Clofenac®

Diclofenac

Analgesic & Anti-inflammatory

COMPOSITION

Clofenac® 25	: Each enteric coated tablet contains Diclofenac Sodium BP 25 mg.
Clofenac® 50	: Each enteric coated tablet contains Diclofenac Sodium BP 50 mg.
Clofenac® SR	: Each enteric coated tablet contains Diclofenac Sodium BP 100 mg in a sustained release formulation.
Clofenac® injection	: Each 3 ml ampoule contains Diclofenac Sodium BP 75 mg.
Clofenac® Plus injection	: Each 2 ml ampoule contains Diclofenac Sodium BP 75 mg and Lidocaine Hydrochloride USP 20 mg .
Clofenac® Gel	: Each 100 gm gel contains 1.16 gm Diclofenac Diethyl ammonium salt which corresponds to 1 gm Diclofenac Sodium BP.
Clofenac® 12.5 Suppository	: Each suppository contains Diclofenac Sodium BP 12.5 mg.
Clofenac® 50 Suppository	: Each suppository contains Diclofenac Sodium BP 50 mg.

PHARMACOLOGY

Clofenac® contains Diclofenac, which is a potent non-steroidal anti-inflammatory drug (NSAID) with marked analgesic and antipyretic properties. It also has some uricosuric effect. The actions of diclofenac appear to be associated principally with the inhibition of prostaglandin synthesis - by inhibiting cyclooxygenase - the enzyme that catalyzes the formation of prostaglandin precursors (endoperoxides) from arachidonic acid. Following oral administration, diclofenac is rapidly absorbed from the gastro-intestinal tract. Peak plasma concentration following ingestion of an enteric coated tablet occurs at about 2 to 3 hours and that following injection occurs within half an hour.

Diclofenac is 99.7% bound to plasma proteins and plasma half-life for the terminal elimination phase is 1-2 hours. Diclofenac enters the synovial fluid, where maximum concentrations are measured 2-4 hours after the peak plasma values have been obtained. The apparent half-life for elimination from the synovial fluid is 3-6 hours. Diclofenac is extensively metabolized to

a range of phenolic compounds. About 60% of the administered dose is excreted via the kidneys in the form of metabolites and less than 1% in unchanged form. The remainder is excreted via the bile in metabolised form.

Clofenac® Plus Injection contains Diclofenac Sodium BP and Lidocaine Hydrochloride USP. Lidocaine is the most widely used local anaesthetic drug. It acts more rapidly and is more stable than most other local anaesthetics. It is a very useful surface anaesthetic. Like other local anaesthetic, lidocaine impairs the generation and conduction of the nerve impulses by slowing depolarization.

The onset of anaesthesia of lidocaine HCl is more rapid and the duration of action is longer. A 1%-2% solution has a duration of action of about 1-2 hours. Binding of lidocaine to plasma proteins is variable and concentration dependent. Approximately 90% of a parenteral dose of lidocaine is rapidly metabolized in the liver. Less than 10% of a dose is excreted unchanged in the urine.

Clofenac® Gel contains diclofenac sodium BP 1% as diclofenac diethyl ammonium salt. It has been designed for external use. The white creamy non-greasy preparation can easily be rubbed into the skin and its aqueous alcoholic base exerts a soothing and cooling effect on the skin. After local application, the active substance penetrates the skin, accumulates in the underlying tissue and combats both acute and chronic inflammatory reaction. The anti-inflammatory and analgesic properties of Clofenac® Gel elicits a clinical response characterized by a marked decrease in inflammatory swelling of traumatic or rheumatic origin. It affords effective relief from tenderness and pain on movement.

INDICATION

Clofenac® tablets, Clofenac® injection, Clofenac® Plus injection and Clofenac® suppositories contain diclofenac sodium, which is used to relief all grades of pain and inflammation in a wide range of conditions including:

a) Arthritic conditions: Rheumatoid Arthritis, Osteoarthritis, Ankylosing spondylitis, Acute gout. **b)** acute musculoskeletal disorders such as periarthritis (e.g., frozen shoulder), tendinitis, tenosynovitis, bursitis. **c)** other painful conditions resulting from trauma, including fracture, low back pain, sprains, strains, dislocations, orthopaedic, dental and other minor surgery.

Clofenac® Plus injection also contains lidocaine, which acts as a local

anaesthetic. Therefore, the possibility of pain at the injection site, which is most likely to occur after intramuscular injection of normal diclofenac, is minimized if Clofenac® Plus Injection is used.

Clofenac® Gel is used for the local symptomatic relief of pain and inflammation in:

a) trauma of the tendons, ligaments, muscles and joints, e.g, due to sprains, strains and bruises, **b)** localised forms of soft tissue rheumatism.

DOSAGE AND ADMINISTRATION

Clofenac® 25 mg and 50 mg enteric coated tablets :

Adults: 75 - 150 mg daily in 2 to 3 divided doses, preferably after food. Dose should be reduced in long term use.

Clofenac® SR : 1 tablet daily, taken whole with liquid, preferably at meal times. If necessary, the daily dose can be increased to 150 mg by supplementation with conventional tablets.

Children: 1-3 mg of diclofenac/kg body wt. daily in divided doses.

Elderly patients: In elderly or debilitated patients, the lowest effective dosage is recommended, although the pharmacokinetics of diclofenac sodium are not impaired to any clinically relevant extent in elderly patients.

Clofenac® injection/Clofenac® Plus injection :

Adults: One ampoule once (or in severe cases, twice) daily by intramuscular injection.

Renal colic: One ampoule once daily intramuscularly. A further ampoule may be administered after 30 minutes, if necessary. The recommended maximum daily dose of diclofenac is 150 mg, by any route. The recommended maximum daily dose of lidocaine is 200 mg.

Children: In juvenile chronic arthritis, 1-3 mg of diclofenac/kg body wt. daily in divided doses.

Elderly patients: In elderly or debilitated patients, the lowest effective dosage is recommended, commensurate with age and physical status.

Clofenac® Gel : Clofenac® Gel should be rubbed gently into the skin. Depending on the size of the affected site to be treated 2 - 4 gm Clofenac® Gel should be applied 3 - 4 times daily and rubbed in lightly. After application, the hands should be washed unless they are the site being treated.

Use in the elderly: The usual adult dosage may be used.

Clofenac® Gel may also be given to further treatment with other dosage forms of Clofenac®. or as prescribed by the physician.

Clofenac® Suppository : Suppository should be administered rectally.
Adults: 50 mg suppository 2-3 times daily. Maximum daily dose is 150 mg.
Children: 12.5 mg suppository 2-3 times daily, or 1-3 mg/kg per day in divided doses.

CONTRAINDICATION AND PRECAUTION

Diclofenac is contra-indicated for those patients who are hypersensitive to diclofenac. In patients with active or suspected peptic ulcer or gastro-intestinal bleeding, or for those patients in whom attacks of asthma, urticaria or acute rhinitis are precipitated by aspirin or other NSAIDs possessing prostaglandin synthetase inhibiting activity, diclofenac is also contra-indicated.

Because of the presence of lidocaine, Clofenac®-Plus injection is also contra-indicated for those patients who are hypersensitive to local anaesthetics of the amide type, although the incidence is very rare. In patients with Adams-Stokes syndrome or with severe degrees of SA, AV, or intraventricular heart block in the absence of an artificial pacemaker, and for those patients who are hypersensitive to any of the excipients used in the formulation (sodium metabisulphite, mannitol, benzyl alcohol, propylene glycol), this injection is also contra-indicated.

Clofenac® Gel is also contra-indicated to those who are hypersensitive to the gel base.

Renal: Patients with severe hepatic, cardiac or renal insufficiency or the elderly should be kept under close 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 should be discontinued.

All patients who are receiving long term treatment with NSAIDs should be monitored as a precautionary measure (e.g., renal, hepatic function and blood counts).

Clofenac® Gel should not be taken by mouth and should not be used under occlusive, airtight dressings. The gel should not be allowed to come in contact with the eyes or mucous membranes.

SIDE EFFECT

Side effects to diclofenac are usually mild and transient. However, if serious side effects occur, diclofenac should be discontinued.

Gastrointestinal: *Occasional*: epigastric pain, other gastro-intestinal disorders (e.g., nausea, vomiting, diarrhoea, abdominal cramps, dyspepsia, flatulence, anorexia).

Rare: gastro-intestinal bleeding, peptic ulcer (with or without bleeding or perforation), bloody diarrhoea. In isolated cases: lower gut disorders (e.g., non-specific haemorrhagic colitis and exacerbations of ulcerative colitis or Crohn's proctocolitis), pancreatitis, glossitis,constipation, etc.

Clofenac® Plus injection: In very rare instances, injection site disorders may occur. In isolated cases, abscesses and local necrosis may occur. The adverse effects due to lidocaine mainly involve the CNS, are usually of short duration, and are dose related. The CNS reactions may be manifested by drowsiness, dizziness, disorientation, confusion, lightheadedness, etc.

Clofenac® Gel is usually well tolerated. Local irritation, erythema, pruritus or dermatitis may occasionally occur. Although the gel has low systemic absorption, yet the possibility of the systemic side-effects cannot be completely excluded because of use to a relatively large area of skin.

DRUG INTERACTION

Clofenac® Gel: No drug interaction during treatment with diclofenac gel have been reported.

All other dosage forms may have the following drug interactions : *Lithium and digoxin*: Diclofenac 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, although clinical investigations do not appear to indicate any influence on anticoagulant effect. *Antidiabetic agents:* Clinical studies have shown that diclofenac can be given together with oral antidiabetic agents without influencing their clinical effect. *Cyclosporin*: Cases of nephrotoxicity have been reported in patients receiving cyclosporin and diclofenac concomitantly.

Methotrexate: Cases of serious toxicity have been reported when methotrexate and NSAIDs are given within 24 hours of each other.

Quinolone antimicrobials: Convulsions may occur due to an interaction between quinolones and NSAIDs. Therefore, caution should be exercised when considering concomitant therapy of NSAID and quinolones. *Other NSAIDs and steroids*: Co-administration of diclofenac with other systemic NSAIDs and steroids may increase the frequency of unwanted effects. With aspirin, the plasma levels of each is lowered, although no clinical significance is known. *Diuretics*: Various NSAIDs areliable to inhibit the activity of diuretics. Concomitant treatment with potassium-sparing diuretics may be associated with increased serum potassium levels. So, serum potassium should be monitored.

USE IN PREGNANCY AND LACTATION

Diclofenac tablets and injection should not be prescribed during pregnancy, unless there are compelling reasons for doing so. The lowest effective dosage should be used. This type of drugs are not recommended during the last trimester of pregnancy. Very small quantities of diclofenac may be detected in breast milk, but no undesirable effects on the infant are to be expected.

Since no experience has been acquired with diclofenac gel in pregnancy or lactation, it is not recommended for use in these circumstances.

STORAGE CONDITION

Protect from heat, light, and moisture.

Clofenac® Suppository: Store below 30˚C.

HOW SUPPLIED

Clofenac® 25	: Box containing 10 x 10 tablets in blister pack.
Clofenac® 50	: Box containing 20 x 10 tablets in blister pack.
Clofenac® SR	: Box containing 10 x 10 tablets in blister pack.
Clofenac® injection	: Box containing 5 x 2 ampoules of 3 ml in blister pack.
Clofenac® Plus injection	: Box containing 2 x 5 ampoules of 2 ml in blister pack.
Clofenac® Gel 10 gm	: Tube containing 10 gm gel.
Clofenac® 12.5 mg Suppository	: Box containing 2 x 5 suppositories in blister pack.
Clofenac® 50 mg Suppository	: Box containing 2 x 5 suppositories in blister pack.