WARNINGS:

There is an increased risk of gastrointestinal bleeding when these agents are used. Use of two or more NSAIDs concomitantly could result in an increase in side-effects. Antibiotics, have been reported in isolated cases. Convulsions, which may have been due to concomitant use of NSAIDs and quinolone

PHARMACOLOGICAL CLASSIFICATION:


PHARMACOLOGICAL ACTION:

Diclofenac is a non-steroidal anti-inflammatory compound (NSAID) with analgesic, anti-inflammatory and anti-ulcer activities. It causes inhibition of the 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 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 metabolized 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 biliary (approximately 30%). Less than 1% is excreted in unchanged form.

INDICATIONS:

K-FENAK is indicated for:

1. The treatment emergency of acute gouty attacks, for a maximum treatment period of 3 days.
2. The treatment of fever or mild to moderate pain of inflammatory origin, for a maximum period of 5 or 6 days.

CONTRA-INDICATIONS:

1. Hyper-sensitivity to diclofenac or to any of the ingredients in the formulation.
2. Hypersensitivity to any other NSAIDs, including aspirin.
3. Gastric or duodenal ulcer.
4. History of peptic ulcer disease or bleeding or perforation (PUB) related to previous NSAIDs.
5. Active or history of recent ulcer haemorrhage/haemorrhagic perforations.
6. Adenocarcinoma of the stomach or history of adenoma affecting(s) acute gastritis or ulcers are precipitated by acetylsalicylic acid or by other medicines which inhibit prostaglandin synthesis.
7. Pregnancy and lactation (see "PREGNANCY AND LACTATION").
8. Porphyria.

WARNING:

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

1. A history of peptic ulcer disease, or of symptoms indicative of, gastrointestinal disease.
2. Ulcerative colitis, Crohn’s disease.
3. Impaired hepatic function.
4. Pre-existing dyspepsia or disorders of bowel 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/aprin: the bioavailability of both K-FENAK and acetylsalicylic acid may be reduced if used concurrently.

Regular use of NSAIDs during the third trimester of pregnancy may result in premature closure of the fetal ductus arteriosus, which may mask signs and symptoms of perforation (PUB), sometimes fatal. The risk of impaired growth of the foetus and closure of the foetal ductus arteriosus (approximately 30%). Less than 1% is excreted in unchanged form.

A reduction in dosage may be required in the elderly, especially the very frail or those with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with treatment. 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.

Special Precautions:

The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or gastrointestinal bleeding, sometimes fatal, have been reported. Other adverse reactions may be nausea, vomiting, diarrhoea, tinnitus, headache, dizziness, hypotension, pneumonitis and vasculitis may occur without prior symptoms.

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 an extracellular volume depletion from any cause, should be carefully monitored because of the role of prostaglandins in maintaining renal blood flow. Diclofenac should be used with caution in patients with a history of ulceration and the elderly. When gastrointestinal bleeding or ulceration occurs in patients receiving K-FENAK, treatment with K-FENAK should be stopped.

K-FENAK should be given with caution to patients with a history of gastrointestinal disease (e.g. ulcerative colitis, Crohn’s disease, haemorrhoids, gastro-intestinal bleeding or perforation). The risk of exacerbation may increase in these patients (see "SIDE-EFFECTS AND SPECIAL PRECAUTIONS").

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. K-FENAK should be discontinued if any of the skin rash, or any other sign of hypersensitivity (see "SIDE-EFFECTS AND SPECIAL PRECAUTIONS").

Lactose.

K-FENAK contains lactose. Patients with rare hereditary problems of galactose intolerance e.g. Galactosaemia, the Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance, should not take K-FENAK.

Lactose may have an effect on the glycemic control of patients with diabetes mellitus.

INTERACTIONS:

Methotrexate:

Concomitant administration of methotrexate with K-FENAK may result in increased methotrexate toxicity (see "WARNING").

Lithium or digoxin:

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

Glucocorticoids:

Gastrointestinal adverse effects may be exacerbated by the concomitant administration of K-FENAK and corticosteroids. Co-administration of K-FENAK and corticosteroids increases the risk of gastrointestinal ulceration or bleeding (PUBs).

Antidiabetic medicines:

K-FENAK may cause either hypo- or hyper-glycaemia. Dosage of antidiabetic medicines may need to be changed.

Anticoagulants:

K-FENAK may enhance the effects of anticoagulants, so that warfarin. There is an increased risk of haemorrhage if K-FENAK is used concomitantly with any anticoagulants. Careful monitoring is necessary.

Ciclosporin:

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

Quinolone antibiotics:

Concomitantly, who may be due to concomitant use of NSAIDs and quinolone antibiotics, have been reported in isolated cases.

NSAIDs:

Use of two or more NSAIDs concomitantly could result in an increase in side-effects.

Antipilet agents and selective serotonin reuptake inhibitors (SSRIs):

There is an increased risk of gasses offered toning when these agents are co-administered with K-FENAK.

PREGNANCY AND LACTATION:

Safety and efficacy in pregnancy and lactation have not been established (see "CONTRA-INDICATIONS").

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

Glucocorticoids:

Less frequent:

Elevated transaminase levels (ALT, AST).

Cardiogenic disorders:

Less frequent:

Glossitis, aphthous stomatitis, haematemesis, epidermal necrolysis, eczema, erythema multiforme, urticaria, angioneurotic oedema (anaphylactic dermatitis).

Lyell’s syndrome (acute toxic epidermal necrolysis), photosensitivity reaction, purpura, including allergic purpura, urticaria, loss of hair.

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