Ketonic®

Ketorolac Tromethamine USP Film Coated Tablet and Injection

DESCRIPTION

Ketonic® is a potent analgesic agent of the non-steroidal anti-inflammatory (NSAID) class. Its mode of action is to inhibit the cyclo-oxygenase enzyme system and hence prostaglandin synthesis and it demonstrates a minimal anti-inflammatory effect at its analgesic dose.

INDICATIONS

Adult Patients: Ketonic® is indicated for the short-term management of moderately severe acute pain that requires analgesia at the opioid level, usually in a postoperative setting. Therapy should always be initiated with **Ketonic®** IM/IV injection & **Ketonic®** tablet is to be used as continuation treatment, if necessary. Combined use of **Ketonic®** IM/IV injection and tablet does not exceed 5 days of use because of the potential of increasing the frequency and severity of adverse reaction associated with the recommended doses.

Paediatric patients: The safety and effectiveness of single dose of **Ketonic®** IM/IV injection have been established in paediatric patients between the ages of 2 and 16 years. Ketorolac Tromethamine as a single injectable dose, has been shown to be effective in the management of moderately severe acute pain that requires analgesia at the opioid level, usually in the postoperative setting. Safety and effectiveness have not been established in paediatric patients below the age of 2 years.

DOSAGE AND ADMINISTRATION

Ketonic® IM/IV Injection:

When administering **Ketonic®** IM/IV injection, the IV bolus must be given over no less than 15 seconds. The IM administration should be given slowly and deeply into the muscle. The analgesic effect begins in ~30 minutes with maximum effect in 1 to 2 hours after dosing IM or IV. Duration of analgesic effect is usually 4 to 6 hours.

Single-Dose Treatment (IM or IV)

Adults patients:

Patients < 65 years of age: One dose of 60 mg (IM) or 30 mg (IV).

Patients ≥ 65 years of age, renally impaired and/or less than 50 kg (110 lbs) of body weight: One dose of 30 mg (IM) or 15 mg (IV).

Paediatric patients (2-16 years):

Paediatric patients should receive only a single dose of 1 mg/kg (IM) up to max. 30 mg or 0.50 mg/kg (IV) up to max. 15 mg.

Multiple-Dose Treatment (IM or IV) in Adults:

Patients < 65 years of age: The recommended dose is 30 mg (IM or IV) Ketorolac Tromethamine injection every 6 hours not exceeding 120 mg/day.

For patients ≥ 65 years of age, renally impaired patients and patients less than 50 kg (110 lbs): The recommended dose is 15 mg Ketorolac Tromethamine injection every 6 hours not exceeding 60 mg/day.

For breakthrough pain, do not increase the dose or the frequency of Ketorolac Tromethamine.

Transition from Ketonic® IM/IV injection to Ketonic® tablet:

Ketonic® tablet should be administered as a continuation therapy to **Ketonic®** IM/IV injection for the management of moderately severe acute pain that requires analgesia at the opioid level.

Adults patients < 65 years of age: 2 tablets as a first oral dose for patients who received 60 mg IM single dose, 30 mg IV single dose or 30 mg multiple doses. **Ketonic®** IM/IV injection followed by 1 tablet every 4 to 6 hours, not to exceed 40 mg/24 h of Ketorolac Tromethamine tablet.

Patients ≥ 65 years of age, renally impaired and / or less than 50 kg (110 lbs) of body weight: 1 tablet as a first oral dose for patients who received 30 mg IM single dose, 15 mg IV single dose or 15 mg multiple dose. **Ketonic®** IM/IV injection a followed by 1 tablet every 4 to 6 hours, not to exceed 40 mg/24h of Ketorolac Tromethamine tablet.

Ketonic® Tablet:

Adults: The usual dose of **Ketonic®** tablet is 10 mg every 4 to 6 hours for pain as required. Doses exceeding 40 mg per day are not recommended. The maximum duration of treatment with the oral formulation is 5 days for post-surgical patients and 7 days for patients with musculoskeletal pain.

Patients under 50 kg, over 65 years of age: The lowest effective dose is recommended.

CONTRAINDICATIONS

Ketorolac Tromethamine is contraindicated:

In patients with active peptic ulcer disease, recent gastrointestinal bleeding or perforation and in patients with a history of peptic ulcer disease or gastrointestinal bleeding.

In patients with advanced renal impairment or in patients at risk for renal failure due to volume depletion.

In labor and delivery because, through its prostaglandin synthesis inhibitory effect, it may adversely affect fetal circulation and inhibit uterine contractions, thus increasing the risk of uterine hemorrhage.

In patients with previously demonstrated hypersensitivity to Ketorolac Tromethamine, allergic manifestations to aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs).

As prophylactic analgesic before any major surgery and is contraindicated intraoperatively when hemostasis is critical because of the increased risk of bleeding.

USE IN PREGNANCY AND LACTATION

As with other drugs known to inhibit prostaglandin synthesis, use of Ketorolac Tromethamine should be avoided in late pregnancy because it may cause premature closure of the ductus arteriosus. There are no adequate and well-controlled studies of Ketorolac Tromethamine in pregnant women. Ketorolac Tromethamine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Because of the possible adverse effects of prostaglandin-inhibiting drugs on neonates, use in nursing mothers is contraindicated.

SIDE-EFFECTS

Body as a Whole: Edema, weight gain, fever, asthenia, hypersensitivity reactions such as anaphylaxis, anaphylactoid reaction, laryngeal edema and tongue edema.

Cardiovascular: Hypertension, palpitation, pallor, syncope, hypotension, flushing.

Dermatologic: Pruritus, rash, urticaria, Lyell's syndrome, Stevens-Johnson syndrome, exfoliative dermatitis, and maculopapular rash.

Gastrointestinal: Nausea, dyspepsia, gastrointestinal pain, diarrhea, constipation, flatulence, fullness of stomach, vomiting, stomatitis, gastritis, rectal bleeding, anorexia, peptic ulceration, GI hemorrhage, GI perforation, melena, acute pancreatitis, hematemesis, esophagitis.

Hemic and Lymphatic: purpura, epistaxis, anemia, eosinophilia, postoperative wound hemorrhage, thrombocytopenia, leukopenia.

Nervous System: Headache, drowsiness, dizziness, tremors, abnormal dreams, hallucinations, euphoria, extrapyramidal symptoms, vertigo, paresthesia, depression, insomnia, nervousness, excessive thirst, dry mouth, abnormal thinking, inability to concentrate, hyperkinesis, stupor, convulsions, psychosis, aseptic meningitis.

Respiratory: Dyspnea, pulmonary edema, rhinitis, cough, asthma, bronchospasm.

Urogenital: Hematuria, proteinuria, oliguria, urinary retention, polyuria, increased urinary frequency, acute renal failure, flank pain with or without hematuria and/or azotemia, interstitial nephritis, hyponatremia, hyperkalemia, hemolytic uremic syndrome.

Special Senses: Abnormal taste, abnormal vision, blurred vision, tinnitus, hearing loss.

DRUG INTERACTIONS

The in vitro binding of ***warfarin*** to plasma proteins is only slightly reduced by Ketorolac Tromethamine. When Ketorolac plasma concentrations reach 5 to 10 μg/mL. Ketorolac does not alter ***digoxin*** protein binding. In vitro studies indicate that, at therapeutic concentrations of ***salicylate*** (300 μg/mL), the binding of Ketorolac was reduced from approximately 99.2% to 97.5%, representing a potential twofold increase in unbound Ketorolac plasma levels.

Ketorolac Tromethamine reduced the diuretic response to ***furosemide*** in normovolemic healthy subjects by approximately 20%.

Concomitant administration of Ketorolac Tromethamine and ***probenecid*** resulted in decreased clearance of Ketorolac and significant increases in Ketorolac plasma levels and terminal half-life. Therefore, concomitant use of Ketorolac Tromethamine and ***probenecid*** is contraindicated.

Inhibition of renal ***lithium*** clearance, leading to an increase in plasma lithium concentration, has been reported with some prostaglandin synthesis-inhibiting drugs. The effect of Ketorolac Tromethamine on plasma lithium has not been studied, but cases of increased lithium plasma levels during Ketorolac Tromethamine therapy have been reported.

Concomitant administration of ***methotrexate*** and some NSAIDs has been reported to reduce the clearance of methotrexate, enhancing the toxicity of methotrexate.

Concomitant use of ***ACE inhibitors*** may increase the risk of renal impairment, particularly in volume-depleted patients.

Sporadic cases of seizures have been reported during concomitant use of Ketorolac Tromethamine and ***antiepileptic drugs*** (phenytoin, carbamazepine).

Hallucinations have been reported when Ketorolac Tromethamine was used in patients taking ***psychoactive drugs*** (fluoxetine, thiothixene, alprazolam).

Ketorolac Tromethamine has been administered concurrently with ***morphine*** in several clinical trials of postoperative pain without evidence of adverse interactions. It has been advised not to mix Ketorolac Tromethamine and morphine in the same syringe.

PRECAUTIONS

Hepatic Effects: Ketorolac Tromethamine should be used with caution in patients with impaired hepatic function or a history of liver disease. Treatment with Ketorolac Tromethamine may cause elevations of liver enzymes, and, in patients with pre-existing liver dysfunction, it may lead to the development of a more severe hepatic reaction. The administration of Ketorolac Tromethamine should be discontinued in patients in whom an abnormal liver test has occurred as a result of Ketorolac Tromethamine therapy.

Hematologic Effects: Ketorolac Tromethamine inhibits platelet aggregation and may prolong bleeding time; therefore, it is contraindicated as a preoperative medication, and caution should be used when hemostasis is critical. Unlike aspirin, the inhibition of platelet function by Ketorolac Tromethamine disappears within 24 to 48 hours after the drug is discontinued. Ketorolac Tromethamine does not appear to affect platelet count, prothrombin time (PT) or partial thromboplastin time (PTT).

PHARMACEUTICAL PRECAUTION

Ketonic® Tablet : Store in a dry place, away from light. Keep out of reach of children.

Ketonic® Injection : Store below 25°C, dry place, away from light. Retain **injection** in carton until time of use. Keep out of reach of children.

PACKAGING

Ketonic® 10 Tablet : Box containing 3 strips of 10 tablets each. Each film coated Tablet contains Ketorolac Tromethamine USP 10 mg.

Ketonic® 30 Injection : Box containing 1 strip of 1 ampoule each. Each 1 ml ampoule contains Ketorolac Tromethamine USP 30 mg.

Ketonic® 60 Injection : Box containing 1 strip of 1 ampoule each. Each 2 ml ampoule contains Ketorolac Tromethamine USP 60 mg.

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Manufactured by

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