milk has been determined during initial and long term dosing conditions (52 days). Piroxicam appeared in breast milk at about 1% to 3% of the maternal plasma concentration. No accumulation of piroxicam occurred in milk relative to that in plasma during treatment. FELDENE is not recommended for use in nursing mothers, as the clinical safety has not been established.

Effects of Ability to Drive and Use Machines

Not applicable to this type of product.

UNDESIRABLE EFFECTS

FELDENE is generally well tolerated. Gastrointestinal symptoms are the most commonly encountered side effects but in most instances do not interfere with the course of therapy. These adverse reactions include stomatitis, anorexia, epigastric distress, nausea, constipation, abdominal discomfort, flatulence, diarrhea, abdominal pain, and indigestion. Gastrointestinal bleeding, perforation and ulceration (see section **SPECIAL WARNINGS AND PRECAUTIONS FOR USE**) have been reported with FELDENE.

Objective evaluations of gastric mucosal appearances and intestinal blood loss show that 20 mg/day of FELDENE administered either in single or divided daily doses is significantly less irritating to the gastrointestinal tract than acetylsalicylic acid.

The following table lists adverse drug reactions (ADRs) within each standard System Organ Class (SOC) by decreasing order of medical seriousness or clinical importance.

Table 1. Adverse Drug Reactions (ADRs) by System Organ Class (SOC) and Council for International Organizations of Medical Science (CIOMS) Frequency Category Listed in Order of Decreasing Medical Seriousness or Clinical Importance Within Each Frequency Category and SOC

System Organ Class	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1,000 to < 1/100	Rare ≥ 1/10,000 to < 1/1,000	Frequency not known (cannot be estimated from the available data)
Blood and lymphatic system disorders				Aplastic anaemia* Haemolytic anaemia* Anaemia* Eosinophilia* Leucopenia* Thrombocytopenia*
Immune system disorders				Anaphylaxis* Serum sickness*
Metabolism and nutrition disorders	Anorexia			Hyperglycaemia* Hypoglycaemia* Fluid retention*
Psychiatric disorders				Depression* Hallucinations* Mental confusion* Mood alterations* Insomnia* Nervousness* Dream abnormalities*
Nervous system disorders	Headache Dizziness Somnolence Vertigo			Aseptic meningitis* Paraesthesia*
Eye disorders		Blurred vision		Eye irritation* Swollen eyes*
Ear and labyrinth disorders	Tinnitus			Hearing impairment*
Cardiac disorders		Palpitations		
Vascular disorders				Vasculitis* Hypertension*
Respiratory, thoracic and mediastinal disorders				Bronchospasm* Dyspnoea* Epistaxis*

System Organ Class	**Common ≥ 1/100 to < 1/10**	**Uncommon ≥ 1/1,000 to < 1/100**	**Rare ≥ 1/10,000 to < 1/1,000**	**Frequency not known (cannot be estimated from the available data)**
Gastrointestinal disorders	Epigastric distress Nausea Constipation Abdominal discomfort Flatulence Abdominal pain Diarrhoea Indigestion Vomiting	Stomatitis		Perforation* Ulceration* Pancreatitis* Gastrointestinal bleeding (including hematemesis and melena)* Gastritis* Ano-rectal reactions to suppositories presenting as local pain, burning, pruritus and tenesmus and rare instances of rectal bleeding*
Hepatobiliary disorders				Fatal hepatitis* Jaundice*

System Organ Class	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1,000 to < 1/100	Rare ≥ 1/10,000 to < 1/1,000	Frequency not known (cannot be estimated from the available data)
Skin and subcutaneous tissue disorders	Skin rash Pruritis			Angioedema* Stevens-Johnson syndrome* Toxic epidermal necrolysis (Lyell's disease)* Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome)* Vesiculo bullous reactions* Dermatitis exfoliative* Erythema multiforme* Photoallergic reactions* Fixed drug eruption* Non-thrombocytopenic purpura (Henoch-Schoenlein)* Onycholysis* Alopecia* Urticaria*
Renal and urinary disorders				Renal failure* Nephrotic syndrome* Glomerulonephritis* Interstitial nephritis*
Reproductive system and breast disorders				Female fertility decreased*
General disorders and administration site conditions	Edema (mainly of the ankle)			

System Organ Class	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1,000 to < 1/100	Rare ≥ 1/10,000 to < 1/1,000	Frequency not known (cannot be estimated from the available data)
Investigations	Reversible elevations of BUN Decreases in hemoglobin and hematocrit unassociated with obvious gastrointestinal bleeding Increased serum transaminase levels Weight increase	Reversible elevations of creatinine		Positive ANA* Weight decrease*

* Adverse Drug Reaction (ADR) identified post-marketing
Abbreviations: BUN = blood urea nitrogen; ANA = antinuclear antibody.

OVERDOSE

In the event of acute overdosage with FELDENE, supportive and symptomatic therapy is indicated. There are no specific antidotes. Emesis and/or gastric lavage and/or activated charcoal may be considered dependent upon amount ingested and time since ingestion. Studies indicate that administration of activated charcoal may result in reduced absorption and re-absorption of piroxicam thus reducing the total amount of active drug available.

POSOLOGY AND METHOD OF ADMINISTRATION

Undesirable effects may be minimized by using the minimum effective dose for the shortest duration necessary to control symptoms.

Dosage

Rheumatoid Arthritis, Osteoarthritis (Arthrosis, Degenerative Joint Disease), Ankylosing Spondylitis
The recommended starting dose is 20 mg given as a single daily dose. The majority of patients will be maintained on 20 mg daily.

Acute Gout

Because of its GI safety profile (see sections **CONTRAINDICATIONS** and **SPECIAL WARNINGS AND PRECAUTIONS FOR USE**), piroxicam should not be used in first-line treatment for acute gout when an NSAID is indicated. For the same reason, it should not be used to treat acute gout in patients most at risk of developing serious GI adverse events (see section **SPECIAL WARNINGS AND PRECAUTIONS FOR USE**). Therapy should be initiated by a single dose of 40 mg, followed on the next 4 to 6 days with 40 mg daily, given in single or divided doses. FELDENE is not indicated for the long term management of gout.

Acute Musculoskeletal Disorders
Because of its GI safety profile (see sections **CONTRAINDICATIONS** and **SPECIAL WARNINGS AND PRECAUTIONS FOR USE**), piroxicam should not be used in first-line treatment for acute musculoskeletal disorders when an NSAID is indicated. For the same reason, it should not be used to treat acute musculoskeletal disorders in patients most at risk of developing serious GI adverse events (see section **SPECIAL WARNINGS AND PRECAUTIONS FOR USE**). Therapy should be initiated with 40 mg daily for the first two days given in single or divided doses. For the remainder of the 7 to 14 day treatment period, the dose should be reduced to 20 mg daily.

Usage in Children
Dosage recommendation for use in children has not been established.

Administration

Oral (Dispersible Tablets)

FELDENE dispersible tablets can be swallowed whole with a fluid, or may be dispersed in a minimum of 50 ml of water and then swallowed.

FELDENE FDDF should be placed on the tongue to disperse and then swallowed with the saliva. FELDENE FDDF dissolves almost instantly in the mouth in the presence of saliva.

SUPPLY

FELDENE Flash 20 mg, box of 3 envelopes @ 1 blister @ 10 fast dissolving tablets;
Reg. No. DKI 9584800681A1

STORE IN DRY PLACE BELOW 30°C

PRESCRIPTION ONLY.

HARUS DENGAN RESEP DOKTER

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Catalent UK Swindon Zydis Limited, United Kingdom

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