Front

YUKON®

(Ketorolac Tromethamine)

10 mg

Tablet

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COMPOSITION:

Yukon Tablet 10 mg:

Each film coated tablet contains:

Ketorolac tromethamine USP ..... 10 mg.

Product Specs.: USP

WARNINGS AND PRECAUTIONS

Ketorolac Tromethamine is not indicated for use in paediatric patients and it is NOT indicated for minor or chronic painful conditions. Increasing the dose of Ketorolac Tromethamine beyond a daily maximum of 40 mg in adults will not provide better efficacy but will increase the risk of developing serious adverse events.

GASTROINTESTINAL RISK:

Ketorolac Tromethamine, including Ketorolac Tromethamine can cause peptic ulcers, gastrointestinal bleeding and/or perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Therefore, Ketorolac Tromethamine is CONTRAINDICATED in patients with active peptic ulcer disease, in patients with recent gastrointestinal bleeding or perforation, and in patients with a history of peptic ulcer disease or gastrointestinal bleeding. Elderly patients are at greater risk for serious gastrointestinal events.

CARDIOVASCULAR RISK:

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

RENAL RISK:

Ketorolac Tromethamine is CONTRAINDICATED in patients with advanced renal impairment and in patients at risk for renal failure due to volume depletion.

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.

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

RISK DURING LABOR AND DELIVERY: The use of Ketorolac Tromethamine in labor and delivery is contraindicated because it may adversely affect fetal circulation and inhibit uterine contractions.

CONCOMITANT USE WITH NSAIDS:

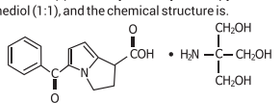
Ketorolac Tromethamine is CONTRAINDICATED in patients currently receiving aspirin or NSAIDs because of the cumulative risk of inducing serious NSAID-related side effects.

SPECIAL POPULATIONS:

Dosage should be adjusted for patients 65 years or older, for patients under 50 kg (110 lbs) of body weight and for patients with moderately elevated serum creatinine.

DESCRIPTION:

Ketorolac Tromethamine is a member of the pyrrolo-pyrrole group of nonsteroidal anti-inflammatory drugs (NSAIDs). The chemical name for ketorolac tromethamine is (±)-5-benzoyl-2,3-dihydro-1H-pyrrolizine-1-carboxylic acid, compound with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1), and the chemical structure is.



Ketorolac Tromethamine is a racemic mixture of [-]S and [+]R ketorolac Tromethamine. Ketorolac Tromethamine may exist in three crystal forms. All forms are equally soluble in water. Ketorolac Tromethamine has a pKa of 3.5 and an n-octanol/water partition coefficient of 0.26. The molecular weight of Ketorolac Tromethamine is 376.41. Its molecular formula is $C_{19}H_{24}N_2O_6$.

Ketorolac Tromethamine is available as round, white, film-coated, red-printed tablets. Each tablet contains 10 mg Ketorolac Tromethamine, the active ingredient, with added lactose, magnesium stearate and microcrystalline cellulose. The white film-coating contains hydroxypropyl methylcellulose, polyethylene glycol and titanium dioxide.

CLINICAL PHARMACOLOGY:

Pharmacodynamics:

Ketorolac Tromethamine is a nonsteroidal anti-inflammatory drug (NSAID) that exhibits analgesic activity. The mechanism of action of ketorolac, like that of other NSAIDs, is not completely understood but may be related to prostaglandin synthetase inhibition. The biological activity of Ketorolac Tromethamine is associated with the S-form. Ketorolac Tromethamine possesses no sedative or anxiolytic properties. The peak analgesic effect of Ketorolac Tromethamine occurs within 2 to 3 hours and is not statistically significantly different over the recommended dosage range of KetorolacTromethamine. The greatest difference between large and small doses of Ketorolac Tromethamine is in the duration of analgesia.

Pharmacokinetics:

Ketorolac tromethamine is a racemic mixture of [-]S- and [+]R-enantiomeric forms, with the S-form having analgesic activity.

Comparison of IV, IM and Oral Pharmacokinetics:

In adults, the extent of bioavailability following administration of the oral form of Ketorolac tromethamine and the IM form of ketorolac tromethamine was equal to that following an IV bolus. Linear Kinetics In adults, following administration of single oral doses of Ketorolac tromethamine or IM or IV doses of ketorolac tromethamine in the recommended dosage ranges, the clearance of the racemate does not change. This implies that the pharmacokinetics of ketorolac tromethamine in adults, following single or multiple IM or IV doses of ketorolac tromethamine or recommended oral doses of Ketorolac tromethamine, are linear. At the higher recommended doses, there is a proportional increase in the concentrations of free and bound racemate.

Absorption: Ketorolac tromethamine is 100% absorbed after oral administration. Oral administration of Ketorolac tromethamine after a high-fat meal resulted in decreased peak and delayed time-to-peak concentrations of ketorolac tromethamine by about 1 hour. Antacids did not affect the extent of absorption.

Distribution: The mean apparent volume (Vβ) of ketorolac tromethamine following complete distribution was approximately 13 liters. This parameter was determined from single dose data. The ketorolac tromethamine racemate has been shown to be highly protein bound (99%). Nevertheless, plasma concentrations as high as 10 µg/mL will only occupy approximately 5% of the albumin binding sites. Thus, the unbound fraction for each enantiomer will be constant over the therapeutic range. A decrease in serum albumin, however, will result in increased free drug concentrations. Ketorolac tromethamine is excreted in human milk.

Metabolism: Ketorolac tromethamine is largely metabolized in the liver. The metabolic products are hydroxylated and conjugated forms of the parent drug. The products of metabolism, and some unchanged drug, are excreted in the urine.

Excretion: The principal route of elimination of ketorolac and its metabolites is renal. About 92% of a given dose is found in the urine, approximately 40% as metabolites and 60% as unchanged ketorolac. Approximately 6% of a dose is excreted in the feces. There is little or no inversion of the R- to S- form in humans. The half-life of the ketorolac tromethamine S-enantiomer was approximately 2.5 hours (SD±0.4) compared with 5 hours (SD±1.7) for the R-enantiomer.

INDICATIONS AND USAGE:

Carefully consider the potential benefits and risks of Ketorolac tromethamine and other treatment options before deciding to use Ketorolac tromethamine. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

Acute pain in adult patients: Ketorolac tromethamine 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. Therapy should always be initiated with IV or IM dosing of ketorolac tromethamine, and Ketorolac tromethamine is to be used only as continuation treatment, if necessary. The total combined duration of use of Ketorolac tromethamine and ketorolac tromethamine is not to exceed 5 days of use because of the potential of increasing the frequency and severity of adverse reactions associated with the recommended doses. Patients should be switched to alternative analgesics as soon as possible, but Ketorolac tromethamine oral therapy is not to exceed 5 days.

DOSAGE AND ADMINISTRATION:

Carefully consider the potential benefits and risks of Ketorolac Tromethamine and other treatment options before deciding to use Ketorolac tromethamine. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals. In adults, the combined duration of use of IV or IM dosing of Ketorolac Tromethamine and Ketorolac Tromethamine is not to exceed 5 days. In adults, the use of Ketorolac Tromethamine is only indicated as continuation therapy to IV or IM dosing of Ketorolac Tromethamine.

Transition from IV or IM dosing of ketorolac tromethamine (single- or multiple dose) to multiple-dose Ketorolac

Back

Tromethamine:

Patients age 17 to 64: 20 mg PO once followed by 10 mg q4-6 hours prn not >40 mg/day

Patients age ≥ 65, renally impaired, and/or weight 40 mg/day

Note:

Oral formulation should not be given as an initial dose

Use minimum effective dose for the individual patient

Do not shorten dosing interval of 4 to 6 hours

Total duration of treatment in adult patients: the combined duration of use of IV or IM dosing of ketorolac tromethamine and Ketorolac tromethamine is not to exceed 5 days.

The following table summarizes Ketorolac Tromethamine dosing instructions in terms of age group:

Patient Population	Yukon (following IV or IM dosing of ketorolac tromethamine)
Age > years	Oral not approved
Adult Age 17 to 64 years	20 mg once, then 10 mg q4-6 hours prn not>40 mg/day
Adult Age ≥ 65 years, renally impaired, and/or weight 50 kg	10 mg once, then 10 mg q4-6 hours prn not>40 mg/day

CONTRAINDICATIONS:

- Ketorolac Tromethamine is contraindicated in patients with previously demonstrated hypersensitivity to ketorolac tromethamine.
- Ketorolac Tromethamine is contraindicated in patients with active peptic ulcer disease, in patients with recent gastrointestinal bleeding or perforation and in patients with a history of peptic ulcer disease or gastrointestinal bleeding.
- Ketorolac Tromethamine should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients.
- Ketorolac Tromethamine is contraindicated as prophylactic analgesic before any major surgery.
- Ketorolac tromethamine is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.
- Ketorolac Tromethamine is contraindicated in patients with advanced renal impairment or in patients at risk for renal failure due to volume depletion.
- 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.
- 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 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 and probenecid is contraindicated. The concomitant use of ketorolac tromethamine and pentoxifylline is contraindicated.

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. These NSAID-related complications can be serious in certain patients for whom Ketorolac tromethamine is indicated, especially when the drug is used inappropriately.

In patients taking Ketorolac tromethamine, the most frequently reported adverse experiences in approximately 1% to 10% of patients are:

Gastrointestinal (GI) experiences including:

abdominal pain, constipation/diarrhea, dyspepsia, flatulence, GI fullness, GI ulcers. (gastric/duodenal), gross bleeding/perforation, heartburn, nausea, stomatitis, vomiting.

Other experiences:

abnormal renal function, anemia, dizziness, drowsiness, edema, elevated liver enzymes, headaches, hypertension, increased bleeding time, injection site pain, pruritus, purpura, rashes, tinnitus, sweating.

USE IN SPECIFIC POPULATIONS:

Pregnancy:

In late pregnancy, as with other NSAIDs, Ketorolac Tromethamine should be avoided because it may cause premature closure of the ductus arteriosus.

Lactation:

Exercise caution when ketorolac is administered to a nursing woman. Available information has not shown any specific adverse events in nursing infants; however, instruct patients to contact their infant's health care provider if they note any adverse events.

Paediatric use:

Ketorolac tromethamine is not indicated for use in paediatric patients. The safety and effectiveness of Ketorolac Tromethamine in paediatric patients below the age of 17 have not been established.

Geriatric use:

Because Ketorolac Tromethamine may be cleared more slowly by the elderly who are also more sensitive to the dose-related adverse effects of NSAIDs, extreme caution, reduced dosages, and careful clinical monitoring must be used when treating the elderly with Ketorolac Tromethamine.

Renal impairment:

Ketorolac Tromethamine is contraindicated in patients with serum creatinine concentrations indicating advanced renal impairment. Ketorolac Tromethamine should be used with caution in patients with impaired renal function or a history of kidney disease because it is a potent inhibitor of prostaglandin synthesis. Because patients with underlying renal insufficiency are at increased risk of developing acute renal decompensation or failure, the risks and benefits should be assessed prior to giving Ketorolac Tromethamine to these patients.

Hepatic impairment:

Ketorolac tromethamine should be used with caution in patients with impaired hepatic function or a history of liver disease. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of a more severe hepatic reaction while on therapy with Ketorolac Tromethamine. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), Ketorolac Tromethamine should be discontinued.

OVERDOSAGE:

Symptoms and Signs Symptoms:

following acute NSAID 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.

Treatment:

Patients should be managed by symptomatic and supportive care following a 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). Forced diuresis, alkalization of urine, hemodialysis or hemoperfusion may not be useful due to high protein binding. Single overdoses of Ketorolac Tromethamine have been variously associated with abdominal pain, nausea, vomiting, hyperventilation, peptic ulcers and/or erosive gastritis and renal dysfunction which have resolved after discontinuation of dosing.

INSTRUCTIONS:

- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

Yukon Tablet 10 mg : Pack of 3 x 10 tablets.

ہدایات:

۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

گرمی، دھوپ اور نمی سے بچائیں۔

بچوں کی پہنچ سے دور رکھیں۔

صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

FOR FURTHER INFORMATIONS PLEASE CONTACT:

CCL

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