

Avorek
(Diclofenac Potassium)

ایوریک

CARDIOVASCULAR RISK

NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.

Diclofenac potassium is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery.

GASTROINTESTINAL RISK

NSAIDs cause an increased risk of serious gastrointestinal adverse events including inflammation, 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.

COMPOSITION
Each **Avorek** 50mg film coated tablet contains 50 mg of diclofenac potassium.

MECHANISM OF ACTION
Diclofenac potassium is a nonsteroidal anti-inflammatory drug (NSAID) that exhibits analgesic, anti-inflammatory and antipyretic properties. The mechanism of action of diclofenac potassium, like that of other NSAIDs, is not completely understood but may be related to prostaglandin synthesis inhibition.

PHARMACOKINETIC PROPERTIES
Absorption
Diclofenac is rapidly and completely absorbed after oral administration. Food intake does not affect absorption. However, there is delay in onset of absorption. Diclofenac undergoes first-pass metabolism and is extensively metabolised. Only about 50% of the absorbed dose is systemically available. Peak plasma concentration after one 50 mg tablet was 3.9 µmol/l after 20-60 minutes.
Distribution
Diclofenac is highly bound to plasma proteins (99.7%), chiefly albumin (99.4%).
Elimination
The terminal half-life in plasma is 1-2 hours. Approx. 60% of the dose administered is excreted in the urine in the form of metabolites, and less than 1% as unchanged substance. The remainder of the dose is eliminated as metabolites through the bile in the faeces.
Special Population
Pediatric Use
Safety and effectiveness in pediatric patients have not been established.
Geriatric use
As with any NSAIDs, caution should be exercised in treating the elderly (65 and older).
Hepatic Insufficiency
Hepatic metabolism accounts for almost 100% of diclofenac potassium elimination. Dose adjustment is required in patients with hepatic disease.
Renal Insufficiency
Diclofenac pharmacokinetics has been investigated in subjects with renal insufficiency. No differences in the pharmacokinetics of diclofenac have been detected in studies of patients with renal impairment. In patients with renal impairment AUC values and elimination rate were comparable to those in healthy subjects.

INDICATIONS
Rheumatoid arthritis
Osteoarthritis
Low back pain
Migraine attacks
Acute musculo-skeletal disorders and trauma such as periarthritis (especially frozen shoulder), tendinitis, tenosynovitis, bursitis, sprains, strains and dislocations, relief of pain in fractures.
Ankylosing spondylitis
Acute gout
Control of pain and inflammation in orthopaedic, dental and other minor surgery
Pyrophosphate arthropathy and associated disorders
Primary dysmenorrhea

DOSAGE AND ADMINISTRATION
Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms.
The tablets should be swallowed whole with liquid, preferably before meals, and must not be chewed or divided.
Adults: The recommended daily dose is 100-150mg in two or three divided doses.
In migraine an initial dose of 50 mg should be taken at the first signs of an impending attack. In cases where relief 2 hours after the first dose is not sufficient, a further dose of 50 mg may be taken. If needed, further doses of 50 mg may be taken at intervals of 4-6 hours, not exceeding a total dose of 200 mg per day.

UNDESIRABLE EFFECTS
If serious side-effects occur, diclofenac potassium should be withdrawn.
Frequency estimate: Frequent:> 10%, occasional:> 1-10%, rare:>0.001-1%, isolated cases: <0.001%.
Gastrointestinal tract:
Occasional: Epigastric pain, other gastrointestinal disorders (e.g. nausea, vomiting, diarrhoea, abdominal cramps, dyspepsia, flatulence, anorexia).
Rare: Gastritis, gastrointestinal bleeding (haematemesis, melaena, and bloody diarrhoea), gastrointestinal ulcers with or without bleeding or perforation (sometimes fatal, particularly in the elderly) may occur.
In isolated cases: Aphthous stomatitis, glossitis, oesophageal lesions, lower gut disorders (e.g. non-specific haemorrhagic colitis and exacerbations of ulcerative colitis or Crohn's proctocolitis, colonic damage and stricture formation), pancreatitis, constipation.
Central Nervous System disorders:
Occasional: Headache, dizziness, or vertigo.
Rare: Drowsiness, tiredness, hypotension.
In isolated cases: Disturbances of sensation, paraesthesia, memory disturbance, disorientation, insomnia, irritability, convulsions, depression, confusion, hallucinations, malaise, anxiety, nightmares, tremor, psychotic reactions, aseptic meningitis (especially in patients with existing auto-immune disorders, such as systemic lupus erythematosus and mixed tissue disease), with symptoms such as fever, stiff neck, headache, nausea and vomiting.
Special senses:
Isolated cases: Disturbances of vision (blurred vision, optic neuritis, diplopia), impaired hearing, tinnitus, taste disturbances.
Skin:
Occasional: Rashes or skin eruptions.
Rare: Urticaria.
In isolated cases: Bullous eruptions, eczema, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome, (acute toxic epidermolysis), erythroderma (exfoliative dermatitis), loss of hair, photosensitivity reactions, purpura including allergic purpura.
Kidney:
Rare: Oedema.
In isolated cases: Acute renal insufficiency, urinary abnormalities (e.g. haematuria, proteinuria), interstitial nephritis, nephrotic syndrome, papillary necrosis.
Liver:
Occasional: Elevation of serum aminotransferase enzymes (ALT, AST).
Rare: Liver function disorders including hepatitis (in isolated cases fulminant) with or without jaundice.
Blood:
In isolated cases: Thrombocytopenia, leucopenia, agranulocytosis, haemolytic anaemia, aplastic anaemia.
Vascular:
Isolated cases: Vasculitis.
Respiratory:
Isolated cases: Pneumonitis.
Cardiovascular system:
Isolated cases: Palpitations, chest pain, hypertension, congestive heart failure.
Other organ systems:
Isolated cases: Impotence.
Hypersensitivity:
Hypersensitivity reactions have been reported following treatment with NSAIDs. These consist of (a) non-specific allergic reactions and anaphylaxis (b) respiratory tract reactivity comprising of 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 epidermal necrolysis and erythema multiforme). Clinical trial and epidemiological data suggest that use of diclofenac, particularly at high doses (150mg daily) and in long term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction

or stroke).

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Lithium and digoxin: Diclofenac potassium may increase plasma concentrations of lithium and digoxin.

Anticoagulants: There are isolated reports of an increased risk of haemorrhage with the combined use of diclofenac and anticoagulant therapy. Therefore, close monitoring of such patients is required. As with other nonsteroidal anti-inflammatory agents, diclofenac in a high dose can reversibly inhibit platelet aggregation.

Antidiabetic agents: There have been isolated reports of hypoglycaemic and hyperglycaemic effects which have required adjustment to the dosage of hypoglycaemic agents.

Methotrexate: Cases of serious toxicity have been reported when methotrexate and NSAIDs are given within 24 hours of each other. This interaction is mediated through accumulation of methotrexate resulting from impairment of renal excretion in the presence of the NSAID.

Quinolone antimicrobials: Convulsions may occur due to an interaction between quinolones and NSAIDs. This may occur in patients with or without a previous history of epilepsy or convulsions.

Other NSAIDs including cyclooxygenase-2 selective inhibitors and corticosteroids: Co-administration of diclofenac potassium with aspirin or corticosteroids may increase the risk of gastrointestinal bleeding or ulceration. Avoid concomitant use of two or more NSAIDs

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding.

Diuretics: Like other NSAIDs, diclofenac potassium may inhibit the activity of diuretics. Concomitant treatment with potassium-sparing diuretics may be associated with increased serum potassium levels, which should therefore be monitored frequently.

Cardiac glycosides: Concomitant use of cardiac glycosides and NSAIDs in patients may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

Antihypertensives: Concomitant use of NSAIDs with antihypertensive drugs (i.e. beta-blockers, angiotensin converting enzyme (ACE) inhibitors, diuretics) may cause a decrease in their antihypertensive effect via inhibition of vasodilatory prostaglandin synthesis.

Ciclosporin and Tacrolimus: Cases of nephrotoxicity have been reported in patients receiving concomitant ciclosporin and NSAIDs, including diclofenac sodium. Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus. This might be mediated through renal antiprostaglandin effects of both NSAID and calcineurin inhibitor.

WARNINGS

In all patients: Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms.

The use of diclofenac potassium with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided.

Elderly: The elderly have increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal.

Gastrointestinal: Close medical surveillance is imperative in patients with symptoms indicative of gastrointestinal disorders, with a history suggestive of gastric or intestinal ulceration, with ulcerative colitis, or with Crohn's disease as these conditions may be exacerbated.

Hepatic: Close medical surveillance is also imperative in patients suffering from impairment of hepatic function.

Hypersensitivity reactions: As with other nonsteroidal anti-inflammatory drugs, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur without earlier exposure to the drug.

Like other NSAIDs, diclofenac potassium may mask the signs and symptoms of infection due to its pharmacodynamic properties.

PRECAUTIONS:

Renal: Patients with renal, cardiac or hepatic impairment and the elderly should be kept under surveillance, since the use of NSAIDs may result in deterioration of renal function. The lowest effective dose should be used and renal function monitored.

Hepatic: If abnormal liver function tests persist or worsen, clinical signs or symptoms consistent with liver disease develop or if other manifestations occur (eosinophilia, rash), diclofenac potassium should be discontinued. Hepatitis may occur without prodromal symptoms.

Haematological: Diclofenac potassium may reversibly inhibit platelet aggregation. Patients with defects of haemostasis, bleeding diathesis or haematological abnormalities should be carefully monitored.

Long term treatment: All patients who are receiving nonsteroidal anti-inflammatory agents should be monitored as a precautionary measure e.g. renal function, hepatic function (elevation of liver enzymes may occur) and blood counts. This is particularly important in the elderly.

Respiratory disorders: Like other drugs that inhibit prostaglandin synthetase activity, diclofenac sodium and other NSAIDs can precipitate bronchospasm if administered to patients suffering from, or with a previous history of bronchial asthma.

Cardiovascular and cerebrovascular effects: Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

Use of diclofenac, particularly at high dose (150mg daily) and in long term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke).

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with diclofenac after careful consideration. Similar consideration should be made before initiating long-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidemia, diabetes mellitus, and smoking).

SLE and mixed connective tissue disease: In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis.

Dermatological: Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs, including diclofenac potassium. Patients appear to be at the highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. Diclofenac potassium should be discontinued at the first appearance of skin rash, mucosal lesions or any other signs of hypersensitivity.

PREGNANCY

Pregnancy category C

There are no adequate and well controlled studies in pregnant women. Use in the last trimester of pregnancy is contraindicated.

Lactation

NSAIDs should if possible be avoided when breastfeeding.

OVERDOSE

Symptoms: Symptoms include headache, nausea, vomiting, epigastric pain, gastrointestinal bleeding, rarely diarrhoea, disorientation, excitation, coma, drowsiness, tinnitus, fainting, occasionally convulsions. In rare cases of significant poisoning acute renal failure and liver damage are possible.

Therapeutic measures: Patients should be treated symptomatically as required. Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adults gastric lavage should be considered within one hour of ingestion of potentially toxic amounts. Frequent or prolonged convulsions should be treated with intravenous diazepam.

CONTRAINDICATIONS

- Hypersensitivity to the active substance or any of the excipients.
- Patients with active, or a history of, gastrointestinal ulcers, bleeding or perforation (two or more distinct episodes of proven ulceration or bleeding).
- Patients who have previously shown hyper-sensitivity reactions (e.g. asthma, angioedema, urticaria or acute rhinitis) to ibuprofen, aspirin or other nonsteroidal anti-inflammatory drugs.
- Severe hepatic, renal and heart failure.
- Perioperative pain treatment in the setting of coronary artery bypass graft surgery.
- During the last trimester of pregnancy.
- History of gastrointestinal bleeding or perforation, relating to previous NSAID therapy.

PRESENTATION

Avorek 50 mg Tablet: 2x10'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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An ISO Certified Company

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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۔