The principal route of elimination of ketorolac and its metabolites is renal. About 92% of a given dose (L/kg) in normal adult subjects (n=37), the total clearance of 30 mg IV-administered ketorolac ∞ 6.1 (8.0-39.1)

Ketorolac tromethamine can cause peptic ulcers, gastrointestinal bleeding and/or perforation of the gastrointestinal tract. These events may occur at any time during therapy, with an increased risk during long-term use. Although most cases appear to recover, some patients will require surgery and follow-up care for complications.

RISK DURING LABOR AND DELIVERY

Ketorolac tromethamine is CONTRAINDICATED as prophylactic analgesic before any major surgery.

Ketorolac tromethamine is CONTRAINDICATED in patients with advanced renal impairment and in individuals who are dehydrated, with low blood volume, or who are hypotensive.

Oral ketorolac tromethamine is indicated only as continuation treatment following IV or IM dosing of ketorolac tromethamine injection (see WARNINGS).

**WARNINGS**

- **Contraindications**: Ketorolac tromethamine is CONTRAINDICATED for neuraxial (epidural or intrathecal) administration due to its potential to cause spinal or epidural anesthetic effects. The concomitant use of ketorolac tromethamine and pentoxifylline is contraindicated. The concomitant use of ketorolac tromethamine and probenecid is contraindicated.

- **Adverse Reactions**: Ketorolac tromethamine can cause serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines. These events may occur at any time during therapy, with an increased risk during long-term use. The most serious risks associated with ketorolac tromethamine are:

  - Stomach pain
  - Vomiting
  - Diarrhea
  - Constipation

- **Interactions**: Ketorolac tromethamine is contraindicated in patients on concomitant therapy that affects hemostasis, including prophylactic low-dose heparin or aspirin.
Clinical trials of several COX-2 selective and nonselective NSAIDs of up to three weeks' duration found that, at therapeutic doses, these drugs may cause elevated liver enzymes, which may persist for some time after treatment discontinuation. The use of ketorolac tromethamine, as with any drug known to inhibit cyclooxygenase (COX), may cause serious skin side effects such as exfoliative dermatitis, SJS, and TEN, which can be fatal. These serious events may occur in patients without a history of hypersensitivity to aspirin-type drugs and may occur after a single dose. The risk of serious skin side effects can be decreased by using the lowest effective dose for the shortest duration consistent with clinical needs.

The recommended dose is 30 mg ketorolac tromethamine injection every 6 hours. The maximum daily dose is 120 mg. In patients with creatinine clearance ≤30 mL/min, dose adjustment is not necessary as renal impairment does not influence ketorolac's elimination. The elimination half-life of ketorolac was found to be approximately 3.3 hours in patients with creatinine clearance 10 to 30 mL/min and approximately 15.1 hours in patients with creatinine clearance ≤10 mL/min. Therefore, concomitant use of ketorolac tromethamine and probenecid is contraindicated. The terminal elimination half-life of ketorolac was approximately threefold from 5.4 to 17.8 mcg/h/mL and terminal half-life increased approximately twofold from 6.6 to 13.2 hours after oral administration in patients with impaired hepatic function (see CLINICAL PHARMACOLOGY). The elimination half-life was increased to 15.1 hours in patients with impaired renal and hepatic function.

Alternatively, ketorolac tromethamine injection may be administered by intravenous infusion at a rate of 150 mcg/min. The injection must be given over 5 minutes or more. The maximum of 60 mg/day may be given by continuous intravenous infusion. The maximum 120 mg/day of ketorolac tromethamine may be given by intermittent intravenous infusion in patients who are unable to take oral medication.

Ketorolac tromethamine should be used with caution in patients with impaired hepatic function or a history of liver disease and should not be administered to patients with this form of aspirin sensitivity. Ketonuria may be observed, especially in patients with diabetes mellitus.

Ketorolac tromethamine should not be administered to patients with asthma, bronchospasm, respiratory depression, pneumonia, or nasal congestion. The use of ketorolac tromethamine injection with other NSAIDs or salicylates is not recommended. The concurrent use of ketorolac tromethamine and anticoagulants should be done extremely cautiously, and patients taking anticoagulants should have their prothrombin times monitored more frequently than usual. In patients taking ketorolac tromethamine or other NSAIDs in clinical trials, the most frequently reported adverse events were dyspepsia, which occurred in 6.2% of patients, headache, which occurred in 5.1% of patients, and upper respiratory tract infections, which occurred in 3.9% of patients. Other reported adverse events included anemia, leukopenia, hypotension, aphthous stomatitis, allergic reactions, central nervous system effects, gastrointestinal bleeding and perforation, arterial and venous thrombosis, changes in renal function, Sally's syndrome, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur in patients without a history of hypersensitivity to aspirin-type drugs and may occur after a single dose. The risk of serious skin side effects can be decreased by using the lowest effective dose for the shortest duration consistent with clinical needs.

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