

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-201 / S-018

APPROVED LABELING

APPEARS THIS WAY ON ORIGINAL

VOLTAREN®

diclofenac sodium
Delayed-Release (enteric-coated) Tablets

CATAFLAM®

diclofenac potassium
Immediate-Release Tablets

Prescribing Information

INDICATIONS: Diclofenac, as the sodium or potassium salt, is a nonsteroidal anti-inflammatory drug (NSAID) indicated for the relief of signs and symptoms of osteoarthritis and rheumatoid arthritis. The chemical structures are shown in Figure 1.

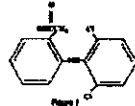


Figure 1
A is the sodium salt of diclofenac sodium
B is the potassium salt of diclofenac potassium

Contraindications and Warnings: Diclofenac is contraindicated in patients with a history of asthma, peptic ulcer disease, or gastrointestinal bleeding. It should be used with caution in patients with a history of hypertension, heart failure, or renal impairment. Diclofenac may increase the risk of bleeding, especially in patients taking anticoagulants or antiplatelet drugs. Patients should be advised to avoid alcohol consumption while taking diclofenac. Diclofenac may cause dizziness, lightheadedness, or fainting, especially when standing up quickly. Patients should be advised to avoid driving or operating machinery until they know how they react to the drug. Diclofenac may cause gastrointestinal side effects, including nausea, vomiting, constipation, and diarrhea. Patients should be advised to avoid taking diclofenac with other NSAIDs or aspirin. Diclofenac may cause liver enzyme elevations. Patients should be advised to avoid taking diclofenac with other drugs that may affect the liver. Diclofenac may cause kidney injury. Patients should be advised to avoid taking diclofenac with other drugs that may affect the kidneys. Diclofenac may cause cardiovascular side effects, including increased blood pressure and heart failure. Patients should be advised to avoid taking diclofenac with other drugs that may affect the cardiovascular system. Diclofenac may cause central nervous system side effects, including dizziness, lightheadedness, or fainting. Patients should be advised to avoid taking diclofenac with other drugs that may affect the central nervous system. Diclofenac may cause allergic reactions. Patients should be advised to avoid taking diclofenac with other drugs that may increase the risk of allergic reactions. Diclofenac may cause drug interactions. Patients should be advised to avoid taking diclofenac with other drugs that may interact with it.

Clinical Pharmacology

Pharmacodynamics: Diclofenac, like aspirin and ibuprofen, is a nonselective anti-inflammatory drug (NSAID). In pharmacologic studies, diclofenac has shown anti-inflammatory, analgesic, and antipyretic activity. In non-clinical studies, diclofenac has been shown to inhibit cyclooxygenase (COX) activity, resulting in decreased production of prostaglandins, which are mediators of inflammation and pain. Diclofenac may also have a direct effect on pain receptors. Diclofenac has been shown to be effective in the treatment of osteoarthritis and rheumatoid arthritis. Diclofenac has been shown to be effective in the treatment of pain and inflammation. Diclofenac has been shown to be effective in the treatment of fever. Diclofenac has been shown to be effective in the treatment of menstrual pain. Diclofenac has been shown to be effective in the treatment of postoperative pain. Diclofenac has been shown to be effective in the treatment of acute gouty arthritis. Diclofenac has been shown to be effective in the treatment of acute bursitis. Diclofenac has been shown to be effective in the treatment of acute tendinitis. Diclofenac has been shown to be effective in the treatment of acute epicondylitis. Diclofenac has been shown to be effective in the treatment of acute calcific tendonitis. Diclofenac has been shown to be effective in the treatment of acute low back pain. Diclofenac has been shown to be effective in the treatment of acute neck pain. Diclofenac has been shown to be effective in the treatment of acute migraine. Diclofenac has been shown to be effective in the treatment of acute tension headaches. Diclofenac has been shown to be effective in the treatment of acute sinusitis. Diclofenac has been shown to be effective in the treatment of acute otitis media. Diclofenac has been shown to be effective in the treatment of acute otitis externa. Diclofenac has been shown to be effective in the treatment of acute conjunctivitis. Diclofenac has been shown to be effective in the treatment of acute allergic rhinitis. Diclofenac has been shown to be effective in the treatment of acute allergic conjunctivitis. Diclofenac has been shown to be effective in the treatment of acute allergic dermatitis. Diclofenac has been shown to be effective in the treatment of acute allergic asthma. Diclofenac has been shown to be effective in the treatment of acute allergic rhinitis. Diclofenac has been shown to be effective in the treatment of acute allergic conjunctivitis. Diclofenac has been shown to be effective in the treatment of acute allergic dermatitis. Diclofenac has been shown to be effective in the treatment of acute allergic asthma.

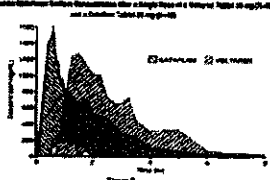


Figure 2
Plasma concentration-time profiles of diclofenac sodium (50 mg) and diclofenac potassium (50 mg).

Only 37% of the absorbed dose of diclofenac from Voltaren is systemically available, due to first-pass metabolism. Peak plasma levels are achieved in 2 hours in fasting normal volunteers, with a range from 1 to 4 hours. The area under the plasma-concentration curve (AUC) is dose-proportional within the range of 25 mg to 100 mg. Peak plasma levels are lower than dose-proportional and are approximately 1.8, 1.3, and 1.8 ng/mL for 25-mg, 50-mg, and 100-mg doses, respectively. It should be noted that the administration of several immediate-release Voltaren tablets may not yield equivalent results in peak concentration as the administration of a tablet of a higher strength. This is probably due to the suggested gastric emptying of tablets only 2-3 hours. Also reported are concentrations of Voltaren 50 mg tablets, diclofenac did not reach steady-state plasma levels.

When Voltaren tablets are taken, there is usually a delay in the onset of analgesia of 1 to 4 hours, with effects lasting up to 10 hours at 100 mg. Diclofenac sodium (Voltaren) is rapidly and extensively absorbed from the gastrointestinal tract, with approximately 90% of the dose being absorbed within 15 minutes of dosing with Cataflam. Peak plasma levels are achieved in approximately 1 hour in fasting normal volunteers, with a range from 1 to 2 hours. Only 37% of the absorbed dose of diclofenac from Cataflam is systemically available, due to first-pass metabolism. The extent of absorption of diclofenac from Cataflam tablets is comparable to that from a buffered tablet of diclofenac potassium. Diclofenac and potassium of Cataflam 75 mg tablets, as a percentage of appropriate plasma amounts.

The extent of diclofenac absorption is not significantly affected when Cataflam is taken with food. However, the rate of absorption is reduced by food, as indicated by a delay in T_{max} and increase in C_{max} values by approximately 30%.

Pharmacokinetics: A single administration of diclofenac sodium (50 mg) as a delayed-release tablet, with the first dose given during a meal at approximately 2 hours, results in a significantly higher plasma concentration and longer half-life than the immediate-release tablet. About 30% of the dose is absorbed in the first 2 hours, and about 60% of the dose is absorbed in the first 4 hours. The plasma concentration of diclofenac sodium (50 mg) as a delayed-release tablet is significantly higher than that of the immediate-release tablet. The plasma concentration of diclofenac sodium (50 mg) as a delayed-release tablet is significantly higher than that of the immediate-release tablet. The plasma concentration of diclofenac sodium (50 mg) as a delayed-release tablet is significantly higher than that of the immediate-release tablet.

Pharmacokinetics: A single administration of diclofenac sodium (50 mg) as a delayed-release tablet, with the first dose given during a meal at approximately 2 hours, results in a significantly higher plasma concentration and longer half-life than the immediate-release tablet. About 30% of the dose is absorbed in the first 2 hours, and about 60% of the dose is absorbed in the first 4 hours. The plasma concentration of diclofenac sodium (50 mg) as a delayed-release tablet is significantly higher than that of the immediate-release tablet. The plasma concentration of diclofenac sodium (50 mg) as a delayed-release tablet is significantly higher than that of the immediate-release tablet. The plasma concentration of diclofenac sodium (50 mg) as a delayed-release tablet is significantly higher than that of the immediate-release tablet.

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In patients receiving less than 60 mg (2.5 mg), or whose hepatic or renal function is impaired, or other disease states, the following information is provided for the physician's reference. In patients receiving less than 60 mg (2.5 mg), or whose hepatic or renal function is impaired, or other disease states, the following information is provided for the physician's reference. In patients receiving less than 60 mg (2.5 mg), or whose hepatic or renal function is impaired, or other disease states, the following information is provided for the physician's reference.

INDICATIONS AND USAGE

Chlorzoxazone is indicated for the relief of moderate to severe pain in patients with musculoskeletal conditions. It is contraindicated in patients with known hypersensitivity to chlorzoxazone or any of its components. It is contraindicated in patients with known hypersensitivity to chlorzoxazone or any of its components. It is contraindicated in patients with known hypersensitivity to chlorzoxazone or any of its components.

Contraindications

Known hypersensitivity to chlorzoxazone or any of its components. Known hypersensitivity to chlorzoxazone or any of its components. Known hypersensitivity to chlorzoxazone or any of its components.

Warnings

Patients should be advised that chlorzoxazone may cause drowsiness, dizziness, and blurred vision. Patients should be advised that chlorzoxazone may cause drowsiness, dizziness, and blurred vision. Patients should be advised that chlorzoxazone may cause drowsiness, dizziness, and blurred vision.

Adverse Reactions

The most common adverse reactions observed in patients receiving chlorzoxazone are drowsiness, dizziness, and blurred vision. The most common adverse reactions observed in patients receiving chlorzoxazone are drowsiness, dizziness, and blurred vision. The most common adverse reactions observed in patients receiving chlorzoxazone are drowsiness, dizziness, and blurred vision.

Drug Interactions

Chlorzoxazone may interact with other central nervous system depressants, including alcohol, barbiturates, and sedatives. Chlorzoxazone may interact with other central nervous system depressants, including alcohol, barbiturates, and sedatives. Chlorzoxazone may interact with other central nervous system depressants, including alcohol, barbiturates, and sedatives.

How Supplied

Chlorzoxazone is available in the following strengths: 250 mg tablets, 375 mg tablets, and 500 mg tablets. Chlorzoxazone is available in the following strengths: 250 mg tablets, 375 mg tablets, and 500 mg tablets. Chlorzoxazone is available in the following strengths: 250 mg tablets, 375 mg tablets, and 500 mg tablets.

How to Use

Chlorzoxazone should be taken orally with or without food. Chlorzoxazone should be taken orally with or without food. Chlorzoxazone should be taken orally with or without food. Chlorzoxazone should be taken orally with or without food.

Storage and Stability

Chlorzoxazone tablets should be stored at room temperature. Chlorzoxazone tablets should be stored at room temperature. Chlorzoxazone tablets should be stored at room temperature. Chlorzoxazone tablets should be stored at room temperature.

CLINICAL PHARMACOLOGY

Chlorzoxazone is a centrally acting muscle relaxant. Chlorzoxazone is a centrally acting muscle relaxant. Chlorzoxazone is a centrally acting muscle relaxant. Chlorzoxazone is a centrally acting muscle relaxant.

Pharmacokinetics

Chlorzoxazone is rapidly absorbed after oral administration. Chlorzoxazone is rapidly absorbed after oral administration. Chlorzoxazone is rapidly absorbed after oral administration. Chlorzoxazone is rapidly absorbed after oral administration.

Pharmacodynamics

Chlorzoxazone acts as a centrally acting muscle relaxant. Chlorzoxazone acts as a centrally acting muscle relaxant. Chlorzoxazone acts as a centrally acting muscle relaxant. Chlorzoxazone acts as a centrally acting muscle relaxant.

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/s/

Carmen DeBellas
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