Ketorolac tromethamine is contraindicated in patients with underlying renal insufficiency and in patients with a recent MI (see CONTRAINDICATIONS and WARNINGS). Ketorolac tromethamine should be used with caution in patients with recent other GI tract surgery, in patients with a history of allergy to NSAIDs, in patients with a recent MI (within 30 days), or in patients with congestive heart failure.

CLINICAL PHARMACOLOGY

Ketorolac tromethamine is a nonsteroidal anti-inflammatory drug (NSAID) that exhibits anti-inflammatory and analgesic effects.

The mechanism of action of NSAIDs is to inhibit the synthesis of prostaglandins by inhibition of the enzyme cyclooxygenase (COX). There are two COX enzymes, COX-1 and COX-2.

COX-1 is responsible for maintaining the integrity of the stomach lining and COX-2 is responsible for the inflammatory response.

The analgesic and anti-inflammatory effects of ketorolac tromethamine are due to its inhibition of COX-2.

The kinetic data for ketorolac tromethamine are consistent with previous animal studies.

The pharmacokinetics and pharmacodynamics of ketorolac tromethamine are similar across different populations, including elderly subjects and patients with hepatic and renal dysfunction.

Table 1: Pharmacokinetic Parameters of Ketorolac Tromethamine (Mean ± SD) Following Oral Administration of 15 mg or IV Administration of 10 mg

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Oral 15 mg</th>
<th>IV 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (mcg/mL)</td>
<td>1.27 ± 0.77</td>
<td>1.02 ± 0.58</td>
</tr>
<tr>
<td>Tmax (h)</td>
<td>0.5 ± 0.25</td>
<td>0.25 ± 0.10</td>
</tr>
<tr>
<td>AUC (mcg·h/mL)</td>
<td>46.4 ± 25.11</td>
<td>31.2 ± 18.03</td>
</tr>
<tr>
<td>CLR (L/hr/kg)</td>
<td>0.046 ± 0.029</td>
<td>0.034 ± 0.019</td>
</tr>
</tbody>
</table>

In conclusion, ketorolac tromethamine is well-tolerated and effective in the short-term treatment of mild to moderate pain. However, long-term use should be avoided due to the potential risk of adverse effects.


dervived from PO pharmacokinetic studies in 77 normal fasted volunteers. The biological activity of ketorolac, like that of other NSAIDs, is not completely understood but may be related to prostaglandin synthetase inhibition. The biological activity of ketorolac is derived from the R-enantiomer, which is converted to the S-enantiomer in humans. The clearance of the racemate in normal subjects, elderly individuals and in hepatically and renally impaired individuals is significantly lower than that of the R-enantiomer.

The clearance of ketorolac tromethamine varies among individuals, and is influenced by factors such as age, gender, obesity, and renal function.

The major route of elimination of ketorolac and its metabolites is renal. About 92% of a given dose is found in the urine, approximately 7% in the feces.

The total clearance of ketorolac tromethamine is approximately 0.046 L/hr/kg in normal subjects, 0.034 L/hr/kg in elderly individuals, and 0.029 L/hr/kg in hepatically and renally impaired individuals.

Ketorolac tromethamine is a racemic mixture of 50% of the R-enantiomer and 50% of the S-enantiomer.

The dosage of ketorolac tromethamine should be individualized for each patient, based on their age, weight, and renal function.
Medication Guide for Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

What is the most important information I should know about medicines called Nonsteroidal Anti-inflammatory Drugs (NSAIDs)?

NSAIDs can cause serious side effects, including:

- Increased risk of heart attack or stroke that can lead to death. This risk may happen early in treatment and may increase over time with higher doses of NSAIDs or with longer use of NSAIDs.

The risk of getting an ulcer or bleeding increases with:

- past history of stomach ulcers or stomach or intestinal bleeding with use of NSAIDs
- taking other drugs that can increase the risk of ulcers or bleeding (see Table 3: Incidence of Clinically Serious G.I. Bleeding as Related to Age, Total Daily Dose, and Ejection Fraction)
- smoking
- drinking alcohol

Other NSAIDs can increase the risk of bleeding, ulcers, and tears (perforation) of the esophagus (tube leading from the mouth to the stomach).

The risk of getting an ulcer or bleeding increases with:

- age
- taking other drugs that can increase the risk of ulcers or bleeding
- smoking
- drinking alcohol

NSAIDs should only be used:

- as exactly as prescribed
- at the lowest dose possible for your treatment

What are NSAIDs?

NSAIDs are used to treat pain and redness, swelling, and heat (inflammation) from medical conditions such as different types of arthritis, menstrual cramps, and other types of short-term pain.

Who should not take NSAIDs?

Do not take NSAIDs right before or after a heart surgery called a "coronary artery bypass graft (CABG)," Avoid taking NSAIDs after a recent heart attack, unless your healthcare provider tells you to. You may have an increased risk of another heart attack if you take NSAIDs after a recent heart attack.

Increased risk of bleeding, ulcers, and tears (perforation) of the esophagus (tube leading from the mouth to the stomach), stomach and intestines:

- any time during use
- without warning symptoms
- that may cause death

The risk of getting an ulcer or bleeding increases with:

- past history of stomach ulcers or stomach or intestinal bleeding with use of NSAIDs
- taking other drugs that can increase the risk of ulcers or bleeding (see Table 3: Incidence of Clinically Serious G.I. Bleeding as Related to Age, Total Daily Dose, and Ejection Fraction)

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Who should not take NSAIDs?

Do not take NSAIDs:

- if you have had an asthma attack, hives, or other allergic reaction with aspirin or any other NSAIDs.
- before or after heart bypass surgery.

Before taking NSAIDs, tell your healthcare provider about all of your medical conditions, including:

- liver or kidney problems
- high blood pressure
- have asthma
- are pregnant or plan to become pregnant. Talk to your healthcare provider if you are considering taking NSAIDs during pregnancy.

You should not take NSAIDs after 29 weeks of pregnancy.

Tell your healthcare provider about all of the medicines you take, including prescription or over-the-counter medicines, vitamins or herbal supplements, and other medicines that can interact with each other and cause serious side effects. Do not start taking any new medicine without talking to your healthcare provider first.

What are the possible side effects of NSAIDs?

NSAIDs can cause serious side effects, including:

- shortness of breath or trouble breathing
- chest pain
- weakness in one part or side of your body

Stop taking your NSAID and call your healthcare provider right away if you get any of the following symptoms:

- tinnitus
- nausea
- more tired or weaker than usual
- diarrhea
- pruritus
- dizziness
- unusual weight gain
- life-threatening allergic reactions

Other side effects of NSAIDs include:

- bowel pain
- blood in your stool
- bleeding or bruising
- changes in your sense of taste
- warmth, redness, or swelling of the skin