

Inflamatix

(Flurbiprofen)

انفلامیٹکس

COMPOSITION

Each **Inflamatix** 100mg tablet contains 100mg of flurbiprofen.

Each **Inflamatix** SR 200mg capsule contains 200mg of flurbiprofen as SR pellets.

CLINICAL PHARMACOLOGY

Pharmacodynamics

Flurbiprofen is a nonsteroidal anti-inflammatory drug that exhibits anti-inflammatory, analgesic, and antipyretic activities in animal models. The mechanism of action of flurbiprofen, like that of other nonsteroidal anti-inflammatory drugs, is not completely understood but may be related to prostaglandin synthesis inhibition.

Pharmacokinetics

Absorption: The mean oral bioavailability of flurbiprofen tablets 100 mg is 96% relative to an oral solution. Flurbiprofen is rapidly absorbed with peak plasma concentrations occurring at about 2 hours. Administration of flurbiprofen with either food or antacids may alter the rate but not the extent of flurbiprofen absorption.

Distribution: Both flurbiprofen enantiomers are more than 99% bound to plasma proteins, primarily albumin. Flurbiprofen is poorly excreted into human milk.

Metabolism: Several flurbiprofen metabolites have been identified in human plasma and urine. In vitro studies have demonstrated that cytochrome P450 2C9 plays an important role in the metabolism of flurbiprofen to its major metabolite, 4'-hydroxy-flurbiprofen. The 4'-hydroxy-flurbiprofen metabolite showed little anti-inflammatory activity in animal models of inflammation. Flurbiprofen does not induce enzymes that alter its metabolism.

Excretion: Following dosing with flurbiprofen, less than 3% is excreted unchanged in the urine, with about 70% of the dose eliminated in the urine as parent drug and metabolites. The mean terminal disposition half-lives (t_{1/2}) of R and S-flurbiprofen are similar, about 4.7 and 5.7 hours, respectively. There is little accumulation of flurbiprofen following multiple doses.

Special Populations

Pediatric: The pharmacokinetics of flurbiprofen has not been investigated in pediatric patients.

Geriatric: Flurbiprofen pharmacokinetics were similar in geriatric arthritis patients, younger arthritis patients, and young healthy volunteers receiving flurbiprofen tablets 100 mg as either single or multiple doses.

Hepatic insufficiency: Hepatic metabolism may account for >90% of flurbiprofen elimination, so patients with hepatic disease may require reduced doses of flurbiprofen compared to patients with normal hepatic function. Flurbiprofen plasma protein binding may be decreased in patients with liver disease and serum albumin concentrations below 3.1 g/dL.

Renal insufficiency: Elimination of flurbiprofen metabolites may be reduced in patients with renal impairment.

INDICATIONS AND USAGE

1. Rheumatoid arthritis and osteoarthritis
2. Dental pain
3. Dysmenorrhea
4. Ankylosing Spondylitis(Arthritis of the spine)
5. Swollen joints, frozen shoulder, bursitis(Inflammation of the bursa), tendinitis, tenosynovitis(Inflammation of the covering layer of tendons).
6. Low back pain, strain and sprain

DOSAGE AND ADMINISTRATION

As with other nonsteroidal anti-inflammatory drugs, the lowest dose should be sought for each patient. Therefore, after observing the response to initial therapy with **Inflamatix** tablets, the physician should adjust the dose and frequency to suit an individual patient's needs. The usual daily dose of **inflamatix** 100mg tablet is 200mg daily in divided dose. In patients with severe symptoms or disease of recent origin or during acute exacerbations, the total daily dosage may be increased to 300mg in divided dose. The usual daily dose of **Inflamatix** SR 200mg capsule is one capsule each evening, after food.

UNDESIRABLE EFFECTS

Gastrointestinal disorders: The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur. Nausea, vomiting, diarrhoea, dyspepsia, flatulence, constipation, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease have been reported following flurbiprofen administration. Less frequently, gastritis, has been observed. Pancreatitis has been reported very rarely.

Immune system disorders: Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of (a) non-specific allergic reactions and anaphylaxis, (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angioedema and, more rarely exfoliative and bullous dermatoses (including toxic epidermal necrolysis and erythema multiforme).

Cardiac disorders and Vascular disorders: Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.

Clinical trial and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with an increased risk of arterial thrombotic events (for example myocardial infarction or stroke).

Respiratory, thoracic and mediastinal disorders: Respiratory tract reactivity (asthma, bronchospasm, dyspnoea). Other adverse events reported less commonly and for which causality has not necessarily been established include:

Blood and lymphatic system disorders: Thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia and haemolytic anaemia.

Psychiatric disorders: Depression, confusional state & hallucination.

Nervous system disorders: Cerebrovascular accident, optic neuritis, headache, paraesthesia, dizziness, and somnolence. Aseptic meningitis (especially in patients with existing autoimmune disorders, such as systemic lupus erythematosus and mixed connective tissue disease) with symptoms of stiff neck, headache, nausea, vomiting, fever or disorientation.

Eye disorders: Visual disturbance.

Ear and labyrinth disorders: Tinnitus & vertigo.

Hepatobiliary disorders: Abnormal liver function, hepatitis and jaundice.

Skin and subcutaneous tissue disorders: Skin disorders including rash, pruritus, urticaria, purpura and very rarely, bullous dermatoses (including Stevens-Johnson syndrome, toxic epidermal necrolysis and erythema multiforme) and photosensitivity reaction.

Renal and urinary disorders: Toxic nephropathy in various forms, including interstitial nephritis, nephrotic syndrome and renal failure.

General disorders: Malaise & fatigue.

DRUG INTERACTIONS

Antacids: Administration of flurbiprofen to volunteers under fasting conditions or with antacid suspension yielded similar serum flurbiprofen-time profiles in young adult subjects (n=12).In geriatric subjects (n=7), there was a reduction in the rate but not the extent of flurbiprofen absorption.

Aspirin: Concurrent administration of flurbiprofen and aspirin resulted in 50% lower serum flurbiprofen concentrations. This effect of aspirin (which is also seen with other nonsteroidal anti-inflammatory drugs) has been demonstrated in patients with rheumatoid arthritis (n=15) and in healthy volunteers (n=16).

Beta-adrenergic blocking agents: Flurbiprofen pretreatment attenuated the hypotensive effect of a single dose of propranolol but not atenolol. Flurbiprofen did not appear to affect the beta-blocker- mediated reduction in heart rate. Flurbiprofen did not affect the pharmacokinetic profile of either drug.

Cimetidine, Ranitidine: In normal volunteers (n=9), pretreatment with cimetidine or ranitidine did not affect flurbiprofen pharmacokinetics, except for a small (13%) but statistically significant increase in the area under the serum concentration curve of flurbiprofen in subjects who received cimetidine.

Digoxin: In studies of healthy males (n=14), concomitant administration of flurbiprofen and Digoxin did not change the steady state serum levels of either drug.

Diuretics: Studies in healthy volunteers have shown that, like other nonsteroidal anti-inflammatory drugs, flurbiprofen can interfere with the effects of furosemide. Although results have varied from study to study, effects have been shown on furosemide-stimulated diuresis, natriuresis, and kaliuresis. Other nonsteroidal anti-inflammatory drugs that inhibit prostaglandin synthesis have been shown to interfere with thiazide and potassium-sparing diuretics.

Lithium: In a study of 11 women with bipolar disorder receiving lithium carbonate at a dosage of >0.2 mmol/L). Nonsteroidal anti-inflammatory drugs have also been reported to decrease the renal clearance of lithium by about 20%.

Oral Hypoglycemic Agents: In a clinical study, flurbiprofen was administered to adult diabetics who were already receiving glyburide (n=4), metformin (n=2), chlorpropamide with phenformin (n=3), or glyburide with phenformin (n=6). Although there was a slight reduction in blood sugar concentrations during concomitant administration of flurbiprofen and hypoglycemic agents, there were no signs or symptoms of hypoglycemia.

WARNINGS

Gastrointestinal (GI) Effects - Risk of GI Ulceration, Bleeding, and Perforation: Serious GI toxicity, such as inflammation, bleeding, ulceration, or perforation of the stomach, small intestine, or large intestine, can occur at any time, with or without warning symptoms, in patients treated with nonsteroidal anti-inflammatory drugs. Minor upper GI problems, such as dyspepsia, are common and may also occur at any time during therapy.

Anaphylactic Reactions: As with other nonsteroidal anti-inflammatory drugs, anaphylactic reactions may occur in patients without known prior exposure to flurbiprofen. If an anaphylactic reaction occurs, the patient should immediately seek emergency help.

Advanced Renal Disease: Treatment with flurbiprofen is not recommended in patients with advanced kidney disease. However, if therapy with a nonsteroidal anti-inflammatory drug must be initiated, close monitoring of the patient's kidney function is advisable.

PRECAUTIONS

General

Hepatic effects: Borderline elevations of one or more liver tests may occur in up to 15% of patients taking nonsteroidal anti-inflammatory drugs, including flurbiprofen. These laboratory abnormalities may progress, may remain unchanged, or may be transient with continuing therapy. Notable elevations of ALT or AST (approximately three or more times the upper limit of normal) have been reported in approximately 1% of patients in clinical trials with nonsteroidal anti-inflammatory drugs. In addition, rare cases of severe hepatic reactions have been reported, including jaundice, fulminant hepatitis, liver necrosis, and hepatic failure, some of them with fatal outcomes. A patient with symptoms and/or signs suggesting liver dysfunction, or with abnormal liver test values, should be evaluated for evidence of the development of a more severe hepatic reaction while on therapy with flurbiprofen. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (eg, eosinophilia, rash, etc.), flurbiprofen should be discontinued.

Renal effects: Caution should be used when initiating treatment with flurbiprofen in patients with considerable dehydration. It is advisable to rehydrate patients first and then start therapy. Caution is also recommended in patients with preexisting kidney disease as with other nonsteroidal anti-inflammatory drugs, long-term administration of flurbiprofen has resulted in renal papillary necrosis and other renal medullary changes. A second form of renal toxicity has been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of a nonsteroidal anti-inflammatory drug may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, or liver dysfunction, as well as those taking diuretics or ACE inhibitors, and the elderly. Discontinuation of nonsteroidal anti-inflammatory drug therapy is usually followed by recovery to the pretreatment state.

Hematological effects: Anemia is sometimes seen in patients receiving nonsteroidal anti-inflammatory drugs, including flurbiprofen. This may be due to fluid retention, GI blood loss, or an incompletely described effect upon erythropoiesis. Patients on long-term treatment with nonsteroidal anti-inflammatory drugs, including patients receiving flurbiprofen who may be adversely affected by alterations in platelet function, such as those with coagulation disorders or patients receiving anticoagulants, should be carefully monitored.

Fluid retention and edema: Fluid retention and edema have been observed in some patients taking nonsteroidal anti-inflammatory drugs. Flurbiprofen should be used with caution in patients with fluid retention, hypertension, or heart failure.

Preexisting asthma: flurbiprofen should not be administered to patients with aspirin sensitive asthma and should be used with caution in patients with preexisting asthma.

Vision changes: Blurred and/or diminished vision has been reported with the use of flurbiprofen and other nonsteroidal anti-inflammatory drugs. Patients experiencing eye complaints should have ophthalmologic examinations.

Laboratory Tests: Patients on long-term treatment with nonsteroidal anti-inflammatory drugs should have their complete blood count and chemistry profile checked periodically. If clinical signs and symptoms consistent with liver or renal disease develop, systemic manifestations occur (eg, eosinophilia, rash etc.), or abnormal liver tests persist or worsen, flurbiprofen should be discontinued.

Pregnancy: Teratogenic effects: Pregnancy Category C.

No developmental abnormalities were seen in reproductive studies conducted in mice and rabbits. However, animal reproduction studies are not always predictive of human response. There are no adequate and well-controlled studies in pregnant women.

Nonteratogenic effects: Because of the known effects of nonsteroidal anti-inflammatory drugs on the fetal cardiovascular system (closure of ductus arteriosus), use during late pregnancy should be avoided.

Nursing Mothers: Concentrations of flurbiprofen in breast milk and plasma of nursing mothers suggest that a nursing infant could receive approximately 0.10 mg flurbiprofen per day in the established milk of a woman taking flurbiprofen 200 mg/day. Because of possible adverse effects of prostaglandin-inhibiting drugs on neonates, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established.

Geriatric Use: Clinical experience with flurbiprofen suggests that elderly patients may have a higher incidence of gastrointestinal complaints than younger patients, including ulceration, bleeding, flatulence, bloating, and abdominal pain.

CONTRAINDICATIONS

Known hypersensitivity to flurbiprofen. Flurbiprofen should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other nonsteroidal anti-inflammatory drugs. Severe, rarely fatal, anaphylactic-like reactions to nonsteroidal anti-inflammatory drugs have been reported in such patients.

OVER DOSAGE

Symptoms following acute overdoses with nonsteroidal anti-inflammatory drugs are usually limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain, which are generally reversible with supportive care. Gastrointestinal bleeding can occur. Hypertension, acute renal failure, respiratory depression and coma may occur, but are rare. Anaphylactic reactions have been reported with therapeutic ingestion of nonsteroidal anti-inflammatory drugs, and may occur following an overdose. Patients should be managed by symptomatic and supportive care following overdose with a nonsteroidal anti-inflammatory drug. There are no specific antidotes. Emesis and/or activated charcoal (60 to 100 g in adults, 1 to 2 g/kg in children) and/or osmotic cathartic may be indicated in patients seen within 4 hours of ingestion with symptoms, or following a large overdose (5 to 10 times the usual dose). Forced diuresis, alkalization of urine, hemodialysis, or hemoperfusion may not be useful due to high protein binding.

PRESENTATION

Inflamatix 100mg tablets: 3x10's/pack.

Inflamatix SR 200mg capsules: 1x10's/pack.

Dosage:

As directed by the physician.

Instructions:

Store below 30°C.

Protect from sunlight & moisture.

Keep out of the reach of children.

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Detailed prescribing information is available on request.



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An ISO Certified Company

LFT/010/02

خوراک:

ڈاکٹر کی ہدایت کے مطابق۔

ہدایات:

دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

دھوپ اور نمی سے بچائیں۔

بچوں کی پہنچ سے دور رکھیں۔