VOREN® SUPPOSITORIES

Ingredient(s):
Voren Suppositories 12.5mg:
Each supp. contains:
Diclofenac Sodium 12.5mg
Voren Suppositories 25mg:
Each supp. contains:
Diclofenac Sodium 25mg
Voren Suppositories 50mg:
Each supp. contains:
Diclofenac Sodium 50mg

Pharmacology (Summary of Pharmacodynamic and Pharmacokinetics):
1. Diclofenac is a potent non-steroidal anti-inflammatory (NSAID) with analgesic and antipyretic properties. It also has some uricosuric effect. Diclofenac inhibits cyclo-oxygenase activity with a reduction in the tissue production of prostaglandins such as Prostaglandin F2a and Prostaglandin E2. The anti-inflammatory effect, measured in the adjuvant-induced arthritis model, is greater than that of aspirin and similar to indomenthacin. Diclofenac causes gastric erosions and prolongs the bleeding time.
2. Although Diclofenac Sodium does not alter the cause of the underlying disease, it has been found to relieve pain, reduce fever, swelling, and tenderness, and increase mobility in patients with rheumatic of the types indicated.
3. The rectally administered Diclofenac Sodium is rapidly and almost completely absorbed and distributed to blood, liver and kidneys. The plasma concentration shows a linear relationship to the amount of drug administered.
4. The plasma AUC values for unchanged Diclofenac Sodium following rectal administration are within the same range as those of the oral doses of enteric coated tablets.

Indication(s):
Chronic rheumatic arthritis, degenerative osteoarthritis and painful post-operative inflammation.

Dosage and Administration:
Adult: 100mg, usually to be used at night. Maximum total daily dose is 150mg.
Children: 0.5 - 2mg/kg body weight daily, in 2 - 3 divided doses.
To be inserted deep into the rectum.
To be dispensed by the physician's prescription.
As a general recommendation, the dose should be individually adjusted. Adverse effects may be minimized by using the lowest effective dose for the shortest possible duration necessary to control symptoms (see section Precaution/Warning).

Established cardiovascular disease or significant cardiovascular risk factors
Treatment with diclofenac is generally not recommended in patients with established cardiovascular diseases (congestive heart failure, established ischemic heart disease, peripheral arterial disease) or uncontrolled hypertension. If needed, patients with established cardiovascular disease, uncontrolled hypertension, or significant risk factors for cardiovascular disease (e.g. hypertension, hyperlipidaemia, diabetes mellitus and smoking) should be treated with diclofenac only after careful consideration and only at doses ≤100 mg daily if treated for more than 4 weeks (see section Precaution/Warning).

Contraindication(s):
1. Voren suppository should not be used in patients who have shown hypersensitivity to Diclofenac Sodium.
2. It is contraindicated in patients with any inflammatory lesions of the rectum or anus, and in patients with recent history of rectal and anal bleeding.
3. It should not be given to children under 12 months of age.
4. It is contraindicated in patients with active or suspected peptic ulcer or gastric-intestinal bleeding.
5. It is contraindicated in patients in whom attack of asthma, urticaria or acute rhinitis are precipitated by aspirin or other NSAIDs.
6. It is contraindicated with in patient with severe cardiac failure (see section Precaution/Warning).

Side Effect(s) / Adverse Reaction(s):
Local irritation; itching, burning and increased bowel movement.
Central nervous system: dizziness, headache, insomnia, drowsiness
Hematologic system: hemolytic anemia, aplastic anemia, agranulocytosis.
Dermatologic system: rash, pruritis, skin eruptions, eczema, urticaria and erythema.
Hepatic: jaundice, hepatitis
Ophthalmological: blurred vision.
Allergic: hypersensitivity reaction.
Cardiac disorder : Uncommon*: Myocardial infraction, cardiac failure, palpitations, chest pain.
*The frequency reflects data from long-term treatment with a high dose (150mg/day).

Description of selected adverse drug reactions

Arteriothrombotic events
Meta-analysis and pharmacoepidemiological data point towards an increased risk of arteriothrombotic events (for example myocardial infarction) associated with the use of diclofenac, particularly at a high dose (150mg daily) and during long-term treatment (see section Precaution/Warning).

Precaution(s) / Warning(s):
1. Caution should be exercised in patients with a history of blood dyscrasias or disorders of coagulation.
2. Observational studies have indicated that non-selective NSAIDs may be associated with an increased risk of serious cardiovascular events, principally myocardial infarction, which may increase with dose or duration of use. Patients with cardiovascular disease or cardiovascular risk of an adverse cardiovascular event in patient taking NSAID, especially in those with cardiovascular risk factors, the lowest effective dose should be used for the shortest possible duration. There is no consistent evidence that the concurrent use of aspirin mitigates the possible increased risk of serious cardiovascular thrombotic events associated with NSAID use.
3. NSAIDs may lead to the onset of new hypertension or worsening the pre-existing hypertension and patients taking anti-hypertensive with NSAIDs may have an impaired anti-hypertensive response. Caution is advised when prescribing NSAIDs to patients with hypertension. Blood pressure should be monitored closely during initiation of NSAID treatment and at regular intervals thereafter.
4. Fluid retention and oedema have been observed in some patients taking NSAIDs, hence caution is advised in patients with fluid retention or heart failure.
5. All NSAIDs can cause gastrointestinal discomfort and rarely serious, potentially fatal gastrointestinal effects such as ulcers, bleeding and perforation which may increase with dose or duration of use, but can occur at any time without warning. Caution is advised in patients with risk factors for gastrointestinal events e.g. the elderly, those with a history of serious gastrointestinal events, smoking and alcoholism. When gastrointestinal bleeding or ulceration occurs in patients receiving NSAIDs, the drug should be withdrawn immediately. Doctors should warn patients about signs and symptoms of serious gastrointestinal toxicity. The concurrent use of aspirin and NSAIDs also increases the risk of serious gastrointestinal adverse events.
6. NSAIDs may very rarely cause serious cutaneous adverse events such as exfoliative dermatitis, toxic epidermal necrolysis (TEN) and Stevens-Johnson Syndrome (SJS), which can be fatal and occur without warning. These serious adverse events are idiosyncratic and are independent of dose or duration of use. Patients should be advised of the signs and symptoms of serious skin reaction and to consult their doctor at the first appearance of a skin rash or any other sign of hypersensitivity.
7. The anti-inflammatory, antipyretic, and analgesic effects of Voren may mask the normal signs of infections. The physician should be alert to any development of infection in patients receiving Voren.
8. Patients with severe hepatic, cardiac or renal insufficiency or the elderly should be kept under close surveillance.
9. Use of diclofenac in patients with hepatic porphyria may trigger an attack.
10. **Cardiovascular effects**
Treatment with NSAIDs including diclofenac, particularly at high dose and in long term, maybe associated with an increased risk of serious cardiovascular thrombotic events (including myocardial infraction and stroke).
Treatment with diclofenac is generally not recommended in patients with established cardiovascular diseases (congestive heart failure, established ischemic heart diseases, peripheral arterial diseases) or uncontrolled hypertension. If needed, patients with established cardiovascular diseases, uncontrolled hypertension, or significant risk factors for cardiovascular disease (e.g. hypertension, hyperlipidaemia, diabetes melilitus and smoking) should be treated with diclofenac only after careful consideration and only at doses ≤100mg daily when treatment continues for more than 4 weeks.
As the cardiovascular risks of diclofenac may increase with dose and duration of exposure, the lowest effective daily dose should be used for the shortest duration possible. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically, especially when treatment continues for more than 4 weeks.
Patients should remain alert for the signs and symptoms of serious arteriothrombotic events (e.g. chest pain, shortness of breath, weakness, slurring of speech), which can occur without warnings. Patients should be instructed to see a physician immediately in case of such an event.

WARNINGS

RISK OF GI ULCERATION, BLEEDING AND PERFORATION WITH NSAID

Serious GI toxicity such as bleeding, ulceration and perforation can occur at any time, with or without warning symptoms, in patients treated with NSAID therapy. Although minor upper GI problems (eg. dyspepsia) are common, usually developing early in therapy, prescribers should remain alert for ulceration and bleeding in patients treated with NSAIDs even in the absence of previous GI tract symptoms.

Studies to date have not identified any subset of patients not at risk of developing peptic ulceration and bleeding. Patients with prior history of serious adverse events and other risk factors associated with peptic ulcer disease (eg. alcoholism, smoking, and corticosteroid therapy) are at increased risk. Elderly or debilitated patients seem to tolerate ulceration or bleeding less than other individuals and account for most spontaneous reports for fatal GI events.

Drug Interaction(s):
The drug has an affinity for serum albumin, and may displace other drugs which are also bound to albumin. Concomitant treatment with Potassium sparing diuretics may be associated with increased serum Potassium level. Concomitant administration with Aspirin is not recommended because Voren is displaced from binding site and resulting in lower plasma concentration and peak plasma levels. Concurrent therapy with Voren and Warfarin requires close monitoring of patients to be certain that no change in their anticoagulant dosage is required. Patients with altered renal function should be observed for the development of the specific toxicities of concomitant administration of Voren and Digoxin, Methotrexate and Cyclosporine. Patients receiving oral hypoglycemic should be observed for signs of toxicity to these drugs.

Symptoms and Treatment for Overdosage, and Antidote(s):
Symptoms of overdose reported have generally reflected, the renal and CNS toxicities of this medication. More serious overdosage effects such as, acute renal failure, convulsion and coma have been reported.
Should accidental overdosage occur, supportive and symptomatic treatment is indicated for complication, eg. hypotension, renal failure, convulsions and respiratory depression. Because it is firmly bound to plasma proteins, hemodialysis and peritoneal dialysis may be of little value.

Shelf-Life:
3 years from the date of manufacture.

Storage Condition(s):
Store at temperature below 25°C. Protect from light and moisture.

Product Description(s) & Packing(s):
Voren Suppositories 12.5mg:
A white to pale yellow color spindle suppository.
10 supp. per strip, 10 strips per box.
Voren Suppositories 25mg:
A white to pale yellow color spindle suppository.
10 supp. per strip, 10 strips per box.
Voren Suppositories 50mg:
A white to pale yellow color spindle suppository.
10 supp. per strip, 10 strips per box.

Manufacturer and Product Registration Holder:
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Ordering Line:1 800 88 3027
Product Info: 1 800 88 3679

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