Lisodim SR Tablets

لائیسوڈم ایس آر گولیاں

(ڈائی کلوفینک سوڈیم ایکسٹینڈڈ ریلیز ٹیبلٹس)

(Diclofenac Sodium Extended-Release Tablets USP)

COMPOSITION: Each film coated sustained release tablet contains:
Diclofenac Sodium USP ... 100mg. [USP Specs.]

DESCRIPTION: Lisodim SR Tablets 100mg contains Diclofenac Sodium, which belongs to the group of medicines called non-steroidal anti-inflammatory drugs (NSAIDs), it reduces pain and inflammation. **Lisodim SR** Tablets 100mg specially formulated to release the Diclofenac Sodium slowly.

CLINICAL PHARMACOLOGY:
Mechanism of Action: The mechanism of action of Diclofenac, like that of other NSAIDs, is not completely understood but involves inhibition of cyclooxygenase (COX-1 and COX-2). Diclofenac is a potent inhibitor of prostaglandin (PG) synthesis in vitro. Diclofenac concentrations reached during therapy have produced in vivo effects. Prostaglandins sensitize afferent nerves and potentiate the action of bradykinin in inducing pain in animal models. Prostaglandins are mediators of inflammation.

PHARMACOKINETICS: After ingestion of the Diclofenac slow release tablet, the active principle is slowly released into the gastrointestinal contents. Once released from the tablet, diclofenac is rapidly absorbed from the gastrointestinal tract but is subject to first-pass metabolism. Peak plasma concentrations occur about 4.5 hours after administration of the prolonged release tablets when taken with a meal. Food and antacids decrease the rate but not the extent of absorption of Diclofenac. The systemic availability of Diclofenac from the SR formulations is on average 82% of that achieved with the same dose of enteric-coated tablets (possibly due to release rate dependent first-pass metabolism). The active substance is 99.7% bound to plasma proteins, mainly albumin. Diclofenac enters the synovial fluid and peak synovial fluid concentrations at steady state exceed plasma concentrations. Furthermore, elimination from the synovial fluid is slower than from plasma. Diclofenac and its metabolites cross the placenta and traces of diclofenac have been found in the milk of lactating women. The half-life for the terminal elimination phase is 3 hours. Approximately 60% of the administered dose is excreted via the kidneys in the form of metabolites and less than 1% in unchanged form. About 30% of the dose is excreted via the bile in metabolised form. Five Diclofenac metabolites have been identified in human plasma and urine. The metabolites include 4'-hydroxy-, 5-hydroxy-, 3'-hydroxy-, 4',5-dihydroxy- and 3'-hydroxy-4'-methoxy-Diclofenac. The major Diclofenac metabolite, 4'-hydroxy-Diclofenac, has very weak pharmacologic activity. The formation of 4'-hydroxy Diclofenac is primarily mediated by CYP2C9. Both Diclofenac and its oxidative metabolites undergo glucuronidation or sulfation followed by biliary excretion. Acylglucuronidation mediated by UGT2B7 and oxidation mediated by CYP2C8 may also play a role in Diclofenac metabolism. CYP3A4 is responsible for the formation of minor metabolites, 5-hydroxy- and 3'-hydroxy-Diclofenac. In patients with renal dysfunction, peak concentrations of metabolites 4'-hydroxy- and 5-hydroxy-Diclofenac were approximately 50% and 4% of the parent compound after single oral dosing compared to 27% and 1% in normal healthy subject.

INDICATIONS: Adults and elderly: Relief of all grades of pain and inflammation in a wide range of conditions, including: **(i)** arthritic conditions: rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, acute gout. **(ii)** acute musculo-skeletal disorders such as periarthritis (for example frozen shoulder), tendinitis, tenosynovitis, bursitis. **(iii)** other painful conditions resulting from trauma, including fracture, low back pain, sprains, strains, dislocations, orthopaedic, dental and other minor surgery.
Children: Diclofenac Sodium 100mg sustain-release tablets are not suitable for children.

DOSAGE AND ADMINISTRATION: Adults: One 100mg Diclofenac sodium prolonged-release tablet daily. If necessary, the daily dosage can be increased to 150mg by supplementation with the conventional dosage forms containing Diclofenac Sodium 25mg or 50mg. The recommended maximum daily dose of Diclofenac Sodium is 150mg.

SPECIAL POPULATIONS: Elderly: In particular it is recommended that the lowest effective dosage be used in frail elderly patients or those with a low body weight and the patient should be monitored for GI bleeding during NSAID therapy.
Cardiovascular and significant cardiovascular risk factors: Diclofenac is contraindicated in patients with established congestive heart failure (NYHA II-IV), ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease. Patients with congestive heart failure (NYHA-I) or significant risk factors for cardiovascular disease should be treated with Diclofenac only after careful consideration. Since cardiovascular risks with Diclofenac may increase with dose and duration of exposure, the lowest effective daily dose should be used and for the shortest duration possible.
Renal impairment: Diclofenac is contraindicated in patients with renal failure. Caution is advised when administering diclofenac to patients with mild to moderate renal impairment.
Hepatic impairment: Diclofenac is contraindicated in patients with hepatic failure. Caution is advised when administering diclofenac to patients with mild to moderate hepatic impairment.

CONTRAINDICATIONS: • Active, gastric or intestinal ulcer, bleeding or perforation. • History of gastrointestinal bleeding or perforation, relating to previous NSAIDs therapy. • Last trimester of pregnancy. • Hepatic failure. • Renal failure. • Established congestive heart failure (NYHA-II-IV), ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease. • Like other non-steroidal anti-inflammatory drugs (NSAIDs), Diclofenac is also contraindicated in patients in whom attacks of asthma, angioedema, urticarial or acute rhinitis are precipitated by ibuprofen, acetylsalicylic acid or other nonsteroidal anti-inflammatory drugs.

WARNINGS AND PRECAUTIONS: Gastrointestinal effects: Gastrointestinal bleeding (haematemesis, melaena), ulceration or perforation, which can be fatal has been reported with all NSAIDs including Diclofenac, and may occur at any time during treatment, with or without warning symptoms or a previous history of serious gastrointestinal (GI) events. They generally have more serious consequences in the elderly. If gastrointestinal bleeding or ulceration occurs in patients receiving Diclofenac, the medicinal product should be withdrawn.

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Hepatic impairment: Close medical surveillance is required when prescribing Diclofenac to patients with impairment of hepatic function, as their condition may be exacerbated. As with other NSAIDs, including Diclofenac, values of one or more liver enzymes may increase. During prolonged treatment with diclofenac, regular monitoring of hepatic function is indicated as a precautionary measure. 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.
Renal impairment: As fluid retention and oedema have been reported in association with NSAID therapy, including Diclofenac, particular caution is called for and in patients with impaired cardiac or renal function, history of hypertension, the elderly, patients receiving concomitant treatment with diuretics or medicinal products that can significantly impact renal function, and in those 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 Diclofenac in such cases. Discontinuation of therapy is usually followed by recovery to the pre-treatment state.
Skin effects: Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs, including Diclofenac. Diclofenac Sodium tablets should be discontinued at the first appearance of skin rash, mucosal lesions or any other signs of hypersensitivity.
Haematological effects: During prolonged treatment with Diclofenac, as with other NSAIDs, monitoring of the blood count is recommended. Diclofenac may reversibly inhibit platelet aggregation. Patients with defects of haemostasis, bleeding diathesis or haematological abnormalities should be carefully monitored.
Pre-existing asthma: Like other drugs that inhibit prostaglandin synthetase activity, Diclofenac sodium and other NSAIDs can precipitate bronchospasm if administered to patients suffering from, or with a previous history of bronchial asthma.

PREGNANCY AND LACTATION:
Pregnancy: Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. If Diclofenac is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible. Consequently, diclofenac sodium tablets are contraindicated during the third trimester of pregnancy.
Breast-feeding: Like other NSAIDs, Diclofenac passes into the breast milk in small amounts. Therefore, Diclofenac should not be administered during breast feeding in order to avoid undesirable effects in the infant.

SIDE EFFECTS: The following common side effects include those reported with either short-term or long-term use.
Nervous system disorders: Headache & dizziness.
Ear and labyrinth disorders: Vertigo & Vertigo.
Gastrointestinal disorders: Common: Nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, flatulence & anorexia.
Hepatobiliary disorders: Transaminases increased.
Skin and subcutaneous tissue disorders: Rash.

DRUG INTERACTIONS: Lithium: If used concomitantly, Diclofenac may raise plasma concentrations of lithium. Monitoring of the serum lithium level is recommended.
Digoxin: If used concomitantly, Diclofenac may raise plasma concentrations of digoxin. Monitoring of the serum digoxin level is recommended.
Diuretics and Anti-hypertensive agents: Like other NSAIDs, concomitant use of Diclofenac with diuretics or antihypertensive agents (e.g. beta-blockers, angiotensin converting enzyme (ACE) inhibitors) may cause a decrease in their antihypertensive effect via inhibition of vasodilatory prostaglandin synthesis. Therefore, the combination should be administered with caution and patients, especially the elderly, should have their blood pressure periodically monitored. Patients should be adequately hydrated.
Drugs known to cause hyperkalemia: Concomitant treatment with potassium-sparing diuretics, ciclosporin, tacrolimus or trimethoprim may be associated with increased serum potassium levels, which should therefore be monitored frequently.
Antidiabetics: Clinical studies have shown that Diclofenac can be given together with oral antidiabetic agents without influencing their clinical effect. However, there have been isolated reports of hypoglycaemic and hyperglycaemic effects necessitating changes in the dosage of the antidiabetic agents during treatment with diclofenac. For this reason, monitoring of the blood glucose level is recommended as a precautionary measure during concomitant therapy.
Methotrexate: Diclofenac can inhibit the tubular renal clearance of methotrexate hereby increasing methotrexate levels. Caution is recommended when NSAIDs, including diclofenac, are administered less than 24 hours before treatment with methotrexate, since blood concentrations of methotrexate may rise and the toxicity of this substance be increased.

OVERDOSE: Symptoms: There is no typical clinical picture resulting from diclofenac over dosage. Over dosage can cause symptoms such as headache, nausea, vomiting, epigastric pain, gastrointestinal haemorrhage, diarrhoea, dizziness, disorientation, excitation, coma, drowsiness, tinnitus, fainting or convulsions. In the case of significant poisoning acute renal failure and liver damage are possible.
Therapeutic measure: Management of acute poisoning with NSAIDs, including diclofenac, essentially consists of supportive measures and symptomatic treatment. Supportive measures and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastrointestinal disorder, and respiratory depression. Activated charcoal may be considered after ingestion of a potentially toxic overdose, and gastric decontamination (e.g. vomiting, gastric lavage) after ingestion of a potentially life threatening overdose.

INSTRUCTIONS: Store below 30°C. Protect from heat, light and moisture. Keep out of the reach of children.

PRESENTATION: Lisodim SR Tablets 100mg are available in a blister pack of 30's.

ہدایات: ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

Manufactured by: **NABIQASIM INDUSTRIES (PVT.) LTD.**
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