Diclogesic® (Diclofenac Sodium)

DESCRIPTION:

Diclogesic® (diclofenac sodium) is a non-steroidal anti-inflammatory agent with marked anti-rheumatic, analgesic antipyretic properties.

Inactive Ingredients:

Diclogesic® 25 & 50 Tablets: Silica colloidal anhydrous, microcrystalline cellulose, maize starch, povidone, magnesium stearate, lactose monohydrate, sodium starch glycolate, simethicone, sodium hydroxide, methacrylic acid ethyl acrylate copolymer, triethyl citrate, talc, titanium dioxide, Yellow color (E104) / **Diclogesic® 25** Tablets, Yellow color (E110) / **Diclogesic® 50** Tablets , macrogol.

Diclogesic® Retard 100 Tablets: Hypromellose, microcrystalline cellulose, povidone, magnesium stearate, talc, titanium dioxide, macrogol, brown color.

Diclogesic® Retard 100 Capsules: Sucrose, maize starch, stearic acid, sodium acetate phthalate, salified methacrylic copolymer, macrogol, talc, lactose.

Diclogesic® Suppositories: Silica colloidal anhydrous, L-arginine, white beeswax, hard fat.

PHARMACOLOGY:

Diclofenac is rapidly absorbed when given orally or as rectal suppository. It is absorbed more slowly when given as enteric coated tablet, especially when this dosage form is given with food. Although orally administered diclofenac is almost completely absorbed; it is subject to first-pass metabolism so that about 50% of the drug reaches the systemic circulation in the unchanged form. At therapeutic concentrations, more than 99% of diclofenac is bound to plasma proteins. Diclofenac is eliminated through metabolism and subsequent urinary and biliary excretion of glucuronide and sulfate conjugates of the metabolites. The terminal plasma half-life is about 1 to 2 hours.

INDICATIONS:

Inflammatory and degenerative forms of rheumatism: rheumatoid arthritis, juvenile rheumatoid arthritis, ankylosing spondylitis, osteoarthritis and spondylarthritis. Painful syndromes of the vertebral column.

Non-articular rheumatism. Acute attacks of gout. Post-traumatic and postoperative pain, inflammation, and swelling, e.g. following dental or orthopaedic surgery.

Painful and/or inflammatory conditions in gynaecology, e.g. primary dysmenorrhoea or adnexitis. Migraine attacks (**Diclogesic®** suppositories). As an adjuvant in severe painful inflammatory infections of the ear, nose, or throat, e.g. pharyngotonsillitis, otitis. In keeping with general therapeutic principles, the underlying disease should be treated with basic therapy, as appropriate.

Fever alone is not an indication.

CONTRAINDICATIONS:

Gastric or intestinal ulcer. Known hypersensitivity to the active substance. Like other non-steroidal anti-inflammatory drugs (NSAIDs), **Diclogesic®** is also contraindicated in patients in whom attacks of asthma, urticaria, or acute rhinitis are precipitated by acetylsalicylic acid or other drugs with prostaglandin-synthetase inhibiting activity.

Suppository: proctitis.

SIDE EFFECTS:

Gastrointestinal tract: Occasional: epigastric pain, other gastrointestinal disorders such as nausea, vomiting, diarrhea, abdominal cramps, dyspepsia, flatulence, anorexia. Suppositories: local irritation; Rare: gastrointestinal bleeding (haematemesis, melaena, bloody diarrhea), gastric or intestinal ulcer with or without bleeding or perforation; Isolated cases: aphthous stomatitis, glossitis, oesophageal lesions, diaphragm-like intestinal strictures, lower gut disorders such as non-specific haemorrhagic colitis and exacerbation of ulcerative colitis or Crohn's disease, constipation, pancreatitis, exacerbation of haemorrhoids.

Central (and peripheral) nervous system: Occasional: headache, dizziness, vertigo; Rare: drowsiness; Isolated cases: sensory disturbances, including paresthesias, memory disturbances, disorientation, insomnia, irritability, convulsions, depression, anxiety, nightmares, tremor, psychotic reactions, aseptic meningitis.
Special senses: Isolated cases: disturbances of vision (blurred vision, diplopia), impaired hearing, tinnitus, taste disturbances.
Skin: Occasional: rashes; Rare: urticaria; Isolated cases: bullous eruptions, eczema, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (acute toxic epidermolysis), erythroderma (exfoliative dermatitis), loss of hair, photosensitivity reaction, purpura, including allergic purpura.
Kidney: Rare: oedema; Isolated cases: acute renal failure, haematuria, proteinuria, interstitial nephritis, nephritic syndrome, papillary necrosis.
Liver: Frequent: elevation of serum aminotransferase enzymes (SGOT, SGPT), occasionally moderate (≥3 times the upper limit of normal) or marked (≥8 times the upper limit of normal); Rare: hepatitis with or without jaundice, in isolated cases fulminant.
Blood: Isolated cases: thrombocytopenia, leucopenia, agranulocytosis, haemolytic anaemia, aplastic anaemia.
Hypersensitivity: Rare: hypersensitivity reactions such as asthma, systemic anaphylactic / anaphylactoid reactions including hypotension; Isolated cases: vasculitis, pneumonitis; Cardiovascular system: Isolated cases: palpitation, chest pain, hypertension, congestive heart failure.

WARNINGS AND PRECAUTIONS:

- **Cardiovascular Risk:**
  NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.
  NSAIDs are contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.
- **Gastrointestinal Risk:**
  NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events.

Careful diagnosis and close medical surveillance is imperative in patients with symptoms indicative of gastrointestinal disorders or a history suggestive of gastric or intestinal ulceration, in patients with ulcerative colitis or Crohn's disease, and in patients suffering from impaired hepatic function.
Gastrointestinal bleeding or ulceration/perforation generally have more serious consequences in the elderly. They can occur at any time during treatment, with or without warning symptoms or a previous history.
In the rare cases where gastrointestinal bleeding or ulceration occurs in patients receiving **Diclogesic®**, the drug should be withdrawn. Owing to the importance of prostaglandins in maintaining renal blood flow, particular caution is called for in patients with impaired cardiac or renal function, the elderly, patients being treated with diuretics, and patients with substantial extracellular volume depletion from any cause, e.g. before or after major surgery. Monitoring of renal function is recommended as a precautionary measure when using **Diclogesic®** in such cases. Discontinuation of therapy is usually followed by recovery to the pretreatment state.
Caution is indicated in the elderly on basic medical grounds. In particular, it is recommended that the lowest effective dosage be used in frail elderly patients or those with a low bodyweight.
As with other NSAIDs, values of one or more liver enzymes may increase during treatment with **Diclogesic®**. Although this has been observed with diclofenac in clinical studies and may occur in around 15% of patients, it is rarely accompanied by clinical symptoms. The clinical significance of this phenomenon is unknown. In the majority of cases, increases are borderline. Occasionally (in 2.5%) the increases observed were moderate (≥3-<8 times the upper limit of normal), while the incidence of marked increases (≥8 times the upper limit of normal) remained about 1%. In the above-mentioned clinical studies, liver enzyme elevations were accompanied by clinically apparent liver damage in 0.5% of cases.
The enzyme elevations were generally reversible on discontinuation of the drug. As with other NSAIDs hepatic function should be monitored regularly during long-term treatment with **Diclogesic®**.

If abnormal liver function tests persist or worsen, if clinical signs or symptoms consistent with liver disease (e.g. hepatitis) develop or if other manifestations occur (e.g. eosinophilia, rash, etc.), **Diclogesic®** should be discontinued. In addition to liver enzyme elevations, there have been reports of rare cases of severe hepatic reactions, including jaundice, and isolated cases of fulminant hepatitis with a fatal course.
Hepatitis may occur without prodromal symptoms. Caution is called for when using **Diclogesic®** in patients with hepatic porphyria, since it may trigger an attack. During prolonged treatment with **Diclogesic®**, as with other NSAIDs, monitoring of the blood count is recommended.
Like other NSAIDs, **Diclogesic®** may temporarily inhibit platelet aggregation. Patients with defects of haemostasis should be carefully monitored. As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur without earlier exposure to the drug.
Like other NSAIDs, **Diclogesic®** may mask the signs and symptoms of infection due to its pharmacodynamic properties.
This product contains:
Yellow color (E110): May cause allergic reactions.
Lactose: If the patient has been told by the doctor that he has intolerance to some sugars, he should contact his doctor before taking this medicinal product.
Note: Patients experiencing dizziness or other central nervous system disturbances, including visual disturbances, should not drive or operate machinery.
Pregnancy and lactation: 1st and 2nd trimesters: Pregnancy category B.
Studies in animals have not indicated any risk to the fetus, but no controlled studies have been carried out in pregnant women.
3rd trimester: Pregnancy category D. Owing to the possibility of uterine inertia and/or premature closure of the ductus arteriosus, **Diclogesic®** should not be used.
Following oral doses of 50 mg administered every 8 hours, the active substance passes into the breast milk, but in quantities so small that no undesirable effects on the infant are to be expected.

DRUG INTERACTIONS:

Lithium, digoxin: when given concomitantly, diclofenac may raise plasma concentrations of lithium and digoxin.
Diuretics: like other NSAIDs, diclofenac may reduce the efficacy of diuretics. Concomitant treatment with a potassium-sparing diuretic may be associated with increased serum potassium levels, which should therefore be monitored frequently.
NSAIDs: concomitant administration of systemic NSAIDs may increase the frequency of undesirable effects.
Anticoagulants: although clinical investigations do not appear to indicate that diclofenac affects the action of anticoagulants concomitantly. Close monitoring of such patients is therefore recommended.
Antidiabetics: clinical studies have shown that diclofenac can be given together with oral antidiabetic agents without influencing their clinical effect.However, isolated cases have been reported of both hypoglycemic and hyperglycemic effects necessitating changes in the dosage of antidiabetic agents during treatment with diclofenac.
Methotrexate: caution is called for when NSAIDs are administered less than 24 hours before or after treatment with methotrexate, since blood concentrations of methotrexate may rise and the toxicity of this substrate be increased.
Cyclosporin: the effects of NSAIDs on renal prostaglandins may increase the nephrotoxicity of cyclosporine.
Quinolone antibacterials: there have been isolated reports of convulsions which may have been due to concomitant use of quinolones and NSAIDs.

DOSAGE AND ADMINISTRATION:

Adults: The recommended initial daily dosage is 100-150 mg. In milder cases, as well as for long-term therapy, 75-100 mg daily is usually sufficient. The total daily dosage should be divided into 2-3 doses. To suppress nocturnal pain and morning stiffness, treatment with tablets during the day can be supplemented by the administration of a suppository at bedtime (up to a maximum daily dose of 150 mg). In primary dysmenorrhoea the daily dosage should be individually adjusted and is generally 50-150 mg. Initially a dose

of 50-100 mg should be given and if necessary, raised in the course of several menstrual cycles up to a maximum of 200 mg/day. Treatment should be started upon appearance of the first symptoms and, depending on the symptomatology, continued for a few days.
The tablets should be swallowed whole with liquid, preferably before meals. Treatment of migraine attacks with **Diclogesic®** suppositories should be started with a dose of 100 mg at the first signs of impending attack. Additional suppositories up to 100 mg may be taken on the same day if required. Should the patient require further therapy on the following day, the maximum daily dosage should be limited to 150 mg in divided doses.
Children: Children aged 1 year or over should be given 0.5-2 mg/kg bodyweight daily, in 2-3 divided doses depending on the severity of the disorder. For treatment of juvenile rheumatoid arthritis the daily dosage can be raised up to a maximum of 3 mg/kg, in divided doses.
The 12.5 mg suppositories are for use in children over 5 years of age and weighing 18 kg or more with chronic juvenile rheumatoid arthritis.
Diclogesic® should not be used in children under 1 years of age.
Owing to the high content of active substance, **Diclogesic®** tablets of 50 mg, tablets or capsules of 100 mg and suppositories of 50 mg and 100 mg are not recommended for use in children.

OVERDOSAGE:
Management of acute poisoning with NSAIDs consists essentially of supportive and symptomatic measures. There is no typical clinical picture associated with overdosage of diclofenac.
The following therapeutic measures should be taken in cases of overdosage: Absorption should be prevented as soon as possible after the overdosage by means of gastric lavage and treatment with activated charcoal. Supportive and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastrointestinal irritation, and respiratory depression.
Specific therapy such as forced diuresis, dialysis, or haemoperfusion is unlikely to be helpful in accelerating the elimination of NSAIDs because of their high protein-binding rate and extensive metabolism.

PRESENTATIONS:
Diclogesic® 25 Tablets: Packs of 20 and 500 enteric coated tablets. Each tablet contains 25 mg Diclofenac Sodium.
Diclogesic® 50 Tablets: Packs of 20 and 500 enteric coated tablets. Each tablet contains 50 mg Diclofenac Sodium.
Diclogesic® Retard 100 Tablets: Packs of 10 and 500 film coated tablets. Each tablet contains 100 mg Diclofenac Sodium.
Diclogesic® Retard 100 Capsules: Packs of 12 and 500 capsules. Each capsule contains 100 mg Diclofenac Sodium.
Diclogesic® 12.5 Children Suppositories: Packs of 10 suppositories. Each suppository contains 12.5 mg Diclofenac Sodium.
Diclogesic® 50 Suppositories: Packs of 10 suppositories. Each suppository contains 50 mg Diclofenac Sodium.
Diclogesic® 100 Suppositories: Packs of 5 suppositories. Each suppository contains 100 mg Diclofenac Sodium.
Diclogesic® is also available as gel, 75 mg ampoules and eye drops.

STORAGE CONDITIONS:
Tablets and Capsules: Protect from light. Store in a dry place below 25° C.
Suppositories: Store up to 25° C. Do not freeze.

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