hovid

CLOFENAC SR TABLET

VICLOxx-0 (SIN)3

DESCRIPTION
Round, pink film-coated, bevel-edged with shallow convex faces.

COMPOSITION
Diclofenac Sodium 100 mg/tablet.

ACTIONS AND PHARMACOLOGY
Diclofenac Sodium is a non-steroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic properties. It inhibits the activity of the enzyme cyclo-oxygenase, resulting in decreased formation of precursors of prostaglandins and thromboxanes from arachidonic acid.

Diclofenac SR is a slow release preparation designed to release Diclofenac over a period of time. It is rapidly absorbed after oral administration. Although orally-administered Diclofenac is almost completely absorbed, it is subject to first-pass metabolism so that only 50 to 60% of the drug reaches the systemic circulation in the unchanged form. Diclofenac penetrates synovial fluid, readily crosses the placenta and is excreted in breast milk. It is highly protein bound. The terminal plasma half-life is about 1 to 2 hours. It is metabolised to 4'-hydroxydiclofenac, 5-hydroxydiclofenac, 3'-hydroxydiclofenac and 4',5-dihydroxydiclofenac. It is excreted in the form of glucuronide and sulphate conjugates, mainly in the urine but also in the bile.

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

SIDE EFFECTS/ADVERSE REACTIONS
- Common side effects include nausea, headaches, diarrhoea, epigastric pain, anorexia, dyspepsia, flatulence, abdominal cramps, vertigo and dizziness.
- Skin rashes and eruptions have occasionally been reported and rarely urticaria.
- Isolated effects on the central nervous system include drowsiness, tiredness, impaired hearing, insomnia, irritability, anxiety etc.
- Occasional effects on the kidney include acute renal insufficiency, urinary abnormalities (eg. haematuria, proteinuria), nephrotic syndrome, papillary necrosis and interstitial nephritis.
- Effects on the liver include occasional reports of elevation of serum aminotransferase enzymes (ALT, AST) and rarely liver function disorders.
- Leucopenia, haemolytic anaemia, thrombocytopenia, aplastic anaemia and agranulocytosis have rarely been reported.
- Hypersensitivity reactions (anaphylactic/anaphylactoid systemic reactions, hypotension, bronchospasm) have rarely been reported.
- Many of these cardiovascular effects may occur secondary to NSAID-induced renal function impairment: angina pectoris, irregular heartbeat, congestive heart failure, increased blood pressure and nose bleeds.
- Cases of hair loss, bullous eruptions, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome) and photosensitivity reactions have been reported.

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

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 (150mg daily) and during long-term treatment (see section WARNING AND PRECAUTIONS).

WARNINGS AND PRECAUTIONS
- Patients with a history of gastrointestinal ulceration, haematemesis or melaena should be carefully observed.
- Care should be taken when treating patients with ulcerative colitis, Crohn's disease, haematological abnormalities or bleeding diathesis.
- Caution is recommended in elderly patients and those with renal or hepatic impairment. Monitoring of renal function, hepatic function and blood counts should be performed on long-term NSAID patients, as a precautionary measure.
- Diclofenac sodium may trigger an attack in patients with hepatic porphyria.
- Patients should not drive or operate machinery if they experience dizziness or other central nervous system disturbances.
- Caution in patients who must restrict their sodium intake.
- Diclofenac should be stopped if liver function tests show abnormalities which persist or worsen, or if liver disease develops or if other symptoms such as eosinophilia or rash occur.
- 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 sign of hypersentivity reactions. Discontinue diclofenac sodium immediately if rash occurs.
- **Cardiovascular effects:**
  Treatment with NSAIDs including diclofenac, particularly at high dose and in long term, may be 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 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 mellitus and smoking) should be treated with diclofenac only after careful consideration and only at doses ≤ 100mg 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.

BACK

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 NSAIDs therapy. Although minor upper 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 adverse 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.

USE IN PREGNANCY AND LACTATION

The use of diclofenac sodium is not advisable in pregnancy and lactation.

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.

CONTRAINDICATIONS

- Contraindicated in patients known to be hypersensitive to Diclofenac sodium.
- Contraindicated in patients who when taking aspirin or other non-steroidal anti-inflammatory drugs suffer attacks of asthma, urticaria or acute rhinitis.
- Should not be used in patients with active or suspected peptic ulcer or gastrointestinal bleeding.
- Contraindicated in patients with bone marrow depression.
- The use of high dose diclofenac (150mg/day) for more than 4 weeks is contraindicated in patients with established cardiovascular disease (congestiveheart failure, established ischemic heart disease, peripheral arterial disease) or uncontrolled hypertension.

DRUG INTERACTIONS

- Diclofenac may increase plasma concentrations of lithium, digoxin and methotrexate.
- Concomitant use of diclofenac sodium and other NSAIDs may increase the frequency of side effects.
- Diclofenac may increase cyclosporin nephrotoxicity as a result of their effect on renal prostaglandins.
- There is an increased risk of convulsions if quinolone antibiotics are given while Diclofenac is being taken, and caution is advised when considering their use.
- Increased serum potassium levels may result when Diclofenac is given concomitantly with potassium-sparing diuretics.
  Serum potassium levels should therefore be monitored.
- Care is required when giving anticoagulants with Diclofenac as it may reversibly inhibit platelet aggregation.
- Non-steroidal anti-inflammatory drugs (NSAIDs) may increase the hypoglycemic effect of antidiabetic agents; dosage adjustments of the diabetic agent may be necessary; glipizide and glyburide may not be affected as much as the other oral antidiabetic agents, however, caution with concurrent use is recommended. Diclofenac has also been reported to decrease the effects of antidiabetic agents, leading to hyperglycemia.

SYMPTOMS AND TREATMENT FOR OVERDOSAGE

- **Clinical features:**
  Gastrointestinal symptoms (e.g. abdominal pain, nausea, vomiting); central nervous system effects (eg. lethargy, drowsiness) and renal effects have been reported. More serious effects such as gastrointestinal hemorrhage, acute renal failure, convulsions and coma have also been reported.
- **Treatment for overdosage:**
  Gastric lavage and treatment with activated charcoal should be used as soon as possible after overdosage in order to prevent absorption of the drug. Further treatment is supportive and symptomatic.

DOSAGE AND ADMINISTRATION

- **Adults:**
  Oral, one 100 mg tablet a day. Tablets should be swallowed whole preferably with food.
- **Elderly:**
  Care should be used when treating patients who are frail or have a low body weight as they will in general be more susceptible to adverse reactions. The lowest effective dose should be used in these patients. The standard adult dose may be used for other elderly patients.
- **Children:**
  Not suitable for use in children.

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 (congestiveheart 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 atthe lowest effective daily dose and for the shortest duration possible.

Note: The information given here is limited. For further information, consult your doctor or pharmacist.

Storage:
Store below 25˚C. Protect from moisture.

Presentation/Packing:
Tablet 100 mg x polyethylene bottle of 100's,
Blisters of 1 x 10's, 10 x 10's.
(Not all presentations available locally)

Manufactured by: HOVID Bhd.
121, Jalan Tunku Abdul Rahman, 30010 Ipoh, Malaysia.

Revision date: September 2021