

SCHEDULING STATUS: S3

Except when intended for the emergency treatment of acute gout attacks and when intended for the treatment of post-traumatic conditions such as inflammation, pain and swelling, for a maximum period of 5 days. **S2**

PROPRIETARY NAME (AND DOSAGE FORM):

K - F E N A K (Tablets)

COMPOSITION:

Each coated tablet contains 50 mg of diclofenac potassium.

PHARMACOLOGICAL CLASSIFICATION:

A 3.1 Antirheumatics (anti-inflammatory agents).

PHARMACOLOGICAL ACTION:

Diclofenac is a non-steroidal anti-inflammatory compound (NSAID) with analgesic, antipyretic and anti-inflammatory activities. It causes decreased formation of prostaglandins and thromboxanes through inhibition of the activity of the enzyme cyclo-oxygenase. Prostaglandins play a major role in the aetiology of inflammation, pain and fever and the inhibition of prostaglandin synthesis may have an important bearing on diclofenac's mechanism of action. Diclofenac inhibits platelet aggregation *in vitro*.

Pharmacokinetics:

Diclofenac is well absorbed after oral administration. Peak plasma concentrations are reached within approximately 1 hour. Administration with food slows the rate but does not alter the extent of absorption. There is a substantial first-pass effect (only 50 % of diclofenac is available systemically). Diclofenac is extensively bound to plasma proteins (99 %) and its plasma half-life is 1 to 2 hours. Diclofenac is metabolised in the liver by a cytochrome P450 isozyme of the CYP2C subfamily and excreted in the form of metabolites via the kidneys (approximately 60 %) and faeces (approximately 30 %). Less than 1 % is excreted in unchanged form.

INDICATIONS:

K-FENAK is indicated as short-term treatment in the following acute conditions:

- Painful musculoskeletal conditions;
- Acute attacks of gout;
- Painful post-operative and post-traumatic inflammation and swelling;
- Pain following dental surgery;
- Flare-up of osteoarthritis;
- Non-articular rheumatism;
- Classical migraine headaches;
- Symptomatic treatment of primary dysmenorrhoea.

CONTRA-INDICATIONS:

- Hypersensitivity to diclofenac or to any of the ingredients.
- Hypersensitivity to other NSAIDs including aspirin.
- Gastric or duodenal ulcer.
- Asthmatic patients in whom asthma attacks, acute rhinitis or urticaria are precipitated by acetylsalicylic acid or by other medicines which inhibit prostaglandin synthetase.
- Pregnancy (see "**PREGNANCY AND LACTATION**").
- Porphyria

WARNINGS:

Close medical surveillance and strict accuracy of diagnosis are imperative in patients with:

- a case history suggestive of, or, symptoms indicative of, gastrointestinal disease;
- ulcerative colitis;
- Crohn's disease;
- impaired hepatic function;
- pre-existing dyshaemopoiesis or disorders of blood coagulation.

K-FENAK should be used with caution in patients with renal or hepatic failure.

Concomitant use of **K-FENAK** and methotrexate could result in serious interactions (see "**INTERACTIONS**").

Acetylsalicylic acid / aspirin: The bioavailability of both **K-FENAK** and acetylsalicylic acid may be reduced if used concurrently.

INTERACTIONS:

Methotrexate:

Concurrent administration of methotrexate with **K-FENAK** may result in increased methotrexate toxicity (see "**WARNINGS**").

Lithium or digoxin:

Raised plasma concentrations of lithium or digoxin may occur if taken together with **K-FENAK**.

Glucocorticoids and other NSAIDs:

Gastrointestinal adverse effects may be exacerbated by the concomitant administration of **K-FENAK**. Concurrent treatment with two or more NSAIDs may increase the risk of adverse effects.

Antidiabetic medicines:

K-FENAK may cause both hypo- or hyperglycaemia. Dosage of antidiabetic medicines may need to be changed.

Anticoagulants:

There is an increased risk of haemorrhage if **K-FENAK** is used concurrently with any anticoagulants. Careful monitoring is necessary.

Ciclosporin:

Nephrotoxicity of ciclosporin may be increased by the effects of **K-FENAK** on renal prostaglandins.

Quinolone antibiotics:

Convulsions which may have been due to concomitant use of NSAIDs and quinolone antibiotics, have been reported in isolated cases.

PREGNANCY AND LACTATION:

Safety and efficacy in pregnancy and lactation has not been established.

Use of NSAIDs during the third trimester of pregnancy may result in premature closure of the ductus arteriosus in utero and may possibly lead to persistent pulmonary hypertension in the newborn. The onset of labour may be delayed and its duration longer (see "**CONTRA-INDICATIONS**").

DOSAGE AND DIRECTIONS FOR USE:

Adults:

Initial daily dose: 100 to 150 mg in two to three divided doses, with a maximum daily dose of 150mg in divided doses.

Milder cases: 75 to 100mg daily in divided doses.

Primary dysmenorrhoea: 50 to 150 mg daily in divided doses. Dosage should be individually determined. Treatment should be initiated at onset of symptoms and continued for a few days, depending on intensity of pain.

Classical migraine: 50 mg taken at first signs of an impending attack. If pain relief is not sufficient within 2 hours after the first dose, a second dose of 50 mg may be taken. A third dose may be taken after 4 to 6 hours if necessary but the total daily dose of 150 mg must not be exceeded. The use of **K-FENAK** in children with migraine attacks has not been established.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

Side-effects:

Haematological disorders:

- *Less frequent:* Aplastic anaemia, haemolytic anaemia, agranulocytosis, leucopenia, thrombocytopenia.

Cardiovascular disorders:

- *Less frequent:* Chest pain, congestive heart failure, hypertension, oedema, palpitations.

Neuropsychiatric disorders:

- *Frequent:* Dizziness, headache, nervousness, vertigo.
- *Less frequent:* Aseptic meningitis, tiredness, tremor, convulsions, disturbances of sensation (including paraesthesia), disorientation, insomnia, irritability, memory disturbance, anxiety, depression, nightmares, psychotic reactions.

Gastrointestinal disorders:

- *Frequent:* Anorexia, local irritation, nausea, vomiting, abdominal cramps, dyspepsia, epigastric pain, eructation, diarrhoea, flatulence.
- *Less frequent:* Alteration in taste, aphthous stomatitis, glossitis, haematemesis, oesophageal lesions, gastrointestinal bleeding, peptic ulcer with or without bleeding or perforation, diaphragm-like intestinal strictures, pancreatitis, lower gut disorders such as non-specific haemorrhagic colitis, exacerbation of ulcerative colitis or Crohn's proctocolitis, bloody diarrhoea, melana, constipation.

Genitourinary disorders:

- *Less frequent:* Acute renal failure, interstitial nephritis, nephrotic syndrome, papillary necrosis, urinary abnormalities such as haematuria, proteinuria.

Hepatobiliary disorders:

- *Frequent:* Elevated transaminase levels (ALT, AST).
- *Less frequent:* Fulminant hepatitis, hepatitis with or without jaundice.

Visual disorders:

- *Less frequent:* Disturbances of vision (diplopia, blurred vision).

Skin and subcutaneous tissue disorders:

- *Frequent:* Rash and other skin reactions.
- *Less frequent:* Bullous eruptions, eczema, erythema multiforme, erythroderma (exfoliative dermatitis), Lyell's syndrome (acute toxic epidermolysis), photosensitivity reaction, purpura, including allergic purpura, Stevens Johnson syndrome, urticaria, loss of hair.

Other:

- *Less frequent:* Impaired hearing, tinnitus. Hypersensitivity reactions (such as bronchospasm, anaphylactic systemic reactions including hypotension), pneumonitis and vasculitis may occur without prior exposure to **K-FENAK**. Discontinue treatment immediately.

Special precautions:

Patients who experience dizziness or other central nervous system disturbances while taking **K-FENAK** should refrain from driving a vehicle or operating machinery.

Due to its pharmacodynamic properties **K-FENAK** may mask signs and symptoms of infection.

Gastric bleeding may occur at any time during treatment with **K-FENAK**. Discontinue treatment immediately.

A reduction in dosage may be required in the elderly, especially the very frail or those with a low body mass.

Heart failure may be precipitated in some compromised patients, due to the inherent potential of **K-FENAK** to cause fluid retention.

Patients suffering from renal, hepatic or cardiac impairment or those being treated with diuretics or who have extracellular volume depletion from any cause, should be carefully monitored because of the role of prostaglandins in maintaining renal blood flow.

During prolonged treatment with **K-FENAK**, blood counts and monitoring of renal and hepatic function are indicated. If abnormal liver function tests persist and symptoms of hepatic disease develop, discontinue **K-FENAK**.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

(See "**SIDE-EFFECTS AND SPECIAL PRECAUTIONS**").

Treatment is symptomatic and supportive, especially for convulsions, hypotension, respiratory depression, gastrointestinal irritation and renal failure. Absorption should be prevented as soon as possible after an overdose by means of gastric lavage and activated charcoal.

Specific therapies such as dialysis, haemoperfusion or forced diuresis are of little value in eliminating **K-FENAK** because of its extensive metabolism and high protein binding.

IDENTIFICATION:

White, circular, biconvex, film-coated tablets plain on both sides.

PRESENTATION:

Bliester-packed cartons of 10, 15, 20 and 30 tablets.

STORAGE INSTRUCTIONS:

Store in a dry place below 25°C.

KEEP OUT OF THE REACH OF CHILDREN

REGISTRATION NUMBER:

38/3.1/0651

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

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