DICLOFENAC TABLETS
NEODOL-50

COMPOSITION:
Each enteric-coated tablet contains: Diclofenac Sodium BP 50 mg

CHEMISTRY:
Sodium 2-[(2,6-dichlorophenyl) amino]phenyl]acetate

CATEGORY:
A nonsteroidal anti-inflammatory drug.

PHARMACOOLOGY:
Diclofenac Sodium is a potent inhibitor of cyclooxygenase resulting in reduction of prostaglandin synthesis. It also decreases formation of products of lipo-oxygenase pathway such as leukotriene and reduces polymorph chemo taxis and production of lysosome enzymes and superoxide radicals. Has analgesic and antipyretic activity. It also inhibits platelet aggregation.

PHARMACOKINETICS:
Rapidly and completely absorbed from the gut. Peak plasma levels in 1.5 to 2.5 hrs. Oral bioavailability 50 to 60 % due to first metabolism Cmax and AUC are dose-proportional in the range of 25 to 150 mg. Food delays but does not reduce absorption. Diclofenac enters synovial fluid with sustained high concentrations. Crosses placenta and excreted into breast milk. Extensively metabolised and excreted through bile and urine Terminal half-life is 1.2 to 1.8 hrs.

INDICATIONS AND USES:
Acute and chronic treatment of the signs and symptoms of rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis.

CONTRAINDICATIONS:
Diclofenac is contraindicated in patients with history of Hypersensitivity, or active or suspected peptic ulcer or GI bleeding, and in those who are known to develop asthma, urticarial or other allergic reactions with aspirin or other NSAIDs. Acute porphyria is a contraindication for diclofenac. Hepatic and Renal insufficiency. Not recommended in pregnancy.

The use of high dose diclofenac (150mg/day) for more than 4 weeks is contraindicated in patients with established cardiovascular disease (congestive heart failure, established ischemic heart disease, peripheral arterial disease) or uncontrolled hypertension.

ADVERSE DRUG REACTIONS:
Epigastric pain, nausea, vomiting, diarrhoea, clinical hepatitis, rash, pruritus and depression.

Cardiac disorders
Uncommon*: Myocardial infarction, cardiac failure, palpitations, chest pain
*The frequency reflects data from long-term treatment with high dose (150mg/day)

Description of selected adverse drug reactions
Arteriothrombotic events
Meta-analysis and pharmacoepidemiological data point towards a small 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.

WARNINGS AND PRECAUTIONS:
Gastrointestinal symptoms, ulceration, hematemesis or melaena (which may occur with or without warning symptoms or a previous history and age. Generally more serious in the elderly) ulcerative colitis, Crohn's disease, bleeding diathesis or haematological abnormalities. If abnormal liver function tests persist or worsen, clinical signs or symptoms consistent with liver disease develop or if other manifestations occur (eosinophilia, rash), treatment should be discontinued. Use of Diclofenac Sodium in patients with hepatic porphyria may trigger an attack.

Cardiovascular effects
Treatment with NSAIDs, including diclofenac, particularly at high dose and in long term, may be associated with a small increased risk of serious cardiovascular thrombotic events (including myocardial infarction and stroke).

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 be advised to 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.

DRUG INTERACTIONS:
Serum levels of digoxin and methotrexate are increased as are also those of cyclosporin with their concomitant administration with Diclofenac. Lithium renal clearance is reduced by Diclofenac and lithium side effects may occur during concurrent treatment. Efficacy of diuretics may be reduced by NSAIDs including Diclofenac. Concomitant use of potassium-sparing diuretics may result in increased serum potassium levels. Aspirin displaces Diclofenac from its binding sites.

USE IN PREGNANCY AND LACTATION:
It should be avoided in late pregnancy since such use may lead to premature closure of ductus arteriosus. Like other NSAIDs Diclofenac may inhibit uterine contractions and delay or prolong labour and it is not recommended for use by nursing mothers.

Use of NSAIDs at about 20 weeks gestation or later in pregnancy may cause foetal renal dysfunction leading to oligohydramnios and in some cases, neonatal renal impairment. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Oligohydramnios is often, but not always, reversible with treatment discontinuation.

DOSAGE AND ADMINISTRATION:
Administration as 25 mg and 75mg, patients should be generally maintained on the lowest dosage, consistent with achieving satisfactory and therapeutic response. Encourage to take with food or just after food.

Osteoarthritis : 100 - 150 mg/day in divided doses, 50 mg b.i.d or t.i.d. or 75 mg b.i.d.

Rheumatoid arthritis: 150-200 mg/day, in divided doses, 50 mg t.i.d or q.i.d or 75 mg b.i.d.

Ankylosing spondylitis: 100-125 mg/day, or 25 mg q.i.d with an extra 25 mg extra dose at bed time if necessary.

Special populations
Established cardiovascular disease or significant cardiovascular risk factors
The use of high dose diclofenac (150mg/day) for more than 4 weeks is contraindicated in patients with established cardiovascular disease (congestive heart failure, established ischemic heart disease, peripheral arterial disease) or uncontrolled hypertension. If diclofenac treatment is needed, patients with established cardiovascular disease, uncontrolled hypertension or significant cardiovascular risk factors (e.g. hypertension, hyperlipidaemia, diabetes mellitus and smoking) should be treated only after careful consideration and at doses ≤ 100 mg daily if the treatment is for more than 4 weeks. As the cardiovascular risks of diclofenac may increase with dose and duration of exposure, diclofenac should always be prescribed at the lowest effective daily dose and for the shortest duration possible.

OVERDOSAGE, SYMPTOMS AND ANTIDOTE:
Symptoms may include dizziness, headache, myoclonic encephalopathy, impairment of consciousness, nausea, vomiting, abdominal pain, hematemesis or melaena, peptic ulceration or perforation, jaundice, oliguria or anuria. Gastric lavage should be done as early as possible and the patient should be managed with supportive therapy with dose monitoring.

STORAGE:
Store below 30°C, Keep in a cool, dry place Protect from light.

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