Toroaid

Ketorolac Tromethamine

Tablet/ Injection

Presentation

TOROAID 30 IM/IV Injection: Each ampoule contains 1 ml sterile solution of Ketorolac Tromethamine USP 30 mg for IM/IV injection.
TOROAID 60 IM Injection: Each ampoule contains 2 ml sterile solution of Ketorolac Tromethamine USP 60 mg for IM injection.
TOROAID 10 Tablet: Each film-coated tablet contains Ketorolac Tromethamine USP 10 mg.

Pharmacodynamic Properties: Ketorolac Tromethamine is a non-narcotic analgesic. It is a non-steroidal anti-inflammatory agent that exhibits anti-inflammatory and weak antipyretic activity. Ketorolac Tromethamine inhibits the synthesis of prostaglandins and is considered a peripherally acting analgesic. It does not have known effects on opiate receptors.

Pharmacokinetic Properties: IM: Following intramuscular administration, Ketorolac Tromethamine was rapidly and completely absorbed, a mean peak plasma concentration of 2.2 µg/ml occurring an average of 50 minutes after a single 30 mg dose. The influences of age, kidney and liver function on terminal plasma half-life and mean total clearance are outlined in the table below (estimated from a single 30 mg IM dose of Ketorolac).

Type of subjects	Total clearance (l/hr/kg) mean (range)	Terminal half-life (hrs) mean (range)
Normal subjects (n = 54)	0.023 (0.010 - 0.046)	5.3 (3.5 - 9.2)
Patients with hepatic dysfunction (n = 7)	0.029 (0.013 - 0.066)	5.4 (2.2 - 6.9)
Patients with renal impairment (n =25) (serum creatinine 160 - 430 micromol/l)	0.016 (0.005 - 0.043)	10.3 (5.9 - 19.2)
Renal dialysis patients (n = 9)	0.016 (0.003 - 0.036)	13.6 (8.0 - 39.1)
Healthy elderly subjects (n = 13)(mean age 72)	0.019 (0.013 - 0.034)	7.0 (4.7 - 8.6)

IV: Intravenous administration of a single 10 mg dose of Ketorolac Tromethamine resulted in a mean peak plasma concentration of 2.4 µg/ml occurring an average of 5.4 minutes after distribution of 0.15 L/kg, and a total plasma clearance of 0.35 ml/min/kg. The primary route of excretion of Ketorolac and its metabolites is renal: 91.4% (mean) of a given dose being found in the urine and 6.1% (mean) in the faeces. More than 99% of the Ketorolac in plasma is protein-bound over a wide concentration range.

Oral: Ketorolac Tromethamine is rapidly and completely absorbed following oral administration with a peak plasma concentration of 0.87 mcg/ml occurring 50 minutes after a single 10 mg dose. The terminal plasma elimination half-life averages 5.4 hours (S.D. = 1.0) in healthy subjects. In elderly subjects (mean age 72) it is 6.2 hours (S.D. = 1.0). More than 99% of the Ketorolac in plasma is protein bound. The pharmacokinetics of Ketorolac in man following single or multiple doses are linear. Steady state plasma levels are achieved after 1 day of Q.I.D. dosing. No changes occurred with chronic dosing. Following a single intravenous dose, the volume of distribution is 0.25 L/kg; the half-life is 5 hours and the clearance 0.55 ml/min/kg. The primary route of excretion of Ketorolac and its metabolites (conjugates and the p-hydroxymetabolite) is in the urine (91.4%) and the remainder is excreted in the faeces. A high fat diet decreased the rate, but not the extent of absorption, while antacid had no effect on Ketorolac absorption.

Indications: TOROAID IM/IV injection and tablet is indicated for the short - term management of moderate to severe acute post - operative pain .

Dosage and Administration: TOROAID injection is for administration by intramuscular or bolus intravenous injection. Bolus intravenous doses should be given over no less than 15 seconds. TOROAID should not be used for epidural or spinal administration. The time to onset of analgesic effect following both IV and IM administration is similar and is approximately 30 minutes, with maximum analgesia occurring within one to two hours. The median duration of analgesia is generally four to six hours. Dosage should be adjusted according to the severity of the pain and the patient response. The administration of continuous multiple daily doses of TOROAID intramuscularly or intravenously should not exceed two days because adverse events may increase with prolonged usage. There has been limited experience with dosing for longer periods since the vast majority of patients have transferred to oral medication, or no longer require analgesic therapy after this time. Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms.

Adults: The recommended initial dose of TOROAID is 10 mg, followed by 10 to 30 mg every four to six hours as required. In the initial post-operative period, TOROAID may be given as often as every two hours if needed. The lowest effective dose should be given. A total daily dose of 90 mg for non-elderly and 60 mg for the elderly, renal-impaired patients and patients less than 50 kg should not be exceeded. The maximum duration of treatment should not exceed two days. Reduce dosage in patients under 50 kg. Opioid analgesics (e.g. morphine, pethidine) may be used concomitantly, and may be required for optimal analgesic effect in the early post-operative period when pain is most severe. Ketorolac does not interfere with opioid binding and does not exacerbate opioid related respiratory depression or sedation. When used in association with TOROAID IM/IV, the daily dose of opioid is usually less than that normally required. However, opioid side-effects should still be considered, especially in day-case surgery. For patients receiving parenteral Ketorolac, and who are converted to Ketorolac oral tablets, the total combined daily dose should not exceed 90 mg (60 mg for the elderly, renal-impaired patients and patients less than 50 kg) and the oral component should not exceed 40 mg on the day the change of formulation is made. Patients should be converted to oral treatment as soon as possible.

Elderly: For patients over 65 years, the lower end of the dosage range is recommended; a total daily dose of 60 mg should not be exceeded.

Children (2 to 16 years): ***IM dosing:*** One dose of 1 mg/kg upto maximum of 30 mg. ***IV dosing:*** One dose of 0.5 mg/kg upto maximum of 15 mg.

Oral Dosage and Administration: ***Adults:*** 10 mg every 4 to 6 hours as required. Doses exceeding 40 mg per day are not recommended; maximimum duration of treatment 7 days. For patients receiving parenteral TOROAID, and who are converted to TOROAID oral tablets, the total combined daily dose should not be exceeded 90 mg. Patients should be converted to oral treatment as soon as possible.

Elderly: For elderly 10 mg tablet 6 or 8 hours interval. Patients older than 65 years, doses should be minimized as possible.

Children: TOROAID tablet is contraindicated for patients below 16 years of age.

Contraindications: A history of, or active, peptic ulceration or gastro-intestinal bleeding. Severe heart failure, suspected or confirmed cerebrovascular bleeding, Haemorrhagic diatheses, including coagulation disorders. Hypersensitivity to Ketorolac or any of its ingredients, or other NSAIDs and those patients in whom aspirin or other prostaglandin synthesis inhibitors induce allergic reactions (severe anaphylactic-like reactions have been observed in such patients). The complete or partial syndrome of nasal polyps, angioedema or bronchospasm. Concurrent treatment with other NSAIDs, oxpentifylline, probenecid or lithium salts. Hypovolaemia from any cause or dehydration. Moderate or severe renal impairment (serum creatinine > 160 micromol/L). A history of asthma. Patients who have had operations with a high risk of haemorrhage or incomplete haemostasis. Patients on anti-coagulants including low dose heparin (2500 - 5000 units twelve hourly). During pregnancy, delivery or lactation. Ketorolac is contraindicated as prophylactic analgesia before surgery due to inhibition of platelet aggregation and is contraindicated intra-operatively because of the increased risk of bleeding. Ketorolac is contraindicated in patients currently receiving aspirin.

Side Effects: The following side-effects have been reported with Ketorolac.

Gastro-intestinal: Nausea, dyspepsia, gastro-intestinal pain, gastro-intestinal bleeding, gastritis, oesophagitis, diarrhoea, constipation, flatulence, melaena, peptic ulcer, ulcerative stomatitis, vomiting, perforation, pancreatitis.

Central nervous/musculoskeletal systems: Anxiety, drowsiness, dizziness, headache, sweating, dry mouth, nervousness, depression, euphoria, convulsions, excessive thirst, insomnia, fatigue, vertigo, myalgia, hallucinations, hyperkinesia, hearing loss, tinnitus.

Renal: Nephrotoxicity including increased urinary frequency, oliguria, acute renal failure, hyponatraemia, hyperkalaemia, nephrotic syndrome.

Cardiovascular/haematological: Bradycardia, pallor, purpura, thrombocytopenia, neutropenia, agranulocytosis, , haemolytic anaemia, hypertension, palpitations, chest pain. Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.

Respiratory: Dyspnoea, asthma, pulmonary oedema.

Other: Asthenia, oedema, weight gain, abnormalities of liver function tests, hepatitis, liver failure, jaundice, fever. Injection site pain has been reported in some patients.

Precautions: Undesirable effects of Ketorolac may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms. Patients over the age of 65 years may be at a greater risk of experiencing adverse events than younger patients. Ketorolac can cause gastro-intestinal irritation, ulcers or bleeding in patients with or without a history of previous symptoms. Bronchospasm may be precipitated in patients with a history of asthma. Since Ketorolac Tromethamine and its metabolites are excreted primarily by the kidney, patients with moderate to severe impairment of renal function (serum creatinine greater than 160 micromol/L) should not receive Ketorolac. Fluid retention and oedema have been reported with the use of Ketorolac and it should therefore be used with caution in patients with cardiac decompensation, hypertension or similar conditions. Ketorolac is not an anesthetic agent and possesses no sedative or anxiolytic properties; therefore it is not recommended as a pre-operative medication for the support of anesthesia when these effects are required.

Drug Interactions: Ketorolac should not be used with other NSAIDs or in patients receiving aspirin because of the potential for additive side-effects. Ketorolac did not alter digoxin protein binding. In vitro studies indicated that at therapeutic concentrations of salicylate (300 µg/ml) and above, the binding of Ketorolac was reduced from approximately 99.2% to 97.5%. Therapeutic concentrations of digoxin, warfarin, paracetamol, phenytoin and tolbutamide did not alter Ketorolac protein binding. Because Ketorolac is a highly potent drug and present in low concentrations in plasma, it would not be expected to displace other protein-bound drugs significantly. Care should be taken when administering Ketorolac with anti-coagulants since co-administration may cause an enhanced anti-coagulant effect. Ketorolac and other non-steroidal anti-inflammatory drugs can reduce the anti-hypertensive effect of beta-blockers and may increase the risk of renal impairment when administered concurrently with ACE inhibitors, particularly in volume depleted patients. NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma cardiac glycoside levels when co-administered with cardiac glycosides. Caution is advised when methotrexate is administered concurrently, since some prostaglandin synthesis inhibiting drugs have been reported to reduce the clearance of methotrexate, and thus possibly enhance its toxicity. As with all NSAIDs, caution should be taken when co-administering with cortico-steroids because of the increased risk of gastro-intestinal bleeding. Patients taking quinolones may have an increased risk of developing convulsions. Co-administration with diuretics can lead to a reduced diuretic effect, and increase the risk of nephrotoxicity of NSAIDs. In patients receiving lithium, there is a possible inhibition of renal lithium clearance, increased plasma lithium concentration, and potential lithium toxicity.

Use in Pregnancy and Lactation: There was no evidence of teratogenicity in rats or rabbits studied at maternally-toxic doses of Ketorolac. Prolongation of the gestation period and/or delayed parturition were seen in the rat. Ketorolac and its metabolites have been shown to pass into the foetus and milk of animals. Ketorolac has been detected in human milk at low levels. Safety in human pregnancy has not been established. Congenital abnormalities have been reported in association with NSAID administration in man, however these are low in frequency and do not follow any discernible pattern. Ketorolac is therefore contraindicated during pregnancy, labour or delivery, or in mothers who are breast-feeding.

Storage Conditions: Store in a cool and dry place away from light. Keep out of reach of children.

Commercial Pack:
TOROAID 30 IM/IV Injection: Each box contains 1 blister pack of 1 ampoule of 1 ml sterile solution and 1 sterile disposable syringe.
TOROAID 60 IM Injection: Each box contains 1 blister pack of 1 ampoule of 2 ml sterile solution and 1 sterile disposable syringe.
TOROAID 10 Tablet: Each box contains 3 Alu-Alu blister packs of 10 tablets.

Manufactured by:
general GENERAL Pharmaceuticals Ltd.
Gazipur, Bangladesh
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