DYFENAC TABLET 50MG

MAL19913381AZ

DESCRIPTION:
TABLET
Colour : Light Brown
Shape : Round and Biconvex
Coating : Enteric-coated

CONTENT:
Each Tablet Contains:
Diclofenac Sodium ..... 50 mg

PHARMACODYNAMICS:
Diclofenac may act to block pain impulse generation via a peripheral action, which may involve inhibition of the synthesis of prostaglandins, and possibly inhibition of the synthesis or action of other substances, which sensitize pain receptors to mechanical or chemical stimulation.

PHARMACOKINETICS:
Diclofenac is absorbed from the gastrointestinal tract. Peak plasma concentrations occur about 2 hours after ingestion of enteric-coated tablets. At therapeutic concentrations, it is more than 99% bound to plasma proteins. It is metabolised and excreted mainly in the urine. Small amounts are excreted in the bile.

INDICATIONS:
For the relief of pain and inflammation in conditions such as rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, acute gout, and following some surgical procedures.

RECOMMENDED DOSE:
Adults: 75 - 150 mg daily in 2 or 3 divided doses.
In milder cases as well as for long-term therapy, 75 - 100 mg daily is usually sufficient.
After assessing the risk/benefit ratio in each individual patient, the lowest effective dose for the shortest possible duration should be used.
As a general recommendation, the dose should be individually adjusted. Adverse effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms (see section **WARNINGS AND PRECAUTIONS**).
Established Cardiovascular Disease or Significant Cardiovascular Risk Factors
Treatment with diclofenac is generally not recommended in patients with established cardiovascular disease (congestive heart failure, established ischemic heart disease, peripheral arterial disease) or uncontrolled hypertension. If needed, patients with established cardiovascular disease, uncontrolled hypertension, or significant risk factors for cardiovascular disease (e.g. hypertension, hyperlipidaemia, diabetes melilitus and smoking) should be treated with diclofenac only after careful consideration and only at doses ≤100 mg daily if treated for more than 4 weeks (see section **WARNINGS AND PRECAUTIONS**).

ROUTE OF ADMINISTRATION:
FOR ORAL USE ONLY

CONTRAINDICATIONS:
Peptic ulcer, known hypersensitivity to Diclofenac Sodium. Asthmatic patients in whom attacks of asthma, urticaria, or acute rhinitis are precipitated by Aspirin or by other drugs with prostaglandin-synthesis inhibiting activity.
Severe cardiac failure (see section **WARNINGS AND PRECAUTIONS**).

WARNINGS AND PRECAUTIONS:
It should be given with care to patients with bleeding disorders, cardiovascular diseases, peptic ulceration or a history of such ulceration. In the rare instances where peptic ulceration or gastrointestinal bleeding occurs, the drug should be withdrawn. During prolonged treatment, blood counts and monitoring of hepatic and renal function are indicated as precautionary measures.
Severe cutaneous reactions, including Stevens-Johnson Syndrome and toxic epidermal necrolysis (Lyell's syndrome) have been reported with Diclofenac Sodium. Patients treated with Diclofenac Sodium should be closely monitored for signs of hypersensitivity reactions. Discontinue Diclofenac Sodium immediately if rash occurs.
Cardiovascular Thrombotic Events
Observational studies have indicated that non-selective NSAIDs may be associated with an increased risk of serious cardiovascular events, principally myocardial infarction, which may increase with dose or duration of use. Patients with cardiovascular disease or cardiovascular risk of an adverse cardiovascular event in patient taking NSAID, especially in those with cardiovascular risk factors, the lowest effective dose should be used for the shortest possible duration.
There is no consistent evidence that the concurrent use of aspirin mitigates the possible increased risk of serious cardiovascular thrombotic events associated with NSAID use.
Hypertension
NSAIDS may lead to the onset of new hypertension or worsening the pre-existing hypertension and patients taking antihypertensive with NSAIDs may have an impaired antihypertensive response. Caution is advised when prescribing NSAIDs to patients with hypertension. Blood pressure should be monitored closely during initiation of NSAID treatment and at regular intervals thereafter.
Heart Failure
Fluid retention and oedema have been observed in some patients taking NSAIDs, therefore caution is advised in patients with fluid retention or heart failure.
Gastrointestinal Events
All NSAIDs can cause gastrointestinal discomfort and rarely serious, potentially fatal gastrointestinal effects such as ulcers, bleeding and perforation which may increase with dose or duration of use, but can occur at any time without warning. Caution is advised in patients with risk factors for gastrointestinal events e.g. the elderly, those with a history of serious gastrointestinal events, smoking and alcoholism. When gastrointestinal bleeding or ulceration occur in patients receiving NSAIDs, the drug should be withdrawn immediately. Doctors should warn patient about signs and symptoms of serious gastrointestinal toxicity. The concurrent use of aspirin and NSAIDs also increases the risk of serious gastrointestinal adverse events.
Severe Skin Reactions
NSAIDs may very rarely cause serious cutaneous adverse events such as exfoliative dermatitis, toxic epidermal necrolysis (TEN) and Steven-Johnson Syndrome (SJS), which can be fatal and occur without warning. These serious adverse events are idiosyncratic and are independent of dose or duration of use. Patients should be advised of the signs and symptoms of serious skin reactions and to consult their doctor at the first appearance of a skin rash or any other sign of hypersensitivity.

Adverse effects: Dermatological: Occasional - rashes or skin eruptions.
Cases of hair loss, bullous eruptions, erythema multiforme, Stevens-Johnson Syndrome, toxic epidermal necrolysis (Lyell's syndrome), and photosensitivity reactions have been reported.

Cardiovascular Effects

Treatment with NSAIDs including diclofenac, particularly at high dose and in long term, maybe associated with an increased risk of serious cardiovascular thrombotic events (including myocardial infarction and stroke).
Treatment with diclofenac is generally not recommended in patients with established cardiovascular disease (congestive heart failure, established ischemic heart disease, peripheral arterial disease) or uncontrolled hypertension. If needed, patients with established cardiovascular disease, uncontrolled hypertension, or significant risk factors for cardiovascular disease (e.g. hypertension, hyperlipidaemia, diabetes melilitus and smoking) should be treated with diclofenac only after careful consideration and only at doses ≤100 mg daily when treatment continues for more than 4 weeks.
As the cardiovascular risks of diclofenac may increase with dose and duration of exposure, the lowest effective daily dose should be used for the shortest duration possible. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically, especially when treatment continues for more than 4 weeks.
Patients should remain alert for the signs and symptoms of serious arteriothrombotic events (e.g. chest pain, shortness of breath, weakness, slurring of speech), which can occur without warnings. Patients should be instructed to see a physician immediately in case of such an event.

WARNINGS

RISK OF GI ULCERATION, BLEEDING AND PERFORATION WITH NSAID

Serious GI toxicity such as bleeding, ulceration and perforation can occur at any time, with or without warning symptoms, in patients treated with NSAID therapy. Although minor GI problems (e.g. dyspepsia) are common, usually developing early in therapy, prescribers should remain alert for ulceration and bleeding in patients treated with NSAIDS even in the absence of previous GI tract symptoms.
Studies to date have not identified any subset of patients not at risk of developing peptic ulceration and bleeding. Patients with prior history of serious GI events and other risk factors associated with peptic ulcer disease (e.g. alcoholism, smoking, corticosteroid therapy) are at increased risk. Elderly or debilitated patients seem to tolerate ulceration or bleeding less than other individuals and account for most spontaneous reports for fatal GI events.

Gastrointestinal Effects

NSAIDs, including diclofenac, may be associated with increased risk of gastrointestinal anastomotic leak. Close medical surveillance and caution are recommended when using diclofenac after gastrointestinal surgery.

DRUG INTERACTIONS:

Care should be taken in patients treated with any of the following drugs as interactions have been reported in some patients:
The anti-hypertensive effect of *anti-hypertensive drugs* may be reduced.
The plasma concentrations of *digoxin* and *lithium* may be increased by Diclofenac Sodium.
Increased risk of haemorrhage when non-steroidal anti-inflammatory agents are used in conjunction with *anticoagulants* has been reported, as well as increased risk of hypoglycaemic effect when non-steroidal anti-inflammatory agents are used in conjunction with *antidiabetic agents*.
The effect on renal prostaglandins may increase *cyclosporin* nephrotoxicity.
Methotrexate plasma levels may be increased and result in increased toxicity, therefore, caution should be exercised if Diclofenac Sodium and methotrexate are administered within 24 hours of each other.
Diuretics can increase the risk of nephrotoxicity of NSAIDs and there may be reduced diuretic effect. Serum potassium levels may be raised and should be monitored where there is concomitant treatment with *potassium sparing diuretics*.
NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels when administered together with *cardiac glycosides*.
NSAIDs should not be used for 8-12 days after *mifepristone* administration as NSAIDs can reduce the effect of mifepristone.
Concomitant use of *two or more NSAIDs* (including *aspirin*) should be avoided.
There is an increase risk of GI bleeding when NSAIDs are administered concomitantly with *corticosteroids*.
Animal data indicate that NSAIDs can increase the risk of convulsions associated with *quinolone antibiotics*. Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.

PREGNANCY AND LACTATION:

It should only be used for compelling reasons during pregnancy. This applies particularly to the last 3 months of pregnancy owing to the possibility of uterine inertia and/or premature closure of the ductus arteriousus. Following oral doses of 150 mg daily, Diclofenac Sodium passes into the breast milk only in small quantities that no undesirable effect on the infant are to be expected.

SIDE EFFECTS/ADVERSE REACTIONS:

Gastrointestinal disturbances, peptic ulceration, gastrointestinal bleeding. Other side-effects include headache, dizziness, nervousness, skin rash, pruritus, tinnitus, oedema, depression, drowsiness, insomnia, and blurred vision and other ocular reactions. More severe reactions are rare which include hypersensitivity reactions, impairment of liver and kidney functions, agranulocytosis and thrombocytopenia.

Cardiac Disorders

Uncommon*: Myocardial infarction, cardiac failure, palpitations, chest pain.
* The frequency reflects data from long-term treatment with a high dose (150 mg/day).
Kounis syndrome: Frequency "not known"

Description of Selected Adverse Drug Reactions

Arteriothrombotic events

Meta-analysis and pharmacoepidemiological data point towards an increased risk of arteriothrombotic events (for example myocardial infarction) associated with the use of diclofenac, particularly at a high dose (150 mg daily) and during long-term treatment (see section **WARNINGS AND PRECAUTIONS**).

SYMPTOMS AND TREATMENT OF OVERDOSE:

Symptoms of overdosage include depressed consciousness, hypotension. Treatments include aspiration and gastric lavage and maintain the vital functions and other general measures.

PACKING/PACK SIZE(S):
Blister packs of 100x10's and 10x10's.

JAUHI UBAT DARIPADA KANAK-KANAK
KEEP OUT OF REACH OF CHILDREN

MANUFACTURER/PRODUCT REGISTRATION HOLDER:
DYNAPHARM (M) SDN. BHD. 198001011897 (65683-V)
2497, Mk. 1, Lorong Perusahaan Baru 5,
Kawasan Perusahaan Perai 3,
13600 Perai, Pulau Pinang, Malaysia.

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