

Voren

(Diclofenac Sodium)

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Each **Voren** 25mg enteric coated tablet contains 25mg of diclofenac sodium.
Each **Voren** 50mg enteric coated tablet contains 50mg of diclofenac sodium.
Each **Voren** 50mg Microtech capsule contains 50mg of diclofenac sodium (as enteric coated pellets).
Each **Voren SR** 100mg sustained release tablet contains 100mg of diclofenac sodium.

Diclofenac sodium is a nonsteroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic properties. Diclofenac inhibits prostaglandin synthesis by interfering with the action of prostaglandin synthetase. This inhibitory effect may partially explain its actions.

Absorption: Diclofenac is 100% absorbed after oral administration. However, due to first-pass metabolism, only about 50% of the absorbed dose is systemically available. Food has no significant effect on the extent of diclofenac absorption. However, there is usually a delay in the onset of absorption of 1 to 4.5 hours and a reduction in peak plasma levels of <20%. The same amount of active substance is released and absorbed from SR tablets as from enteric-coated tablets. Mean peak plasma concentrations of diclofenac are reached at 4 hours after 100mg SR. 100mg SR is a modified release preparation and plasma concentrations of diclofenac of 13ng/mL can be recorded at 24 hours after administration. Absorption is unaffected by food.

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). As a result of the slower release of active substance, peak plasma concentrations are lower than for the equivalent enteric-coated tablets. Pharmacokinetic behaviour does not change on repeated administration. Accumulation does not occur, provided the recommended dosage intervals are observed.

Distribution: Diclofenac is more than 99% bound to human serum proteins, primarily to albumin. Diclofenac diffuses into and out of the synovial fluid.

Metabolism: Five diclofenac metabolites have been identified in human plasma and urine.

Excretion: Approximately 65% of the dose is excreted in the urine and approximately 35% in the bile as conjugates of unchanged diclofenac plus metabolites. The terminal half-life of unchanged diclofenac is approximately 2 hours.

Hepatic Insufficiency: Hepatic metabolism accounts for almost 100% of diclofenac sodium elimination, so patients with hepatic disease may require reduced doses of diclofenac sodium compared to patients with normal hepatic function.

Renal Insufficiency: Diclofenac pharmacokinetics has been investigated in subjects with renal insufficiency. No differences in the pharmacokinetics of diclofenac have been detected in studies of patients with renal impairment. In patients with renal impairment (inulin clearance 60-90, 30-60, and <30 mL/min; N=6 in each group), AUC values and elimination rate were comparable to those in healthy subjects.

Acute gout, pain and inflammation in rheumatic disease and in other musculoskeletal disorders, rheumatoid arthritis, osteoarthritis, periarthritis (especially frozen shoulder), low back pain, tendinitis, tenosynovitis, bursitis, sprains, strains and dislocations, relief of pain in fractures, ankylosing spondylitis.

It may be used in the control of pain and inflammation in orthopaedic, dental and other minor surgery.

Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals. The maximum daily dose of diclofenac sodium should not exceed 150 mg.

Adults: One **Voren** tablet 50mg twice daily. Dose can be increased to one **Voren** tablet 50mg thrice daily in severe cases. One **Voren** Microtech capsule 50mg twice daily. Dose can be increased to one **Voren** capsule thrice daily in severe cases. One **Voren** SR tablet 100mg daily. If necessary the daily dosage can be increased to 150 mg by supplementation with the conventional dosage forms containing **Voren** 25 mg or 50mg. Diclofenac sodium tablets should be swallowed whole with liquid preferably at mealtime.

Children: In children the dosage is 1 to 3 mg/kg daily in divided doses.

In patients taking diclofenac sodium, or other NSAIDs, the most frequently reported adverse experiences occurring in approximately 1%-10% of patients are:

Gastrointestinal symptoms including: abdominal pain, constipation, diarrhea, dyspepsia, flatulence, gross bleeding/perforation, heartburn, nausea, GI ulcers (gastric/duodenal) and vomiting.

Abnormal renal function, anemia, dizziness, edema, elevated liver enzymes, headache, increased bleeding time, pruritus, rashes and tinnitus.

Additional adverse experiences reported occasionally include:

Body as a Whole: fever, infection, sepsis.
Cardiovascular System: congestive heart failure, hypertension, tachycardia, syncope.
Digestive System: dry mouth, esophagitis, gastric/peptic ulcers, gastritis, gastrointestinal bleeding, glossitis, hematemesis, hepatitis, jaundice.

Hemic and Lymphatic System: ecchymosis, eosinophilia, leukopenia, melena, purpura, rectal bleeding, stomatitis, thrombocytopenia.

Metabolic and Nutritional: weight changes.

Nervous System: anxiety, asthenia, confusion, depression, dream abnormalities, drowsiness, insomnia, malaise, nervousness, paresthesia, somnolence, tremors, vertigo.

Respiratory System: asthma, dyspnea.

Skin and Appendages: alopecia, photosensitivity, increased sweating.

Special Senses: blurred vision

Urogenital System: cystitis, dysuria, hematuria, interstitial nephritis, oliguria/polyuria, proteinuria, renal failure

Body as a Whole: anaphylactic reactions, appetite changes, death.
Cardiovascular System: arrhythmia, hypotension, myocardial infarction, palpitations, vasculitis.
Digestive System: colitis, eructation, liver failure, pancreatitis.

Hemic and Lymphatic System: agranulocytosis, hemolytic anemia, aplastic anemia, lymphadenopathy, pancytopenia.
Metabolic and Nutritional: hyperglycemia.

Nervous System: convulsions, coma, hallucinations, meningitis.

Respiratory System: respiratory depression, pneumonia.

Skin and Appendages: angioedema, toxic epidermal necrolysis, erythema multiforme, exfoliative dermatitis, Stevens Johnson

skin and appendages: angiodema, toxic epidermal necrolysis, erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, urticaria.

Special Senses: conjunctivitis, hearing impairment.

Aspirin: As with other NSAIDs, concomitant administration of diclofenac and aspirin is not generally recommended because of the potential of increased adverse effects.

Methotrexate: Caution should be used when NSAIDs are administered concomitantly with methotrexate. Methotrexate plasma levels may be increased and result in increased toxicity.

Cyclosporine: Concomitant therapy with diclofenac sodium may increase cyclosporine's nephrotoxicity. Caution should be used when diclofenac sodium is administered with cyclosporine.

ACE Inhibitors: Reports suggest that NSAIDs may diminish the anti-hypertensive effect of ACE inhibitors. This interaction should be given consideration in patients taking NSAIDs concomitantly with ACE inhibitors.

Furosemide: Diclofenac sodium can reduce the natriuretic effect of furosemide and thiazides in some patients. During concomitant therapy with NSAIDs, the patient should be observed closely for signs of renal failure, as well as to assure

Lithium: NSAIDs have produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. Thus, when

Warfarin: The effects of warfarin and NSAIDs on GI bleeding are synergistic, such that users of both drugs together have

a risk of serious GI bleeding higher than users of either drug alone.

PRECAUTIONS

- Diclofenac sodium should not be used concomitantly with diclofenac potassium since both exist in plasma as the same active organic ion.
- Patients on long-term diclofenac sodium treatment should have their hemopoietic system evaluated periodically. Periodic hematologic examinations (CBC and blood film examination) can detect anemias or blood dyscrasias secondary to possible gastrointestinal tract or bone marrow toxicity.
- There is a risk of hyperkalemia with NSAID treatment. Patients most at risk are: the elderly, those having conditions such as diabetes mellitus or renal failure, or those receiving concomitant therapy with B-adrenergic blockers, angiotensin converting enzyme inhibitors or some diuretics.
- In humans there have been reports of acute interstitial nephritis with hematuria, proteinuria, and occasionally nephrotic syndrome.
- In patients with prerenal conditions leading to reduction in renal blood flow or blood volume, renal prostaglandins have a supportive role in the maintenance of renal perfusion. Administration of NSAIDs may precipitate overt renal decompensation due to a dose-dependent reduction in prostaglandin formation. Patients at greatest risk are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics, and the elderly. Recovery to the pretreatment state usually follows discontinuation of NSAID therapy.
- During long-term therapy, kidney function should be monitored periodically.
- If abnormal liver function test results persist or worsen, or if systemic manifestations or clinical signs consistent with liver disease develop, discontinue diclofenac sodium treatment. Liver function should be monitored during long-term treatment with this drug.
- Caution is called for when using diclofenac sodium in patients with hepatic porphyria, since diclofenac sodium may trigger an attack.
- The anti-inflammatory, antipyretic, and analgesic effects of diclofenac sodium may mask the usual signs of infection.
- Blurred and/or diminished vision has been reported with the use of diclofenac sodium and with other NSAIDs. Ophthalmic examination should be carried out at periodic intervals in any patient receiving this drug for an extended period of time.
- As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can occur without prior exposure to drug. Careful questioning for patient history of asthma, nasal polyps, urticaria, and hypotension associated with NSAIDs is important before starting therapy.

WARNINGS

- Caution is required if administered to patients suffering from, or with a previous history of, bronchial asthma since NSAIDs have been reported to cause bronchospasm in such patients.
- NSAIDs should only be given with care to patients with a history of gastrointestinal disease.
- Undesirable effects may be minimised by using the minimum effective dose for the shortest possible duration.
- Side effects are generally more serious in the elderly and if serious, diclofenac sodium should be withdrawn.
- Patients on long term treatment should be monitored and patients with severe hepatic, cardiac or renal insufficiency should be kept under close surveillance as the use of NSAIDs may result in deterioration of renal function. Patients with impaired cardiac or renal function or recovering from major surgery or being treated with diuretics should be considered because of the importance of prostaglandins in maintaining blood flow. The dose should be kept as low as possible and renal function should be monitored in these patients.
- NSAIDs should be given with care to patients with a history of heart failure or hypertension since oedema has been reported in association with NSAIDs administration.
- If there is persistency in abnormal liver function tests or there are symptoms consistent with liver disease or if there are other manifestations such as rash or eosinophilia, diclofenac sodium treatment should be discontinued. Attacks of hepatic porphyria may be triggered in susceptible patients.
- Diclofenac sodium in common with other non-steroidal anti-inflammatory drugs can reversibly inhibit platelet aggregation.

PREGNANCY

Pregnancy Category C: There are no adequate and well-controlled studies in pregnant women. Use of prostaglandin synthetase inhibitors may result in premature closure of the foetal ductus arteriosus or uterine inertia and therefore are not recommended during the last trimester of pregnancy.

NURSING MOTHERS

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from diclofenac sodium, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

GERIATRIC USE

As with any NSAIDs, caution should be exercised in treating the elderly (65 years and older).

OVERDOSE

Symptoms: Symptoms following acute NSAID overdoses are usually limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain, which are generally reversible with supportive care. Gastrointestinal bleeding can occur. Hypertension, acute renal failure, respiratory depression and coma may occur, but are rare. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose.

Treatment: Patients should be managed by symptomatic and supportive care following a NSAID overdose. There are no specific antidotes. Emesis and/or activated charcoal (60 to 100 g in adults, 1 to 2 g/kg in children) and/or osmotic cathartic may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large overdose (5 to 10 times the usual dose). Forced diuresis, alkalization of urine, hemodialysis, or hemoperfusion may not be useful due to high protein binding.

CONTRAINDICATIONS

- **Voren** is contraindicated in patients with known hypersensitivity to diclofenac.
- **Voren** should not be given to patients who have experienced asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients.
- **Voren** is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery.

PRESENTATION

Voren tablet 25mg:	10 x 10's / pack.
Voren tablet 50mg:	10 x 10's / pack.
Voren Microtech capsule 50mg:	10 x 10's / pack.
Voren SR tablet 100mg:	3 x 10's / pack.

Dosage:

As directed by the physician.

Instructions:

Store below 30°C.
Protect from sunlight & moisture.
Keep out of reach of children.

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Detailed prescribing information is available on request.

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LFT/002/02

خوراک :
ڈاکٹر کی ہدایت کے مطابق۔
ہدایات :
دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔