# TROVEX® MR

Ketoprofen 200 mg Capsules

**DESCRIPTION** : Ketoprofen is a nonsteroidal anti-inflammatory drug. Each Trovex® MR 200 mg capsule contains ketoprofen in the form of hundreds of coated pellets.

**COMPOSITION :** Each MR capsule contains :
- Active Ingredient : Ketoprofen 200.00 mg
- Excipients : Sugar, Povidone, Methacrylic acid copolymer, Talc

**CLINICAL PHARMACOLOGY :** Ketoprofen is a nonsteroidal anti-inflammatory drug with analgesic and antipyretic properties shown to have inhibitory effects on prostaglandin and leukotriene synthesis, to have antibradykinin activity, as well as to have lysosomal membrane-stabilizing action.
Trovex® and Trovex® MR capsules both contain ketoprofen. They differ only in their release characteristics. Trovex® capsules release drug in the stomach whereas the pellets in Trovex® MR capsules are designed to resist dissolution in gastric fluid but release drug at a controlled rate in the small intestine.

**INDICATIONS :** Trovex® MR is indicated for the management of the signs and symptoms of rheumatoid arthritis and osteoarthritis. Trovex® MR is not recommended for treatment of acute pain.

**CONTRAINDICATIONS** : Ketoprofen is contraindicated in patients who have shown hypersensitivity to it. It should not be given to patients in whom aspirin or other NSAIDs induce asthma, urticaria, or other allergic-type reactions.

**WARNINGS : Risk of GI Ulceration, Bleeding and Perforation with NSAID Therapy**
Early dyspepsia is common, but symptomatic upper-GI ulcers, gross bleeding, or perforation appear to occur in 1% of patients treated for 3 to 6 months, and in about 2-4% of patients treated for one year.
Patients with a prior history of serious GI events and risk factors known to be associated with peptic ulcer disease, such as alcoholism, smoking, etc., elderly or debilitated patients seem to tolerate ulceration or bleeding less well than other individuals. In considering the use of relatively large doses (within the recommended dosage range), sufficient benefit should offset the potential increased risk of GI toxicity. Patients should be followed for signs and symptoms of ulceration and bleeding.

**GENERAL PRECAUTIONS :** Rare cases of interstitial nephritis or nephrotic syndrome have been reported in humans. A second form of reversible renal toxicity has been seen in patients with conditions leading to a reduction in renal blood flow or blood volume. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics, and the elderly.
Borderline elevations of one or more liver function tests may occur in up to 15% of patients. These abnormalities may progress, remain essentially unchanged, or disappear with continued therapy. Meaningful (3-folds) elevations of ALT or AST occur in less than 1% of patients.
Anemia is commonly observed in rheumatoid arthritis and is sometimes aggravated by NSAIDs, which may produce fluid retention or gastrointestinal blood loss in some patients.
Peripheral edema has been observed in approximately 2% of patients taking ketoprofen. It should be used with caution in patients with fluid retention, hypertension, or heart failure.
**Drug Interactions**
The following drug interactions were studied with ketoprofen doses of 200 mg/day. The possibility of increased interaction should be kept in mind when Trovex® doses greater than 50 mg as a single dose or 200 mg of ketoprofen per day are used concomitantly with highly bound drugs.
1. *Antacids* : Concomitant administration of magnesium and aluminum hydroxide does not interfere with the rate or extent of the absorption of ketoprofen administered as Trovex®.
2. *Aspirin* : Concurrent administration of aspirin decreased ketoprofen protein binding and increased ketoprofen plasma clearance. Therefore, concurrent use of aspirin and ketoprofen is not recommended.
3. *Diuretics* : Hydrochlorothiazide, given concomitantly with ketoprofen, produces a reduction in urinary potassium and chloride excretion compared to hydrochlorothiazide alone. Patients taking diuretics are at greater risk of developing renal failure secondary to a decrease in renal blood flow caused by prostaglandin inhibition.
4. *Digoxin* : Ketoprofen does not alter the serum levels of digoxin.
5. *Warfarin* : Ketoprofen does not significantly interfere with the effect of warfarin on prothrombin time. Bleeding from a number of sites may be a complication of warfarin treatment and GI bleeding a complication of ketoprofen treatment. Concurrent therapy requires close monitoring.
6. *Probenecid* : Probenecid increases both free and bound ketoprofen by reducing its plasma clearance to about one-third, and decreasing its protein binding. Therefore, this combination is not recommended.
7. *Methotrexate*: Ketoprofen, like other NSAIDs, may cause changes in the elimination of methotrexate leading to elevated serum levels of the drug and increased toxicity.
8. *Lithium* : NSAID agents have been reported to increase steady-state plasma lithium levels. It is recommended that plasma lithium levels be monitored when ketoprofen is co-administered with lithium.

**Effect on Blood Coagulation** : Ketoprofen can prolong bleeding time by approximately 3 to 4 minutes from baseline values.
**Teratogenic Effects - Pregnancy Category B** : There are no adequate and well-controlled studies in pregnant women. Because animal teratology studies are not always predictive of the human response, ketoprofen should be used during pregnancy only if the potential benefit justifies the risk. In addition, effects of ketoprofen on labor and delivery in pregnant women are unknown. Because of the effects of prostaglandin-inhibiting drugs on the fetal cardiovascular system (closure of ductus arteriosus), use of ketoprofen during late pregnancy should be avoided.
**Nursing Mothers** : Data on secretion in milk do not exist, so ketoprofen is not recommended for use in nursing mothers.
**Pediatric Use** : Ketoprofen is not recommended for use in pediatric patients.

**ADVERSE REACTIONS** : Minor gastrointestinal effects predominate; upper gastrointestinal symptoms are more common than lower ones. Peptic ulcer or GI bleeding occur in controlled clinical trials in less than 1%.
The incidence of peptic ulceration in patients on NSAIDs is dependent on many risk factors including age, sex, smoking, alcohol use, diet, stress, concomitant drugs such as aspirin and corticosteroids, as well as the dose and duration of treatment with NSAIDs .
Central nervous system side effects follow in frequency, such as headache, dizziness, or drowsiness. Special senses effects (tinnitus, visual disturbance), skin and appendages (rash), urogenital (impairment of renal function, edema, increased BUN, signs or symptoms of urinary-tract irritation) are also found. The incidence of some adverse reactions appears to be dose-related.

**OVERDOSAGE :** Signs and symptoms following acute NSAID overdose are usually limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain, which are generally reversible with supportive care. Respiratory depression, coma, or convulsions have occurred following large ketoprofen overdoses. Gastrointestinal bleeding, hypotension, hypertension, or acute renal failure may occur, but are rare.
Patients should be managed by symptomatic and supportive care following an NSAID overdose. There are no specific antidotes. Gut decontamination may be indicated in patients with symptoms seen within 4 hours (longer for sustained-release products) or following a large overdose (5 to 10 times the usual dose). This should be accomplished via emesis and/or activated charcoal (60 to 100 g in adults, 1 to 2 g/kg in children) with a saline cathartic or sorbitol added to the first dose. Forced diuresis, alkalinization of the urine, hemodialysis or hemoperfusion would not be useful due to ketoprofen's high protein binding.

**DOSAGE AND ADMINISTRATION :** The recommended dose of ketoprofen in otherwise healthy patients is for Trovex® MR 200 mg administered once a day and this daily dose should not be exceeded. Smaller doses of Ketoprofen should be utilized initially in small individuals or in debilitated or elderly patients. Concomitant use of Trovex® and Trovex® MR is not recommended. If minor side effects appear, they may disappear at a lower dose.
In patients with severe end-stage renal impairment, the maximum total daily dose of Ketroprofen should not exceed 100 mg. It is also recommended that the initial dosage of Ketoprofen should be reduced for patients over 75 years of age.
For patients with impaired liver function and serum albumin concentration less than 3.5 g/dl, the maximum initial total daily dose of Ketroprofen should be 100 mg.
To minimize gastrointestinal side effects, Trovex® MR may be taken with antacids, food, or milk.

**Presentation :** Capsules MR 200 mg - Blister pack of 30's
**Storage Conditions :** Store in a dry place at temperatures not exceeding 25°C.
**Do not use after expiry date.**

**THIS IS A MEDICAMENT**
- Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.

Keep medicament out of children's reach

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Zouk Mosbeh, Lebanon
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