KETOR® 10mg Tablets U.S.P.
(Ketorolac Tromethamine)

کیٹور ۱۰ ملی گرام
(کیٹورولیک ٹرومیتھامین) ٹیبلٹس یو ایس پی۔

DESCRIPTION: Ketor (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). 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 376.41g/mol.

COMPOSITION:
Ketor Tablet U.S.P. : Each Film-coated tablet contains:
Ketorolac Tromethamine U.S.P. 10mg

WARNING: KETOR (Ketorolac Tromethamine), 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 and only as continuation treatment following IV or IM dosing of ketorolac tromethamine, if necessary. The total combined duration of use of KETOR and ketorolac tromethamine should not exceed 5 days.
KETOR is not indicated for use in pediatric patients and it is NOT indicated for minor or chronic painful conditions. Increasing the dose of KETOR 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 TORADOL 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, TORADOL 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 (see WARNINGS).

CLINICAL PHARMACOLOGY
Pharmacodynamics: Ketor is a potent analgesic agent of the non-steroidal, anti-inflammatory class (NSAID). Its mode of action is to inhibit the cyclooxygenase enzyme system and hence prostaglandin synthesis and it demonstrates a minimal anti-inflammatory effect at its analgesic dose. Ketor 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. It is not an opioid and, has no known effects on opioid receptors.
Pharmacokinetics: Absorption: Oral administration of Ketor 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 singledose data. The ketorolac tromethamine racemate has been shown to be highly protein bound (99%). Nevertheless, plasma concentrations as high as 10 μ g/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.
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. A single-dose study with 10 mg Ketor (n=9) demonstrated that the S-enantiomer is cleared approximately two times faster than the R-enantiomer and that the clearance was independent of the route of administration. This means that the ratio of S/R plasma concentrations decreases with time after each dose. There is little or no inversion of the R- to S- form in humans.
Preclinical safety data: Cariprazine and its major active metabolites did not induce CYP1A2 and CYP3A4 enzymes and were weak inhibitors of CYP1A2, CYP2C9, CYP2D6, and CYP3A4 in vitro. Cariprazine was also a weak inhibitor of CYP2C19, CYP2A6, and CYP2E1 in vitro. Cariprazine and its major active metabolites are not substrates of P-glycoprotein (P-gp), the organic anion transporting polypeptide 1B1 and 1B3 (OATP1B1 and OATP1B3), and the breast cancer resistance protein (BCRP). Cariprazine and its major active metabolites were poor or non-inhibitors of transporters OATP1B1, OATP1B3, BCRP, organic cation transporter 2 (OCT2), and organic anion transporters 1 and 3 (OAT1 and OAT3) in vitro. The major active metabolites were also poor or non-inhibitors of transporter P-gp although cariprazine was probably a P-gp inhibitor based on the theoretical GI concentrations at high doses in vitro.

INDICATIONS
Ketor is indicated for the short-term management of moderate to severe acute postoperative pain.

CONTRAINDICATIONS
Ketor is contraindicated in patients with previously demonstrated hypersensitivity to ketorolac tromethamine. Ketor 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. Ketor 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. Ketor is contraindicated as prophylactic analgesic before any major surgery. Ketor is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery. Ketor is contraindicated in patients with advanced renal impairment or in patients at risk for renal failure due to volume depletion. Ketor 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. Ketor 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. Ketor 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 Ketor and probenecid is contraindicated. The concomitant use of ketorolac tromethamine and pentoxifylline is contraindicated.

USE IN SPECIFIC POPULATION
Pregnancy In late pregnancy, as with other NSAIDs, Ketor should be

avoided because it may cause premature closure of the ductus arteriosus Labor and Delivery The use of Ketor 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. Nursing Mothers 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. Pediatric Use Ketor is not indicated for use in pediatric patients. The safety and effectiveness of Ketor in pediatric patients below the age of 17 have not been established.

ADVERSE REACTIONS

Adverse reaction rates increase with higher doses of Ketor. Practitioners should be alert for the severe complications of treatment with Ketor, such as GI ulceration, bleeding and perforation, postoperative bleeding, acute renal failure, anaphylactic and anaphylactoid reactions and liver failure.

PRECAUTIONS

Ketor cannot be expected to substitute for corticosteroids or to treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to disease exacerbation. Patients on prolonged corticosteroid therapy should have their therapy tapered slowly if a decision is made to discontinue corticosteroids. The pharmacological activity of Ketor in reducing inflammation may diminish the utility of this diagnostic sign in detecting complications of presumed noninfectious, painful conditions. Hepatic Effect Ketor 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 Ketor. These laboratory abnormalities may progress, may remain un-changed, or may be transient with continuing therapy.

Hematologic Effect Anemia is sometimes seen in patients receiving NSAIDs, including Ketor. This may be due to fluid retention, occult or gross GI blood loss, or an incompletely described effect upon erythropoiesis. Patients on long-term treatment with NSAIDs, including Ketor, should have their hemoglobin or hematocrit checked if they exhibit any signs or symptoms of anemia. NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients. Unlike aspirin, their effect on platelet function is quantitatively less, of shorter duration, and reversible. Patients receiving Ketor who may be adversely affected by alterations in platelet function, such as those with coagulation disorders or patients receiving anticoagulants, should be carefully monitored.

Preexisting Asthma Patients with asthma may have aspirin-sensitive asthma. The use of aspirin in patients with aspirin-sensitive asthma has been associated with severe bronchospasm which can be fatal. Since cross reactivity, including bronchospasm, between aspirin and other nonsteroidal anti-inflammatory drugs has been reported in such aspirin-sensitive patients, Ketor should not be administered to patients with this form of aspirin sensitivity and should be used with caution in patients with preexisting asthma.

Drug Interactions: Ketorolac is highly bound to human plasma protein (mean 99.2%). There is no evidence in animal or human studies that Ketor induces or inhibits hepatic enzymes capable of metabolizing itself or other drugs. Warfarin, Digoxin, Salicylate, and Heparin The in vitro binding of warfarin to plasma proteins is only slightly re-duced by ketorolac tromethamine (99.5% control vs 99.3%) when ketorolac plasma concentrations reach 5 to 10 g/mL. Ketorolac does not alter digoxin protein binding. In vitro studies indicate that, at therapeutic concentrations of salicylate (300 g/mL), the binding of ketorolac was reduced from approximately 99.2% to 97.5%, representing a potential two fold increase in unbound ketorolac plasma levels. Therapeutic concentrations of digoxin, warfarin, ibuprofen, naproxen, piroxicam, acetaminophen, phenytoin and tolbutamide did not alter ketorolac tromethamine protein binding. In a study involving 12 adult volunteers, Ketor was coadministered with a single dose of 25 mg warfarin, causing no significant changes in pharmacokinetics or pharmacody-namics of warfarin. In another study, ketorolac tromethamine dosed IV or IM was given with two doses of 5000 U of heparin to 11 healthy volunteers, resulting in a mean template bleeding time of 6.4 minutes (3.2 to 11.4 min) compared to a mean of 6.0 minutes (3.4 to 7.5 min) for heparin alone and 5.1 minutes (3.5 to 8.5 min) for placebo. Although these results do not indicate a significant interaction between Ketor and warfarin or heparin, the administration of Ketor to patients taking anticoagulants should be done extremely cautiously, and patients should be closely monitored.

DOSAGE AND ADMINISTRATION

Carefully consider the potential benefits and risks of Ketor and other treatment options before deciding to use Ketor. 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 Ketor is not to exceed 5 days. In adults, the use of Ketor 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 multipledose) to multiple-dose Ketor: 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.

DOSAGE

As directed by the physician.

INSTRUCTIONS

Store below 30°C. Protect from heat, light and moisture.
Keep all medicines out of the reach of children.

PRESENTATION

7's, 10's, 14's, 20's, 28's, 30's in Alu-Alu Blister with carton.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات: ۳۰°ڈگری سینٹی گریڈ سے کم پر رکھیں۔
گرمی، روشنی اور نمی سے محفوظ رکھیں۔
تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

For detailed information
please contact:

Genix Pharma (Pvt.) Ltd.

44,45-B, Korangi Creek Road, Karachi-75190, Pakistan.
UAN: +92-21-111-10-10-11, **Email:** info@genixpharma.com

ISO 9001:2015 ISO 14001:2015 ISO 45001:2018
www.genixpharma.com