Bosch

For Medical Professional only

DOLO-K® 50 mg TABLETS

(Diclofenac Potassium)

ڈولو۔کے ۵۰ ملی گرام ٹیبلیٹس

(ڈکلوفینک پوٹاشیم)

DESCRIPTION:
Dolo-K (Diclofenac potassium) is a benzeneacetic acid derivative, available as tablets of 50 mg for oral administration. The chemical name is 2-[(2,6-dichlorophenyl)amino] benzeneacetic acid, monopotassium salt. The molecular weight is 334.25. Its molecular formula is $C_{14}H_{10}Cl_2NKO_2$.

Composition:
Each film coated tablet contains:
Diclofenac Potassium U.S.P..... 50 mg.
(Product Specs.: U.S.P.)

CLINICAL PHARMACOLOGY:
Pharmacodynamic properties:
Pharmacotherapeutic group: Non-steroidal anti-inflammatory drug (NSAID).ATC code: M01A B05
Dolo-K tablets contain the potassium salt of diclofenac, a non-steroidal compound with pronounced and clinically demonstrable analgesic, anti-inflammatory and anti-pyretic properties.
Diclofenac Potassium is a potent inhibitor of prostaglandin biosynthesis and a modulator of arachidonic acid release and uptake. Diclofenac Potassium tablets have a rapid onset of action and are therefore suitable for the treatment of acute episodes of pain and inflammation.

PHARMACOKINETIC PROPERTIES:
Absorption
Diclofenac Potassium is rapidly and completely absorbed from oral administration. Food intake does not affect absorption.
Peak plasma concentration after one 50 mg coated tablet was 3.9 µmol/l after 20-60 minutes. The plasma concentrations show a linear relationship to the size of the dose. Diclofenac undergoes first-pass metabolism and is extensively metabolised.

Distribution
Diclofenac Potassium is highly bound to plasma proteins (99.7%), chiefly albumin (99.4%) Diclofenac was detected in a low concentration (100ng/mL) in breast milk in one nursing mother. The estimated amount ingested by an infant consuming breast milk is equivalent to a 0.03 mg/kg/day dose.

Biotransformation
The biotransformation of Diclofenac Potassium involves partly glucuronidation of the intact molecule but mainly single and multiple hydroxylation followed by glucuronidation.

Elimination
The total systemic clearance of Diclofenac Potassium in plasma is 263 ± 56 ml/min (mean ± SD). The terminal half-life in plasma is 1 – 2 hours. Repeated oral administration of Diclofenac Potassium tablets for 8 days in daily doses of 50 mg t.i.d. does not lead to accumulation of diclofenac potassium in the plasma. 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.

Specific Populations
The age of the patient has no influence on the absorption, metabolism, or excretion of Diclofenac Potassium.
In patients suffering from renal impairment, no accumulation of the unchanged active substance can be inferred from the single-dose kinetics when applying the usual dosage schedule. At a creatinine clearance of <10 ml/min the theoretical steady-state plasma levels of metabolites are about four times higher than in normal subjects. However, the metabolites are ultimately cleared through the bile.
In the presence of impaired hepatic function the kinetics and metabolism are the same as for patients without liver disease.

THERAPEUTIC INDICATIONS:
- Rheumatoid arthritis
- Osteoarthrosis
- 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

DOSAGE AND ADMINISTRATION:

Adults

The recommended daily dose is 100-150mg in two or three divided doses. For mild cases, 75-100mg daily in two or three divided doses is usually sufficient.

In migraine an initial dose of 50mg 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 50mg may be taken. If needed, further doses of 50mg may be taken at intervals of 4-6 hours, not exceeding a total dose of 200mg per day.

Specific Population

Paediatric population

For children over 14 years of age, the recommended daily dose is 75-100mg in two or three divided doses. Diclofenac Potassium Tablets are not recommended for children under 14 years of age.

The use of Diclofenac Potassium tablets in migraine attacks has not been established in children.

Elderly

Although the pharmacokinetics of diclofenac potassium are not impaired to any clinically relevant extent in elderly patients, nonsteroidal anti-inflammatory drugs should be used with particular caution in such patients who generally are more prone to adverse reactions.

CONTRAINDICATIONS:

Hypersensitivity to the active substance or any of the excipients.

- Active, gastric or intestinal ulcer, bleeding or perforation.
- History of gastrointestinal bleeding or perforation, relating to previous NSAID therapy.
- Active, or history of recurrent peptic ulcer / hemorrhage.
- Last trimester of pregnancy.
- Hepatic failure.
- Renal failure.
- Established congestive heart failure (NYHA II-IV), ischemic heart disease, peripheral arterial disease and cerebrovascular disease.
- Like other non-steroidal anti-inflammatory drugs (NSAIDs), Diclofenac Potassium is also contraindicated in patients in whom attacks of asthma, angioedema, urticaria or acute rhinitis are precipitated by ibuprofen, acetylsalicylic acid or other nonsteroidal anti-inflammatory drugs.

WARNINGS AND PRECAUTIONS:

General

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms. The concomitant use of Diclofenac Potassium with systemic NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided due to the absence of any evidence demonstrating synergistic benefits and the potential for additive undesirable effects. Caution is indicated in the elderly on basic medical grounds. In particular, it is recommended that the lowest effective dose be used in frail elderly patients or those with a low body weight.

As with other nonsteroidal anti-inflammatory drugs including Diclofenac Potassium, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur without earlier exposure to the drug . Presenting symptoms of such reactions can include chest pain occurring in association with an allergic reaction to Diclofenac Potassium.

Lactose:

Product contains lactose.

Possibility of untoward reaction for patient with celiac disease relating to the use of such excipients.

Gastrointestinal effects:

Gastrointestinal bleeding (haematemesis, melaena) ulceration or perforation which can be fatal has been reported with all NSAIDs including diclofenac and may occur at any time during treatment, with or without warning symptoms or a previous history of serious GI events. They generally have more serious consequences in the elderly. If gastrointestinal bleeding or ulceration occurs in patients receiving Diclofenac Potassium, the drug should be withdrawn.

As with all NSAIDs, including Diclofenac Potassium , close medical surveillance is imperative and particular caution should be exercised when prescribing diclofenac in patients with symptoms indicative of gastrointestinal disorders, or with a history suggestive of gastric or intestinal ulceration, bleeding or perforation.

To reduce the risk of GI toxicity in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation, and in the elderly, the treatment should be initiated and maintained at the lowest effective dose. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant use of medicinal products containing low dose acetylsalicylic acid (ASA) aspirin or medicinal products likely to increase gastrointestinal risk.

Hepatic effects:

Close medical surveillance is required when prescribing Diclofenac Potassium to patients with impairment of hepatic function as their condition may be exacerbated.As with other NSAIDs, including diclofenac potassium, values of one or more liver enzymes may increase. During prolonged treatment with Diclofenac Potassium, regular monitoring of hepatic function is indicated as a precautionary measure.

Renal effects:

As fluid retention and oedema have been reported in association with NSAIDs therapy, including Diclofenac Potassium, particular caution is called for in patients with impaired cardiac or renal function, history of hypertension, the elderly, patients receiving concomitant treatment with diuretics or medicinal products that can significantly impact renal function, and those patients with substantial extracellular volume depletion from any cause. Monitoring of renal function is recommended as a precautionary measure when using Dolo-K in such cases. Discontinuation therapy is usually followed by recovery to the pre-treatment state.

Skin effects:

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. Diclofenac Potassium should be discontinued at the first appearance of skin rash, mucosal lesions or any other signs of hypersensitivity.

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.

Cardiovascular and cerebrovascular effects:
Patients with congestive heart failure (NYHA-I) or patients with significant risk factors for cardiovascular events should only be treated with Diclofenac Potassium after careful consideration.As the cardiovascular risks of diclofenac potassium may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically.

Haematological effects:
Use of diclofenac potassium are recommended only for short term treatment.During prolonged treatment with Diclofenac Potassium, as with other NSAIDs, monitoring of the blood count is recommended.
Diclofenac Potassium may reversibly inhibit platelet aggregation. Patients with defects of haemostasis, bleeding diathesis or haematological abnormalities should be carefully monitored.

Pre-existing asthma:
In patients with asthma, seasonal allergic rhinitis, swelling of the nasal mucosa, chronic obstructive pulmonary diseases or chronic infections of the respiratory tract, reactions on NSAIDs like asthma exacerbation, Quincke's edema or urticaria are more frequent than in other patients.
Like other drugs that inhibit prostaglandin synthetase activity, Diclofenac Potassium sodium and other NSAIDs can precipitate bronchospasm if administered to patients suffering from, or with a previous history of bronchial asthma.

Female fertility:
The use of Diclofenac Potassium may impair female fertility and is not recommended in women attempting to conceive. In women who may have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of Diclofenac Potassium should be considered.

DRUG INTERACTIONS:
The following interactions include those observed with Diclofenac Potassium gastro-resistant tablets and other pharmaceutical forms of Diclofenac Potassium.
Lithium: If used concomitantly, Diclofenac Potassium may increase plasma concentrations of lithium. Monitoring of the serum lithium level is recommended.
Digoxin: If used concomitantly, Diclofenac Potassium may raise plasma concentrations of digoxin. Monitoring of the serum digoxin level is recommended.
Diuretics and antihypertensive agents: Like other NSAIDs, concomitant use of Diclofenac Potassium with diuretics and antihypertensive agents (ACE) inhibitors may cause a decrease in their antihypertensive effect via inhibition of vasodilatory prostaglandin synthesis. Therefore, the combination should be administered with caution and patients, especially the elderly, should have their blood pressure periodically monitored. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy periodically thereafter, particularly for diuretics and ACE inhibitors due to the increased risk of nephrotoxicity.

Drugs known to cause hyperkalemia: Concomitant treatment with potassium-sparing diuretics, ciclosporin, tacrolimus or trimethoprim may be associated with increased serum potassium levels, which should therefore be monitored frequently .

Anticoagulants and anti-platelet agents: Caution is recommended since concomitant administration could increase the risk of bleeding . Although clinical investigations do not appear to indicate that Diclofenac Potassium has an influence on the effect of anticoagulants, there are reports of an increased risk of haemorrhage in patients receiving Diclofenac Potassium and anticoagulant concomitantly . Therefore, to be certain that no change in anticoagulant dosage is required, close monitoring of such patients is required. As with other nonsteroidal anti-inflammatory agents, Diclofenac Potassium in a high dose can reversibly inhibit platelet aggregation.

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

Selective serotonin reuptake inhibitors (SSRIs): Concomitant administration of SSRI's may increase the risk of gastrointestinal bleeding.
Methotrexate: Diclofenac Potassium can inhibit the tubular renal clearance of methotrexate hereby increasing methotrexate levels. Caution is recommended when NSAIDs, including diclofenac potassium, are administered less than 24 hours before treatment with methotrexate, since blood concentrations of methotrexate may rise and the toxicity of this substance be increase.
Ciclosporin: Diclofenac Potassium, like other NSAIDs, may increase the nephrotoxicity of ciclosporin due to the effect on renal prostaglandins. Therefore, it should be given at doses lower than those that would be used in patients not receiving ciclosporin.
Tacrolimus: 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.
Quinolone antibacterials: 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. Therefore, caution should be exercised when considering the use of a quinolone in patients who are already receiving an NSAID.
Phenytoin: When using phenytoin concomitantly with Dolo-K, monitoring of phenytoin plasma concentrations is recommended due to an expected increase in exposure to phenytoin.
Colestipol and cholestyramine: These agents can induce a delay or decrease in absorption of Diclofenac Potassium. Therefore, it is recommended to administer Diclofenac Potassium at least one hour before or 4 to 6 hours after administration of colestipol/ cholestyramine.
Cardiac glycosides: Concomitant use of cardiac glycosides and NSAIDs in patients may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.
Potent CYP2C9 inhibitors: Caution is recommended when co-prescribing Diclofenac Potassium with potent CYP2C9 inhibitors (such as voriconazole), which could result in a significant increase in peak plasma concentrations and exposure to Diclofenac Potassium due to inhibition of diclofenac metabolism.
Zidovudine: Increased risk of haematological toxicity when NSAIDs are

given with zidovudine. There is evidence of an increased risk of hemarthosis and hematoma in HIV(+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

PREGNANCY:
Pregnancy Category C prior to 30 weeks gestation ; Category D starting at 30 weeks gestation. Starting at 30 weeks gestation, DOLO-K, and other NSAIDS, should be avoided by pregnant women as premature closure of the ductus arteriosus in the fetus may occur. Prior to 30 weeks gestation, DOLO-K should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

LACTATION:
Like other NSAIDs, Diclofenac Potassium passes into breast milk in small amounts. Therefore Diclofenac Potassium should not be administered during breast feeding in order to avoid undesirable effects in the infant.

ADVERSE EFFECTS:
Common:
Headache, dizziness, Vertigo, Nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, flatulence, anorexia, Transaminases increased, Rash.
Uncommon:
Myocardial infarction, cardiac failure, palpitations, chest pain,

Rare:
Hypersensitivity, anaphylactic and anaphylactoid reactions, Somnolence, tiredness, Asthma (including dyspnoea), Gastritis, gastrointestinal haemorrhage, haematemesis, diarrhoea haemorrhagic, melaena, gastrointestinal ulcer with or without bleeding or perforation, Hepatitis, jaundice, liver disorder, Urticaria, Edema.

Very Rare:
Thrombocytopenia, leucopoenia, anaemia (including haemolytic and aplastic anaemia), agranulocytosis, Disorientation, depression, insomnia, nightmare, irritability, psychotic disorder, Paraesthesia, memory impairment, convulsion, anxiety, tremor, aseptic meningitis, taste disturbances, cerebrovascular accident, Visual disturbance, vision blurred, diplopia, Tinnitus, hearing impaired, Hypertension, hypotension, vasculitis, Pneumonitis, Colitis (including haemorrhagic colitis and exacerbation of ulcerative colitis or Crohn's disease), constipation, stomatitis (including ulcerative stomatitis), glossitis, oesophageal disorder, diaphragm-like intestinal strictures, pancreatitis, Fulminant hepatitis, hepatic necrosis, hepatic failure, Bullous eruptions, eczema, erythema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), dermatitis exfoliative, loss of hair, photosensitivity reaction, purpura, allergic purpura, pruritus, Acute renal failure, haematuria, proteinuria, nephrotic syndrome, interstitial nephritis, renal papillary necrosis, Impotence.

OVER DOSAGE:
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 a potentially life-threatening overdose. Patients should be observed for at least four hours after ingestion of potentially toxic amounts. Frequent or prolonged convulsions should be treated with intravenous diazepam. Supportive measures should be given for complications such as hypotension, renal failure, gastrointestinal disorder, and respiratory depression.

SHELF LIFE:
3 Years

Presentation:
DOLO-K 50mg tablet in blister pack of 2x10's tablets.

STORAGE AND INSTRUCTION:
Protect from heat, sunlight & moisture, store below 25°C.
The expiration date refer to the product correctly stored at the required condition. Keep out of the reach of children.
Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com.
To be sold on prescription of a registered medical practitioner only.
"Product contains lactose"

ہدایات :

دھوپ، گرمی اور نمی سے محفوظ ۲۵ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
بچّوں کی پہنچ سے دُور رکھیں۔
صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

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