KETOROLAC

A source of KETOROLAC for your facility

Packaging is InformatIV™

- Available in 15 mg per mL, 30 mg per mL and 60 mg per 2 mL single-dose vials
- Easy-to-read drug name and strengths
- Each strength is distinguished by a different color on the caps, labels and cartons
- Unique label and carton design to help products stand out on the shelf
- Preservative-free, AP rated, bar coded and not made with natural rubber latex

KETOROLAC Tromethamine Injection, USP

Please see full prescribing information, including boxed warning, for KETOROLAC Tromethamine Injection, USP, enclosed.
KETOROLAC Tromethamine Injection, USP

INDICATIONS AND USAGE
Ketorolac tromethamine injection is indicated for the short-term (≤5 days) management of moderately severe acute pain that requires analgesia at the opioid level, usually in a postoperative setting.

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

HYPERSENSITIVITY
Hypersensitivity reactions, ranging from bronchospasm to anaphylactic shock, have occurred and appropriate counteractive measures must be available when administering the first dose of ketorolac tromethamine injection (see CONTRAINDICATIONS and WARNINGS). Ketorolac tromethamine is CONTRAINDICATED in patients with previously demonstrated hypersensitivity to ketorolac tromethamine or allergic manifestations to aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs).

WARNINGS
Ketorolac tromethamine is a nonsteroidal anti-inflammatory drug (NSAID), is indicated for the short-term (up to 5 days in adults), management of moderately severe acute pain that requires analgesia at the opioid level. Oral ketorolac tromethamine is indicated only as continuation treatment following IV or IM dosing of ketorolac tromethamine, if necessary. The total combined duration of use of oral ketorolac tromethamine and ketorolac tromethamine injection should not exceed 5 days.

Ketorolac tromethamine and ketorolac tromethamine injection are to be used only as indicated for the short-term (up to 5 days in adults), management of moderately severe acute pain that requires analgesia at the opioid level.

DOSAGE AND ADMINISTRATION

SPECIAL POPULATIONS
Doses of ketorolac tromethamine injection are not to exceed 60 mg (total dose per day) in these patients.

DOSSAGE AND ADMINISTRATION
Ketorolac Tromethamine Tablets
Ketorolac tromethamine tablets are indicated only as continuation therapy to ketorolac tromethamine injection, and the combined duration of use of ketorolac tromethamine injection and ketorolac tromethamine tablets is not to exceed 5 (five) days, because of the increased risk of serious adverse events.

CONTRAINDICATIONS
Ketorolac tromethamine injection is contraindicated in patients with previously demonstrated hypersensitivity to ketorolac tromethamine.

Ketorolac tromethamine injection is contraindicated in patients with active peptic ulcer disease, in patients with recent gastrointestinal bleeding or perforation, in patients with a history of peptic ulcer disease or gastrointestinal bleeding. Elderly patients are at greater risk for serious gastrointestinal events (see WARNINGS).

NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk (see WARNINGS and CLINICAL TRIALS).

Ketorolac tromethamine is CONTRAINDICATED for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery (see WARNINGS).

RENAL RISK
Ketorolac tromethamine is CONTRAINDICATED in patients with advanced renal impairment and in patients at risk for renal failure due to volume depletion (see WARNINGS).

RISK OF BLEEDING
Ketorolac tromethamine inhibits platelet function and is, therefore, CONTRAINDICATED in patients with suspected or confirmed cerebrovascular bleeding, patients with hemorrhagic diathesis, incomplete hemostasis and those at high risk of bleeding (see WARNINGS and PRECAUTIONS).

This SAGENT product meets stringent FDA requirements and is AP rated, preservative-free and not made with natural rubber latex.

To order, or for more information about how to Discover Injectables Excellence® with SAGENT, contact your sales representative, call 1-866-625-1618 or visit www.SagentPharma.com.
KETOROLAC Tromethamine Injection, USP

IMPORTANT SAFETY INFORMATION

(continued from previous page)

- Ketorolac tromethamine injection is contraindicated in patients with advanced renal impairment or in patients at risk for renal failure due to volume depletion.
- Ketorolac tromethamine injection is contraindicated 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.
- Ketorolac tromethamine inhibits platelet function and is, therefore, contraindicated in patients with suspected or confirmed cerebrovascular bleeding, hemorrhagic diathesis, incomplete hemostasis and those at high risk of bleeding.
- Ketorolac tromethamine injection is contraindicated in patients currently receiving aspirin or NSAIDs because of the cumulative risks of inducing serious NSAID-related adverse events.
- The concomitant use of ketorolac tromethamine injection and probenecid is contraindicated.
- The concomitant use of ketorolac tromethamine injection and pentoxifylline is contraindicated.
- Ketorolac tromethamine injection is contraindicated for neuraxial (epidural or intrathecal) administration due to its alcohol content.

WARNINGS

- The total combined duration of use of oral ketorolac tromethamine and IV or IM dosing of ketorolac tromethamine is not to exceed 5 days in adults. Ketorolac tromethamine injection is not indicated for use in pediatric patients.
- Ketorolac tromethamine is contraindicated in patients with previously documented peptic ulcers and/or GI bleeding.
- To minimize the potential risk for an adverse GI event or adverse CV event, the lowest effective dose should be used for the shortest possible duration.
- Use of ketorolac tromethamine in patients who have coagulation disorders should be undertaken very cautiously, and those patients should be carefully monitored.
- In postmarketing experience, postoperative hematomas and other signs of wound bleeding have been reported in association with the peri-operative use of IV or IM dosing of ketorolac tromethamine. Therefore, peri-operative use of ketorolac tromethamine should be avoided and postoperative use be undertaken with caution when hemostasis is critical.
- Ketorolac tromethamine should be used with caution in patients with impaired renal function. There have been reports of acute renal failure, interstitial nephritis and nephrotic syndrome with the use of ketorolac tromethamine.
- Anaphylactoid reactions may occur in patients without prior known exposure to ketorolac tromethamine. Ketorolac tromethamine should not be given to patients with the aspirin triad. This symptom complex typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other NSAIDs. Emergency help should be sought in cases where an anaphylactoid reaction occurs.
- NSAIDs, including ketorolac tromethamine, can lead to onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of CV events. Patients taking thiazides or loop diuretics may have impaired response to these therapies when taking NSAIDs. NSAIDs, including ketorolac tromethamine, should be used with caution in patients with hypertension. Blood pressure (BP) should be monitored closely during the initiation of NSAID treatment and throughout the course of therapy.
- Fluid retention, edema, retention of NaCl, oliguria, elevations of serum urea nitrogen and creatinine have been reported in clinical trials with ketorolac tromethamine. Therefore, ketorolac tromethamine should be used only very cautiously in patients with cardiac decompensation, hypertension or similar conditions.
- NSAIDs, including ketorolac tromethamine, can cause serious skin adverse events such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur without warning. Patients should be informed about the signs and symptoms of serious skin manifestations and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.
- In late pregnancy, as with other NSAIDs, ketorolac tromethamine should be avoided because it may cause premature closure of the ductus arteriosus.

PRECAUTIONS

- Ketorolac tromethamine cannot be expected to substitute for corticosteroids or to treat corticosteroid insufficiency.
- Ketorolac tromethamine should be used with caution in patients with impaired hepatic function or a history of liver disease. Borderline elevations of one or more liver tests may occur in up to 15% of patients taking NSAIDs including ketorolac tromethamine.
- Anemia is sometimes seen in patients receiving NSAIDs, including ketorolac tromethamine. Patients receiving ketorolac tromethamine who may be adversely affected by alterations in platelet function, such as those with coagulation disorders or patients receiving anticoagulants, should be carefully monitored.
- Since cross reactivity, including bronchospasm, between aspirin and other nonsteroidal anti-inflammatory drugs has been reported in patients with aspirin-sensitive asthma, ketorolac tromethamine should not be administered to patients with this form of aspirin sensitivity and should be used with caution in patients with preexisting asthma.
- Ketorolac tromethamine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- The use of ketorolac tromethamine is contraindicated 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.
- The use of ketorolac tromethamine, as with any drug known to inhibit cyclooxygenase/prostaglandin synthesis, may impair fertility and is not recommended in women attempting to conceive.
- Exercise caution when ketorolac is administered to a nursing woman.
- Ketorolac tromethamine is not indicated for use in pediatric patients. The safety and effectiveness of ketorolac tromethamine in pediatric patients below the age of 17 have not been established.
- Extreme caution, reduced dosages, and careful clinical monitoring must be used when treating the elderly with ketorolac tromethamine.

ADVERSE REACTIONS

- Adverse reaction rates increase with higher doses of ketorolac tromethamine. Practitioners should be alert for the severe complications of treatment with ketorolac tromethamine, such as GI ulceration, bleeding and perforation, postoperative bleeding, acute renal failure, anaphylactic and anaphylactoid reactions and liver failure.
- The most frequently reported adverse experiences in approximately 1% to 10% of patients taking ketorolac tromethamine or other NSAIDs in clinical trials are nausea, headaches, abdominal pain, vomiting, flatulence, gross GI bleeding/perforation, stomatitis, constipation/diarrhea, heartburn, dyspepsia and GI ulcers (gastrointestinal). Other adverse experiences are abnormal renal function, drowsiness, injection site pain, rashes, anemia, edema, hypertension, pruritus, tinnitus, dizziness, elevated liver enzymes, increased bleeding time and sweating.

OVERDOSAGE

Symptoms following acute NSAIDs overdoses are usually limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain, which are generally reversible with supportive care. Gastrointestinal bleeding can occur. Hypertension, acute renal failure, respiratory depression and coma may occur, but are rare. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose.

Patients should be managed by symptomatic and supportive care following an NSAIDs overdose. There are no specific antidotes. Emesis and/or activated charcoal (60 g to 100 g in adults, 1 g/kg to 2 g/kg in children) and/or osmotic cathartic may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large oral overdose (5 to 10 times the usual dose).

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see full prescribing information for KETOROLAC Tromethamine Injection, USP.
GASTROINTESTINAL RISK

• Nonsteroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including MI and stroke, which can be fatal. The increased risk for serious CV events appears to be of similar magnitude across different subclasses of NSAIDs, including COX-2 inhibitors. This risk may increase with duration of use. Therefore, NSAIDs should be used at the lowest effective dose for the shortest duration consistent with patient treatment needs (see DOSAGE AND ADMINISTRATION).

HYPERSENSITIVITY

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

• Ketorolac tromethamine inhibits platelet function and is, therefore, CONTRAINDICATED in patients with suspected or confirmed cerebrovascular disease or recent stroke, and those with active peptic ulcer disease or gastrointestinal bleeding. Elderly patients are at greater risk for these events (see WARNINGS and PRECAUTIONS).

• Ketorolac tromethamine is CONTRAINDICATED in the setting of coronary artery bypass graft (CABG) surgery (see WARNINGS).

RENAL RISK

Ketorolac tromethamine is CONTRAINDICATED in patients with advanced renal impairment and in patients at risk for renal failure due to volume depletion (see WARNINGS).

RISK FACTORS

• Hypersensitivity reactions, ranging from rash to anaphylactic shock, have occurred and appropriate countermeasure must be taken.

• Ketorolac tromethamine is associated with an increased risk of upper gastrointestinal events including bleeding, ulcers, and perforation in patients treated for short-term (≤5 days) or long-term (>5 days) for the treatment of pain. These events may occur any time during use of ketorolac tromethamine (see WARNINGS and PRECAUTIONS).

• Because of the potential of increasing the frequency and severity of adverse reactions associated with the recommended doses of ketorolac tromethamine, there have been reports of fatal renal failure in patients receiving the recommended doses of ketorolac tromethamine, and oral ketorolac tromethamine is to be used only as continuation treatment, if necessary.

• Ketorolac tromethamine injection is contraindicated in patients who have previously experienced anaphylactoid or anaphylactic reactions to ketorolac tromethamine or a component of the drug product (see WARNINGS: Anaphylactoid Reactions).

CONTRAINICATIONS

(See also Boxed WARNING)

Ketorolac tromethamine is contraindicated in patients with previously demonstrated hypersensitivity to ketorolac tromethamine. Ketorolac tromethamine injection is contraindicated in patients with recent or concurrent use of aspirin or other NSAIDs due to the potential for increased risk of severe bleeding. Ketorolac tromethamine injection should be used with caution in patients with a history of peptic ulcer disease or gastrointestinal bleeding. Ketorolac tromethamine is not to be used in patients who have experienced adverse reactions to ketorolac tromethamine injection or single-dose preparations after taking aspirin or other NSAIDs. Safe, rarely, rapid, anaphylactic-like reactions to ketorolac have been reported in such patients (see WARNINGS: Anaphylactoid Reactions). Ketorolac tromethamine injection is contraindicated as prophylactic analgesic before any major surgery.

Ketorolac tromethamine injection is contraindicated in the setting of coronary artery bypass graft (CABG) surgery (see WARNINGS).

Ketorolac tromethamine injection is contraindicated in patients with a history of serious adverse events due to ketorolac tromethamine injection, including sensitization reactions or anaphylactoid reactions. Ketorolac tromethamine injection is contraindicated in patients with a history of perioperative advanced renal impairment or in patients at risk for renal failure due to volume depletion (see WARNINGS: for corrections of volume depletion).

Ketorolac tromethamine is contraindicated in labor and delivery, because of its potential to cause premature closure of the ductus arteriosus. In preterm labor (before 34 weeks gestation), ketorolac tromethamine injection is to be used only as a single dose for the shortest duration consistent with patient treatment needs (see WARNINGS: Neonatal Risk).

Ketorolac tromethamine inhibits platelet function and should be used with caution in patients with active peptic ulcer disease or gastrointestinal bleeding. Ketorolac tromethamine is contraindicated in patients currently receiving aspirin or NSAIDs because of the cumulative risks of resulting serious NSAID-related adverse events.

The concurrent use of ketorolac tromethamine injection and pethidine is contraindicated.

The concurrent use of ketorolac tromethamine injection and pentazocine is contraindicated.

Ketorolac tromethamine is contraindicated for use in patients (or in those receiving aspirin or NSAIDs) due to an alcohol or NSAID abstinence or alcohol or NSAID abuse. Use of ketorolac tromethamine injection is contraindicated in patients with severe heart failure; no benefit is expected from the use of ketorolac tromethamine in patients with severe heart failure, worsening heart failure, or death. Use of ketorolac tromethamine injection is contraindicated in patients with severe heart failure; no benefit is expected from the use of ketorolac tromethamine in patients with severe heart failure, worsening heart failure, or death. Use of ketorolac tromethamine injection is contraindicated in patients with severe heart failure; no benefit is expected from the use of ketorolac tromethamine in patients with severe heart failure, worsening heart failure, or death.
Concomitant administration of oral ketorolac tromethamine and aspirin is not generally recommended because of the potential of increased adverse effects. When ketorolac tromethamine is administered with aspirin, its protein binding is reduced, although the clearance of free ketorolac tromethamine treatment (see PRECAUTIONS, ADVERSE REACTIONS).

When ketorolac tromethamine is administered with aspirin, its protein binding is reduced, although the clearance of free ketorolac tromethamine is not altered. The clinical significance of this interaction is not known; however, as with other NSAIDs, concomitant use of ketorolac tromethamine with aspirin should not be administered to patients already taking aspirin and should be used with caution in patients with previous aspirin hypersensitivity.

Information for Patients
Ketorolac tromethamine is a patient-controlled NSAID and may cause serious side effects such as gastrointestinal bleeding or liver failure, which may result in hospitalization and even death. Although serious skin reactions may occur, serious reactions are less common. Patients should be instructed to report any changes in liver function tests persist or worsen, ketorolac tromethamine should be discontinued.

Ketorolac tromethamine should be used with caution in patients with impaired hepatic function or a history of liver disease. Borderline increases in liver enzymes have been observed in some patients taking ketorolac tromethamine without obvious clinical implications. Patients with active liver disease, including those with cirrhosis, should not be given ketorolac tromethamine.

Ketorolac tromethamine is contraindicated 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 and effect of warfarin and NSAIDs, in general, on GI bleeding are synergistic, such that the users of both drugs together have a risk of significant bleeding. Therefore, when the drug is used in patients receiving warfarin, the international normalized ratio should be monitored frequently. In patients taking warfarin, ketorolac tromethamine may cause an increase in the risk of abnormal bleeding and prolonged bleeding time, or in patients on heparin, it may reduce the effectiveness of heparin. In patients on anticoagulant therapy, the anticoagulant effect should be monitored. Changes in the anticoagulant effect may be anticipated in patients taking ketorolac tromethamine. Increased ACT and PT may occur with ketorolac tromethamine administration.

Ketorolac tromethamine is contraindicated in patients with a history of angioedema or asthma associated with the use of aspirin. Cross-reactive sensitivity to other NSAIDs has been reported. Therefore, ketorolac tromethamine should not be administered to patients with previous anaphylaxis or urticaria associated with the use of aspirin, or to those with a history of allergy to aspirin or other NSAIDs.

In late pregnancy, as with other NSAIDs, ketorolac tromethamine should be avoided because it will cause premature closure of the ductus arteriosus.

Hypersensitivity reactions, such as anaphylactoid reactions, urticaria, angioedema, asthma, dyspnea, pruritus, rash, or anaphylaxis, have been reported in patients treated with ketorolac tromethamine. Rash, urticaria, pruritus, or anaphylaxis occurring within 8 hours of the first dose is considered to be an idiosyncratic adverse reaction to ketorolac tromethamine. Patients who develop any rash or pruritus should not receive additional doses of ketorolac tromethamine.

Skin Reactions
Ketorolac tromethamine has been reported to cause urticaria, angioedema, rash, pruritus, or anaphylactic reactions in a small number of patients. These reactions have been attributed to the presence of non-steroidal prostaglandin synthase and drug-related allergic reactions, respectively. If a patient develops urticaria, angioedema, or anaphylactoid reaction with ketorolac tromethamine, this drug should be discontinued and appropriate treatment instituted.