

SoznacTM
(Aceclofenac)
Tablets
100mg

سوزنیک ۱۰۰ ملی گرام
ٹیبلٹس
(ایسکلو فنیک)

QUALITATIVE AND QUANTITATIVE COMPOSITION

SoznacTM Tablet 100mg

Each film-coated tablet contains:

Aceclofenac B.P.100mg

Innovator's Specification

DESCRIPTION

Aceclofenac is a non-steroidal agent with marked anti-inflammatory and analgesic properties.

CLINICAL PHARMACOLOGY

Pharmacodynamics: The mode of action of aceclofenac is largely based on the inhibition to prostaglandin synthesis. Aceclofenac is a potent inhibitor of the enzyme cyclo-oxygenase, which is involved in the production of prostaglandins. **Pharmacokinetics:** After oral administration, aceclofenac is rapidly and completely absorbed as unchanged drug. Peak plasma concentrations are reached approximately 1.25 to 3.00 hours following ingestion. Aceclofenac penetrates into the synovial fluid, where the concentrations reach approximately 57% of those in plasma. The volume of distribution is approximately 25 L. The mean plasma elimination half-life is around 4 hours. Aceclofenac is highly proteinbound (>99%). Aceclofenac circulates mainly as unchanged drug. 4'-Hydroxyaceclofenac is the main metabolite detected in plasma. Approximately two-thirds of the administered dose is excreted via the urine, mainly as hydroxymetabolites.

INDICATION: Aceclofenac is indicated for the relief of pain and inflammation in osteoarthritis, rheumatoid arthritis and ankylosing spondylitis.

CONTRAINDICATIONS: Hypersensitivity to the active substance or to any of the excipients. Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding). NSAIDs are contraindicated in patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema or urticaria) in response to ibuprofen, aspirin, or other nonsteroidal anti-inflammatory drugs. Hepatic failure and renal failure. Patients with established congestive heart failure (NYHA II-IV), ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease. History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy. Active bleedings or bleeding disorders. Aceclofenac should not be prescribed during pregnancy, especially during the last trimester of pregnancy, unless there are compelling reasons for doing so. The lowest effective dosage should be used.

INTERACTIONS: Other analgesics including cyclooxygenase-2 selective inhibitors: Avoid concomitant use of two or more NSAIDs (including aspirin) as this may increase the risk of adverse effects, including GI bleeding.

Anti-hypertensives: NSAID's may reduce the effect of antihypertensives. The risk of acute renal insufficiency, which is usually reversible, may be increased in some patients with compromised renal function (e.g. dehydrated patients or elderly patients) when ACE inhibitors or angiotensin II receptor antagonists are combined with NSAIDs. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.

Diuretics: Aceclofenac, like other NSAIDs, may inhibit the activity of diuretics. Diuretics can increase the risk of nephrotoxicity of NSAIDs. Although it was not shown to affect blood pressure control when co-administered with bendrofluzide, interactions with other diuretics cannot be ruled out. When concomitant administration with potassium-sparing diuretics is employed, serum potassium should be monitored. **Cardiac glycosides, like digoxin:** NSAIDs may

exacerbate cardiac failure, reduce GFR (glomerular filtration rate) and inhibit the renal clearance of glycosides, resulting in increased plasma glycoside levels. The combination should be avoided unless frequent monitoring of glycoside levels can be performed. **Lithium:** Several NSAID drugs inhibit the renal clearance of lithium, resulting in increased serum concentrations of lithium. The combination should be avoided unless frequent monitoring of lithium can be performed.

Methotrexate: The possible interaction between NSAIDs and methotrexate should be born in mind also when low doses of methotrexate are used, especially in patients with decreased renal function. When combination therapy has to be used, the renal function should be monitored. Caution should be exercised if both an NSAID and methotrexate are administered within 24 hours of each other, since NSAIDs may increase plasma levels of methotrexate, resulting in increased toxicity. **Mifepristone:** NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone. **Corticosteroids:** Increased risk of gastrointestinal ulceration or bleeding. **Anti-coagulants:** NSAIDs may enhance the effects of anti-coagulants, such as warfarin. Close monitoring of patients on combined anti-coagulants and Aceclofenac therapy should be undertaken. **Quinolone antibiotics:** Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions. **Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs):** Increased risk of gastrointestinal bleeding. **Cyclosporin, tacrolimus:** Administration of NSAID drugs together with cyclosporin or tacrolimus is thought to increase the risk of nephrotoxicity due to decreased synthesis of prostacyclin in the kidney. During combination therapy it is therefore important to carefully monitor renal function. **Zidovudine:** Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There are indications of an increased risk of haemarthroses and haematoma in HIV(+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen. **Antidiabetic agents:** There have been isolated reports of hypoglycaemic and hyperglycaemic effects. Thus with Aceclofenac, consideration should be given to adjustment of the dosage of hypoglycaemic agents.

USE IN SPECIFIC POPULATION

Pregnancy & Fertility: During the first and second trimester of pregnancy, aceclofenac should not be given unless clearly necessary. If aceclofenac 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. Aceclofenac is contraindicated during the third trimester of pregnancy. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of Aceclofenac should be considered. The use of Aceclofenac be avoided in pregnancy and lactation unless the potential benefits to the other outweigh the possible risks to the foetus.

WARNINGS AND PRECAUTIONS Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms. **Elderly:** The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal.

Respiratory disorders: Caution is required if administered to patients suffering from, or with a previous history of, bronchial asthma since NSAIDs have been reported to precipitate bronchospasm in such patients. **Cardiovascular, Renal and Hepatic Impairment:** The administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics or recovering from major surgery, and the elderly. Renal function should be monitored in these patients. **Renal:** Patients with mild to moderate renal impairment should be kept under surveillance, since the use of NSAIDs may result in deterioration of renal function. The lowest effective dose should be used and renal function monitored regularly. Effects on renal function are usually reversible on withdrawal of Aceclofenac. **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), Aceclofenac should be discontinued. Close medical surveillance is necessary in patients suffering from mild to moderate impairment of hepatic function. Hepatitis may occur without prodromal symptoms. Use of Aceclofenac in patients with hepatic porphyria may trigger an attack. **Cardiovascular and cerebrovascular effects:** Patients with congestive heart failure (NYHA-I) and patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) should only be treated with aceclofenac after careful consideration. As the cardiovascular risks of aceclofenac may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used.

Gastrointestinal bleeding, ulceration and perforation: GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events. The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation, and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk. Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as systemic corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or antiplatelet agents such as aspirin. When GI bleeding or ulceration occurs in patients receiving aceclofenac, the treatment should be withdrawn. **SLE and mixed connective tissue disease:** In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis. **Dermatological:** 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. Aceclofenac should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity. Exceptionally, varicella can trigger serious cutaneous and soft tissues infections complications. **Hypersensitivity reactions:** As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur without earlier exposure to the drug. **Haematological:** Aceclofenac may reversibly inhibit platelet aggregation. Long-term treatment: All patients who are receiving NSAIDs should be monitored as a precautionary measure e.g. renal, hepatic function (elevation of liver enzymes may occur) and blood counts.

ADVERSE REACTIONS The most commonly-observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease have been reported following administration. Pancreatitis has been reported very rarely. Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of (a) non-specific allergic reactions and anaphylaxis (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angiodema and, more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme). Cardiovascular and cerebrovascular: Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment. Exceptionally, occurrence of serious cutaneous and soft tissues infections complications during varicella has been reported in association with NSAID treatment. Other adverse reactions reported less commonly include: Renal: interstitial

nephritis. Neurological and special senses: optic neuritis, reports of aseptic meningitis (especially in patients with existing auto immune disorders, such as systemic lupus erythematosus, mixed connective tissue disease), with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation, confusion, hallucinations, malaise and drowsiness. Haematological: agranulocytosis, aplastic anaemia. Dermatological: Bullous reactions including Stevens Johnson Syndrome and Toxic Epidermal Necrolysis (very rare). Photosensitivity. If serious adverse reactions occur, Aceclofenac should be withdrawn.

DOSAGE AND ADMINISTRATION

Posology Adults: The recommended dose is 200 mg daily, taken as two separate 100 mg doses, one tablet in the morning and one in the evening. **Paediatric population:** There are no clinical data on the use of Aceclofenac in children and therefore it is not recommended for use in children. **Elderly:** If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy. **Renal insufficiency:** There is no evidence that the dosage of Aceclofenac needs to be modified in patients with mild renal impairment, but as with other NSAIDs caution should be exercised. **Hepatic insufficiency:** There is some evidence that the dose of Aceclofenac should be reduced in patients with hepatic impairment and it is suggested that an initial daily dose of 100 mg be used. **Method of administration:** To be taken preferably with or after food. The tablets should be swallowed whole with a sufficient quantity of liquid. **Overdose:** Symptoms include headache, nausea, vomiting, epigastric pain, gastrointestinal irritation, gastrointestinal bleeding, rarely diarrhoea, disorientation, excitation, coma, drowsiness, dizziness, tinnitus, hypotension, respiratory depression, fainting, occasionally convulsions. In cases of significant poisoning acute renal failure and liver damage are possible. **Management** Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adults, gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose. Renal and liver function should be closely monitored. Patients should be observed for at least four hours after ingestion of potentially toxic amounts. In case of frequent or prolonged convulsions, patients should be treated with intravenous diazepam. Other measures may be indicated by the patient's clinical condition. Management of acute poisoning with oral aceclofenac essentially consists of supportive and symptomatic measures for complications such as hypotension, renal failure, convulsions, gastro-intestinal irritation, and respiratory depression.

DOSAGE: As directed by the physician. **INSTRUCTIONS:** Store below 30°C. Protect from heat, light and moisture. Keep all medicines out of the reach of children.

PRESENTATION

Soznac™ Tablet 100mg Available in 1x10's Alu-PVC Blister pack of Tablet.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایت: ۳۰ ڈگری سینٹی گریڈ سے کم پر رکھیں۔

گرمی، روشنی اور نمی سے محفوظ رکھیں۔

تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

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