Toradolin®

ketorolac tromethamine USP

Composition :
Active ingredient: Ketorolac tromethamine USP.
Each ampoule contains 30 mg active ingredient in 1 ml.

Properties and effects :
Toradolin is a potent analgesic agent of the non-steroidal, anti-inflammatory class (NSAID). Its mode of action is to inhibit the cyclo-oxygenase enzyme system and hence prostaglandin synthesis and it demonstrates a minimal anti-inflammatory effect at its analgesic dose. Toradolin 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 :
Following intramuscular administration, ketorolac tromethamine was rapidly and completely absorbed, a mean peak plasma concentration of 2.2 microgram/ml occurring an average of 50 minutes after a single 30 mg dose.

Kinetics in special clinical situations:
Patients with impaired hepatic function from cirrhosis do not have any clinically important changes in ketorolac tromethamine clearance or terminal half life

Indications :
Toradolin ampoules are indicated for the short-term management of moderate to severe acute postoperative pain.

Dosage and administration :
Toradolin ampoules are for administration by intramuscular or bolus intravenous injection. Bolus intravenous doses should be given over no less than 15 seconds. Toradolin ampoules should not be used for epidural or spinal administration.
The time to onset of analgesic effect following both i.v and i.m administration is similar and is approximately 30 minutes, with maximum analgesia occurring within 1 to 2 hrs. The median duration of analgesia is generally 4 to 6 hrs.
Dosage should be adjusted according to the severity of the pain and the patient response.

Duration of treatment: The administration of continuous multiple daily doses of Toradolin intramuscularly or intravenously should not exceed 5 days because adverse events may increase with prolonged usage. There has been limited experience with dosing for longer periods since the vast majority of patients have transferred to oral medication, or no longer require analgesic therapy after this time.

Adults:
10-30 mg initial dose followed by 10-30 mg every 6 hours as required. In the initial postoperative period, Toradolin may be given as often as every 2 hours if needed. The lowest effective dose should be given. A total daily dose of 120 mg for non-elderly and 60 mg for the elderly, renally-impaired patients and patients less than 50 kg should not be exceeded.

For patients receiving Toradolin ampoules, and who are converted to Toradol tablets, the total combined daily dose should not exceed 90 mg (60 mg for the elderly, renally-impaired patients and patients less than 50 kg) and the oral component should not exceed 40 mg on the day the change of dosage form is made. Patients should be converted to oral treatment as soon as possible.

Special dosage instructions :
Elderly patients: For patients over 65 years, the lower end of the dosage range is recommended; a total daily dose of 60 mg should not be exceeded

Children (2 years of age or older):
1.0 mg/kg I.M. or 0.5-1.0 mg/kg I.V followed by 0.5 mg/kg I.V. 6 hourly.
Maximum duration of treatment is 2 days.

Renal impairment: Since ketorolac tromethamine and its metabolites are excreted primarily by the kidney, Toradolin is contraindicated in moderate to severe renal impairment (serum creatinine >160 mol/l); patients with lesser renal impairment should receive a reduced dose (not exceeding 60 mg/day i.v. or i.m.), and their renal status should be closely monitored.

Combination treatment: (See also Incompatibilities) Opioid analgesics (e.g. morphine, pethidine) may be used concomitantly, and may be required for optimal analgesic effect in the early postoperative period when pain is most severe. Ketorolac tromethamine does not interfere with opioid binding and does not exacerbate opioid-related respiratory depression or sedation. When used in association with Toradolin ampoules, the daily dose of opioid is usually less than that normally required. However, opioid side effects should still be considered, especially in day-case surgery.

Contraindications :
- history of peptic ulcer or gastrointestinal bleeding
- suspected or confirmed cerebrovascular bleeding
- hemorrhagic diatheses, including coagulation disorders
- patients with hypersensitivity to ketorolac tromethamine or other NSAIDs and patients in whom aspirin or other prostaglandin synthesis inhibitors induce allergic reactions (severe anaphylactic-like reactions have been observed in such patients)
- patients with the complete or partial syndrome of nasal polyps, angio-edema or bronchospasm
- concurrent treatment with other NSAIDs, probenecid or lithium salts
- hypovolemia from any cause, or dehydration
- moderate or severe renal impairment (serum creatinine >160 mol/l)
- a history of asthma
- patients who have had operations with a high risk of hemorrhage or incomplete hemostasis
- patients on anticoagulants including low-dose heparin (2,500-5,000 units 12-hourly)
- during pregnancy, labor, delivery or lactation

Precautions :
Elderly patients: Patients over the age of 65 years may be at a greater risk of experiencing undesirable effects than younger patients. This age-related risk is common to all NSAIDs. Compared to young adults, the elderly have an increased plasma half-life and reduced plasma clearance of ketorolac tromethamine. With Toradol tablets, a longer dosing interval is advisable (see Dosage and administration).
Gastrointestinal effects: Toradolin can cause gastrointestinal irritation, ulcers or bleeding in patients with or without a history of previous symptoms. Elderly and debilitated patients are more prone to develop these reactions. The incidence increases with dose and duration of treatment.
Respiratory effects: Bronchospasm may be precipitated in patients with a history of asthma.
Renal effects: Drugs that inhibit prostaglandin biosynthesis (including NSAIDs) have been reported to cause nephrotoxicity, including but not limited to glomerular nephritis, interstitial nephritis, renal papillary necrosis, nephrotic syndrome and acute renal failure. In patients with renal, cardiac or hepatic impairment, caution is required.
As with other drugs that inhibit prostaglandin synthesis, elevations of serum urea, creatinine and potassium have been reported with Toradolin and may occur after one dose.
Impaired renal function: Caution should be observed in patients with conditions leading to a reduction in blood volume and/or renal blood flow, where renal prostaglandins have a supportive role in the maintenance of renal perfusion. In these patients, administration of an NSAID may cause a dose-dependent reduction in renal prostaglandin formation and may precipitate overt renal failure. Patients at greatest risk of this reaction are those who are volume-depleted because of blood loss or severe dehydration, patients with impaired renal function, heart failure, liver impairment, the elderly and those taking diuretics. Discontinuation of NSAID therapy is typically followed by recovery to the pretreatment state. Inadequate fluid/blood replacement during surgery, leading to hypovolemia, may lead to renal dysfunction which could be exacerbated when Toradolin is administered. Therefore, volume depletion should be corrected and close monitoring of serum urea and creatinine and urine output is recommended until the patient is normovolemic. In patients on renal dialysis, ketorolac tromethamine clearance was reduced to approximately half the normal rate and terminal half-life increased approximately three-fold.
Fluid retention and edema: Fluid retention and edema have been reported with the use of Toradolin and it should therefore be used with caution in patients with cardiac decompensation, hypertension or similar conditions.
Hepatic effects: Borderline elevations of one or more liver function tests may occur. These abnormalities may be transient, may remain unchanged, or may progress with continued therapy. Meaningful elevations (greater than 3 times normal) of serum glutamate pyruvate transaminase (SGPT/ALT) or serum glutamate oxaloacetate transaminase (SGOT/AST) occurred in controlled clinical trials in less than 1% of patients. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur, Toradolin should be discontinued.
Hematological effects: Patients with coagulation disorders should not receive Toradolin. Patients on anti-coagulation therapy may be at increased risk of bleeding if given Toradolin concurrently. The concomitant use of ketorolac tromethamine and prophylactic low-dose heparin (2,500-5,000 units 12-hourly) has not been studied extensively and may also be associated with an increased risk of bleeding. Patients already on anticoagulants or who require low-dose heparin should not receive ketorolac tromethamine. Patients who are receiving other drug therapy that interferes with hemostasis should be carefully observed. In controlled clinical studies, the incidence of clinically significant postoperative bleeding was less than 1%.
ketorolac tromethamine inhibits platelet aggregation and prolongs bleeding time. In patients with normal bleeding function, bleeding times were raised, but not outside the normal range of 2-11 minutes. Unlike the prolonged effects from aspirin, platelet function returns to normal within 24-48 hours after ketorolac tromethamine is discontinued.

Pregnancy, nursing mothers :
The safety of Toradolin in human pregnancy has not been established. Toradolin is therefore contraindicated during pregnancy, labor or delivery. As ketorolac tromethamine has been detected in human milk at low levels, it is also contraindicated in mothers who are breast-feeding. (There was no evidence of teratogenicity in rats or rabbits studied at maternally-toxic doses of ketorolac tromethamine.)

Undesirable effects :
Gastrointestinal tract: abdominal discomfort, constipation, diarrhea, dyspepsia, eructation, flatulence, fullness, gastritis, gastrointestinal bleeding, gastrointestinal pain, nausea, pancreatitis, peptic ulcer, perforation, stomatitis, vomiting.
Central nervous/musculoskeletal systems: abnormal dreams, abnormal taste and vision, abnormal thinking, aseptic meningitis, convulsions, depression, dizziness, drowsiness, dry mouth, euphoria, excessive thirst, functional disorders, hallucinations, headache, hearing loss, hyperkinesia, inability to concentrate, insomnia, myalgia, nervousness, paresthesia, stimulation, sweating, tinnitus, vertigo.
Urinary tract and kidneys: acute renal failure, flank pain (with or without hematuria), glomerular nephritis, hemolytic uremic syndrome, hyperkalemia, hyponatremia, increased urinary frequency, interstitial nephritis, nephrotic syndrome, oliguria, raised serum urea and creatinine, renal papillary necrosis.
Cardiovascular/hematological systems: bradycardia, flushing, hypertension, pallor, purpura, thrombocytopenia.
Respiratory system: asthma, dyspnea, pulmonary edema.
Skin: exfoliative dermatitis, Lyell's syndrome, maculopapular rash, pruritus, Stevens-Johnson syndrome, urticaria.
Hypersensitivity reactions: anaphylaxis, bronchospasm, flushing and rash, hypotension, laryngeal edema. Such reactions may occur in patients with or without known sensitivity to Toradolin or other NSAIDs.
Bleeding: epistaxis, hematomata, postoperative wound hemorrhage.
Other: abnormal liver function tests, asthenia, edema, injection site pain, weight gain.

Overdosage :
Doses of 360 mg given intramuscularly over an 8-hour interval for 5 consecutive days have caused abdominal pain and peptic ulcers which have healed after discontinuation of dosing. Two patients recovered from unsuccessful suicide attempts. One patient experienced nausea after 210 mg Toradolin, and the other hyperventilation after 300 mg Toradolin.

Incompatibilities :
Toradolin ampoules should not be mixed in a small volume (e.g. in a syringe) with morphine sulphate, pethidine hydrochloride, promethazine hydrochloride or hydroxyzine hydrochloride as precipitation of ketorolac tromethamine will occur. Toradolin ampoules are compatible with normal saline, 5% dextrose, Ringer's solution, Ringer-Lactate solution or Plasmalyte solution. Compatibility with other drugs is unknown.

Stability :
This medicine must not be used after the expiry date (EXP) shown on the pack. Toradolin ampoules must not be used if particulate matter is present in the solution. Keep away from light & store below 30C.

Packs :
5 Ampoules of 1ml in one box

Keep medicine out of reach of children

® Registered Trade Mark

RADIANT

Manufactured by
Radiant Pharmaceuticals Limited
at Popular Pharmaceuticals Limited, Bangladesh

Version: 01

PMR 5316

টোরাডলিন®

কিটোরোলাক ট্রোমেথামিন ইউএসপি

গঠন ঃ

সক্রিয় উপাদান:

প্রতিটি অ্যাম্পুলে আছে কিটোরোলাক ট্রোমেথামিন ইউএসপি ৩০ মি: গ্রা:/ ১ মি.লি.।

বৈশিষ্ট্য ও কার্যকারিতা: টোরাডলিন® একটি শক্তিশালী বেদনানাশক যা নন ষ্টেরয়ডাল এন্টিইনফ্লামেটরী শ্রেনীভুক্ত। ইহা সাইক্লো-অক্সিজিনেজ এনজাইম সিষ্টেমকে বাধা দিয়ে প্রোষ্টাগ্লানডিন সংশ্লেষণ বাধাগ্রস্থ করে।

শোষণ ঃ

ইনজেকশন প্রদানের পর কিটোরোলাক ট্রোমেথামিন খুব দ্রুত এবং সম্পূর্ণ পরিশোষিত হয় এবং একটি ৩০ মি: গ্রা: মাত্রা গ্রহনের ৫০ মিনিট (গড়ে) পর গড় সর্বোচ্চ প্লাজমা ঘনত্ব ২.২ মাইক্রোগ্রাম/মি.লি. পাওয়া যায়।

নির্দেশনা ঃ

টোরাডলিন® স্বল্পকালীন মাঝারী থেকে তীব্র ব্যথায় নির্দেশিত।

মাত্রা ও প্রয়োগ ঃ

পূর্ণ বয়স্ক রোগীর ক্ষেত্রে: প্রাথমিক মাত্রা ১০-৩০ মি.গ্রা. টোরাডলিন® প্রদানের পর ব্যথার তীব্রতা অনুযায়ী ১০-৩০ মি.গ্রা. টোরাডলিন® প্রতি ৬ ঘন্টা অন্তর নির্দেশিত। দৈনিক সর্বোচ্চ মাত্রা ১২০ মি. গ্রা.।

বয়স্ক, কিডনী সমস্যায় আক্রান্ত রোগী ও যাদের ওজন ৫০ কেজির নীচে তাদের ক্ষেত্রে দৈনিক সর্বোচ্চ মাত্রা ৯০ মি. গ্রা.।

মাত্রা নির্দেশ সুবিন্যস্ত করতে হবে ব্যথার তীব্রতা এবং রোগীর প্রতিক্রিয়া অনুসারে।

টোরাডলিন® অ্যাম্পুল শুধুমাত্র স্বল্পকালীন ব্যবহারের জন্য (সর্বোচ্চ পাঁচ দিন পর্যন্ত) এবং ইহা দীর্ঘস্থায়ী ব্যবহারের জন্য পরামর্শ দেওয়া হয় না।

বিরূপ ব্যবহার ঃ

- রোগীর পাকস্থলীর ক্ষত ও পাকতান্ত্রিক রক্তক্ষরণের পূর্ব বৃত্তান্ত যদি থাকে।
- সন্দেহজনক বা নিশ্চিত মস্তিষ্ক ও সংবহন নালিকার রক্তক্ষরণ।
- রক্ত জমাট বাঁধন বিশৃঙ্খলা সহ রক্তক্ষরণজনিত রোগ প্রবণতা।
- কিটোরোলাক বা অন্যান্য NSAID এর প্রতি অতি সংবেদনশীলতা।
- ন্যাসাল পলিপস্, এনজিও ইডিমা অথবা ব্রোঙ্কোস্পাজমের সম্পূর্ন বা আংশিক লক্ষণযুক্ত রোগী।
- অন্যান্য NSAID, অক্সপেনটিফাইলাইন, প্রোবেনিসিড অথবা লিথিয়াম সল্ট এর সাথে সহ চিকিৎসায়।
- যে কোন কারণে ডিহাইড্রেশন বা হাইপোভোলেমিয়া।
- লঘু বা তীব্র বৃক্ক সম্বন্ধীয় দুর্বলতা (সিরাম ক্রিয়েটিনিন>১৬০ মাইক্রোমোল/ লিটারের নিচে)।
- হাঁপানি রোগের পূর্ববৃত্তান্ত যদি থাকে।
- যাদের অস্ত্রোপচার জনিত রক্তক্ষরণের তীব্র আশংকা আছে।
- রক্ত জমাট বাধন রোধী স্বল্পমাত্রার হেপারিন চিকিৎসায় রয়েছে এমন রোগী (১২ ঘন্টায় ২৫০০-৫০০০ ইউনিট)
- গর্ভকালীন সময়ে, প্রসবাবস্থায় এবং প্রসব কালীন সময়ে।

গর্ভাবস্থায় ও স্তন্যদানকারী মায়েদের ক্ষেত্রে ব্যবহার ঃ

গর্ভাবস্থায় ও স্তন্যদানকারী মায়েদের ক্ষেত্রে টোরাডলিন® ব্যবহারের নিরাপত্তা এখনো প্রতিষ্ঠিত হয় নাই। সে কারণে টোরাডলিন® গর্ভকালীন সময়ে, প্রসবাবস্থায়, প্রসব কালীন সময়ে এবং স্তন্যদানকারী মায়েদের ক্ষেত্রে প্রতিনির্দেশিত।

সরবরাহ ঃ

প্রতি বাক্সে আছে ৫ টি অ্যাম্পুল এবং প্রতি অ্যাম্পুলে রয়েছে ৩০ মি. গ্রা. কিটোরোলাক ট্রোমেথামিন।

ওষুধ বিষয়ক সতর্কতা ঃ

আলো থেকে দূরে এবং ৩০° সেঃ তাপমাত্রার নীচে সংরক্ষণ করুন।

প্যাকেট এর উপর লেখা মেয়াদ উত্তীর্নের তারিখ অতিক্রম করলে ওষুধ ব্যবহার করা উচিত নয়।

বিস্তারিত তথ্যের জন্য ইংরেজী অংশ দেখুন।

ওষুধ শিশুদের নাগালের বাইরে রাখুন।

® রেজিস্ট্রার্ড ট্রেডমার্ক

RADIANT

প্রস্তুতকারক
রেডিয়েন্ট ফার্মাসিউটিক্যাল্স লিমিটেড কর্তৃক
পপুলার ফার্মাসিউটিক্যালস লিমিটেড-এ প্রস্তুতকৃত

Toradolin® Tablet

Ketorolac Tromethamine USP

Non-steroidal anti-inflammatory agent.

COMPOSITION:
Each film coated tablet contains Ketorolac Tromethamine USP 10 mg.

CLINICAL PHARMACOLOGY:
TORADOLIN (ketorolac tromethamine) is a non-steroidal anti-inflammatory drug (NSAID) that exhibits analgesic activity mediated by peripheral effects. The mechanism of action of ketorolac, like that of other NSAIDS, is not completely understood, but is believed to be related to prostaglandin synthetase inhibition.

Pharmacokinetics:
The pharmacokinetics are linear following single and multiple dosing. Steady state plasma levels are attained after one day of Q.I.D. dosing.

Following oral administration, peak plasma concentrations of 0.7 to 1.1 g/mL occur at an average of 44 minutes after a single 10 mg dose. The terminal plasma elimination half-life ranges between 2.4 and 9.0 hours in healthy adults, and between 4.3 and 7.6 hours in elderly subjects (mean age 72 years). A high fat meal decreases the rate, but not the extent, of absorption of oral ketorolac tromethamine. The use of an antacid has not been demonstrated to affect the pharmacokinetics of ketorolac.

In renally impaired patients there is a reduction in clearance and an increase in the terminal half life of ketorolac tromethamine (see table 5 below).

A series of studies were carried out in mice, rats, rabbits, monkeys and humans to characterize the pharmacokinetic profile of the free acid of ketorolac and ketorolac tromethamine. The salt form of the compound was later selected for development due to its more rapid and complete absorption.

INDICATIONS:
Orally administered TORADOLIN (ketorolac tromethamine) is indicated for the short-term management (not to exceed 5 days for post-surgical patients or 7 days for patients with musculoskeletal pain) of moderate to moderately severe acute pain, including post-surgical pain (such as general, orthopaedic and dental surgery), acute musculoskeletal trauma pain and post-partum uterine cramping pain. The total duration of combined intramuscular and oral treatment should not exceed 5 days.

For patients with an increased risk of developing CV and/or GI adverse events, other management strategies that do not include the use of NSAIDs should be considered first

Use of TORADOLIN should be limited to the lowest effective dose for the shortest possible duration of treatment in order to minimize the potential risk for cardiovascular or gastrointestinal adverse events TORADOLIN, as a NSAID, does not treat clinical disease or prevent its progression.

TORADOLIN, as a NSAID, only relieves symptoms and decreases inflammation for as long as the patient continues to take it.

Geriatrics (> 65 years of age): Evidence from clinical studies and post-market experience suggests that use in the geriatric population is associated with differences in safety .

Pediatrics (< 18 years of age): Safety and efficacy have not been established in the pediatric population.

DOSE AND ADMINISTRATION:
Dosing Considerations: Use of TORADOLIN should be limited to the lowest effective dose for the shortest possible duration of treatment . In no case is the duration of TORADOLIN treatment to exceed 7 days.

Recommended Dose and Dosage Adjustment
Adults (>18 years of age): Dosage should be adjusted according to the severity of the pain and the response of the patient.

Oral: The usual oral dose of TORADOLIN (ketorolac tromethamine) is 10 mg every 4 to 6 hours for pain as required. Doses exceeding 40 mg per day are not recommended. The maximum duration of treatment with the oral formulation is 5 days for post-surgical patients and 7 days for patients with musculoskeletal pain. TORADOLIN is not indicated for chronic use.

Conversion from Parenteral to Oral Therapy: When TORADOLIN tablets are used as a follow-on therapy to parenteral ketorolac, the total combined daily dose of ketorolac (oral + parenteral) should not exceed 120 mg in younger adult patients or 60 mg in elderly patients on the day the change of formulation is made. On subsequent days, oral dosing should not exceed the recommended daily maximum of 40 mg. Ketorolac IM should be replaced by an oral analgesic as soon as feasible. The total duration of combined intramuscular and oral treatment should not exceed 5 days.

Renal Impairment: TORADOLIN is contraindicated in patients with moderate to severe renal impairment (serum creatinine >442 µmol/L). TORADOLIN should be used with caution in patients with lesser renal impairment (serum creatinine 170 - 442 µmol/L). Such patients should receive a reduced dose o TORADOLIN, and their renal status should be closely monitored. It is recommended that the daily dose be reduced by half; a total daily dose of 60 mg should not be exceeded. Dialysis does not significantly clear ketorolac from bloodstream.

Hepatic Impairment: TORADOLIN is contraindicated in patients with severe liver impairment or active liver disease. Caution should be observed in giving TORADOLIN to patient with mild to moderate hepatic insufficiency.

Elderly, Frail or Debilitated Patients: These patients are at increased risk of the serious consequences of adverse reactions.

Oral: The lowest effective dose is recommended.

Missed Dose
The missed dose should be taken as soon as remembered, and then the regular dosing schedule should be continued. Two doses of TORADOLIN should not be taken at the same time.

Route of administration: Oral

CONTRAINDICATIONS:
TORADOLIN is contraindicated in:

- the peri-operative setting of coronary artery bypass graft surgery (CABG). Although TORADOLIN has Not been studied in this patient population, a selective COX-2 inhibitor NSAID studied in such a setting has led to an increased incidence of cardiovascular/thromboembolic events, deep surgical infections and sternal wound complications
- the third trimester of pregnancy, because of risk of premature closure of the ductus arteriosus and prolonged parturition
- labour and delivery because, through its prostaglandin synthesis inhibitory effect, it may adversely affect fetal circulation and inhibit uterine musculature, thus increasing the risk of uterine haemorrhage
- women who are breastfeeding, because of the potential for serious adverse reactions in nursing infants
- severe uncontrolled heart failure
- known hypersensitivity to TORADOLIN or to other NSAIDs, including any of the components/excipients
- history of asthma, urticaria, or allergic-type reactions after taking ASA or other NSAIDs (i.e. complete or partial syndrome of ASA-intolerance - rhinosinusitis, urticaria/ angioedema, nasal polyps, asthma). Fatal anaphylactoid reactions have occurred in such individuals. Individuals with the above medical problems are at risk of a severe reaction even if they have taken NSAIDs in the past without any adverse reaction. The potential for cross-reactivity between different NSAIDs must be kept in mind.
- active gastric / duodenal / peptic ulcer, active GI bleeding
- inflammatory bowel disease
- cerebrovascular bleeding or other bleeding disorders
- coagulation disorders, post-operative patients with high haemorrhagic risk or incomplete haemostasis in patients with suspected or confirmed cerebrovascular bleeding.
- immediately before any major surgery and intraoperatively when haemostasis is critical because of the increased risk of bleeding
- severe liver impairment or active liver disease
- moderate to severe renal impairment (serum creatinine >442 µmol/L and/or creatinine clearance <30 mL/min or 0.5 mL/sec) or deteriorating renal disease (individuals with lesser degrees of renal impairment are at risk of deterioration of their renal function when prescribed NSAIDs and must be monitored)
- known hyperkalemia.
- concurrent use with other NSAIDs due to the absence of any evidence demonstrating synergistic benefits and potential for additive side effects
- concomitant use with probenecid.
- concomitant use with oxpentifylline.
- children and adolescents aged less than 18 years

Special Populations:
Pregnant Women: TORADOLIN is contraindicated for use during the third trimester of pregnancy because of risk of premature closure of the ductus arteriosus and the potential to prolong parturition (see contraindications) .

Caution should be exercised in prescribing TORADOLIN during the first and second trimesters of pregnancy.

Inhibition of prostaglandin synthesis may adversely affect pregnancy and/or the embryo-foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation after use of a prostaglandin synthesis inhibitor in early pregnancy.

In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.
TORADOLIN is not recommended in labour and delivery because, through their prostaglandin synthesis inhibitory effect, they may adversely affect fetal circulation and inhibit uterine contractions, thus increasing the risk of uterine hemorrhage

Geriatrics: Patients older than 65 years (referred to in this document as older or elderly) and frail or debilitated patients are more susceptible to a variety of adverse reactions from NSAIDs. The incidence of these adverse reactions increases with dose and duration of treatment. In addition, these patients are less tolerant to ulceration and bleeding. Most reports of fatal GI events are in this population. Older patients are also at risk of lower esophageal injury including ulceration and bleeding. For such patients, consideration should be given to a starting dose lower than the one usually recommended, with individual adjustment when necessary and under close supervision.

WARNINGS AND PRECAUTIONS:
Risk of Cardiovascular (CV) Adverse Events: Ischemic Heart Disease, Cerebrovascular Disease, Congestive Heart Failure (NYHA II-IV) .

TORADOLIN is a non-steroidal anti-inflammatory drug (NSAID). Use of some NSAIDs is associated with an increased incidence of cardiovascular adverse events (such as myocardial infarction, stroke or thrombotic events) which can be fatal. The risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.
Caution should be exercised in prescribing TORADOLIN to any patient with ischemic heart disease (including but not limited to acute myocardial infarction, history of myocardial infarction and/or angina), cerebrovascular disease (including but not limited to stroke, cerebrovascular accident, transient ischemic attacks and/or amaurosis fugax) and/or congestive heart failure (NYHA II-IV).

Use of NSAIDs, such as TORADOLIN, can promote sodium retention in a dose-dependent manner, through a renal mechanism, which can result in increased blood pressure and/or exacerbation of congestive heart failure.

Randomized clinical trials with TORADOLIN have not been designed to detect differences in cardiovascular events in a chronic setting. Therefore, caution should be exercised when prescribing TORADOLIN. Risk of Gastrointestinal (GI) Adverse Events
Use of NSAIDs, such as TORADOLIN, is associated with an increased incidence of gastrointestinal adverse events (such as peptic/duodenal ulceration, perforation, obstruction and gastrointestinal bleeding).

SIDE EFFECTS:
Adverse Drug Reaction Overview
The most common adverse reactions encountered with non-steroidal anti-inflammatory drugs are gastrointestinal, of which peptic ulcer, with or without bleeding is the most severe. Fatalities have occurred, particularly in the elderly.

Clinical Trial Adverse Drug Reactions
Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

TORADOLIN TABLETS
SHORT-TERM PATIENT STUDIES
The incidence of adverse reactions in 371 patients receiving multiple 10 mg doses of TORADOLIN (ketorolac tromethamine) for pain resulting from surgery or dental extraction during the postoperative period (less than 2 weeks) is listed below. These reactions may or may not be drug related.

Table 1: Most Common Clinical Trial Adverse Drug Reactions (4-9% and 2-3%)

Body System	Incidence	Adverse Reaction
Nervous System	4-9%	Somnolence, insomnia
	2-3%	Nervousness, headache, dizziness
Digestive System	4-9%	Nausea
	2-3%	Diarrhea, dyspepsia, gastrointestinal pain, constipation
Body as a whole	2-3%	Fever

Table 2: Less Common Clinical Trial Adverse Drug Reactions (≤ 1%)

Nervous System: abnormal dreams, anxiety, dry mouth, hyperkinesia, paresthesia, increased sweating, euphoria, hallucinations

Digestive System: anorexia, flatulence, vomiting, stomatitis, gastritis, gastrointestinal disorder, sore throat

Body as a Whole: asthenia, pain, back pain

Cardiovascular System: increased cough, rhinitis, dry nose

Musculoskeletal System: myalgia, arthralgia

Skin and Appendages: rash, urticaria

Special Senses: vision, ear pain

Urogenital System: dysuria

LONG-TERM PATIENT STUDY
The adverse reactions listed below were reported to be probably related to study drug in 553 patients receiving long-term oral therapy (approximately 1 year) with TORADOLIN.

Table 3: Most Common Clinical Trial Adverse Drug Reactions (10-12%, 4-9% and 2-3%)

Body System	Incidence	Adverse Reaction
Digestive System	10-12%	Dyspepsia, gastrointestinal pain
	4-9%	Nausea, constipation
	2-3%	Diarrhea, flatulence, gastrointe--stinal fullness, peptic ulcers
Nervous System	4-9%	Headache
Metabolic/ Nutritional Disorder	2-3%	Dizziness, somnolence
	2-3%	Edema

Table 4: Less Common Clinical Trial Adverse Drug Reactions (≤ 1%)

Digestive System: Eructation, stomatitis, vomiting, anorexia,

duodenal ulcer, gastritis, gastrointestinal haemorrhage, increased appetite, melena, mouth ulceration, rectal bleeding, sore mouth
Nervous System: Abnormal dreams, anxiety, depression, dry mouth, insomnia, nervousness, paresthesia

Special Senses: Tinnitus, taste perversion, abnormal vision, blurred vision, deafness, lacrimation disorder

Metabolic/Nutritional Disorder: Weight gain, alkaline phosphatase increase, BUN increased, excessive thirst, generalized edema, hyperuricemia

Skin & Appendages: Pruritus, rash, burning sensation skin

Body as a Whole: Asthenia, pain, back pain, face edema, hernia

Musculo-skeletal System: Arthralgia, myalgia, joint disorder

Cardiovascular System: Chest pain, chest pain substernal, migraine

Respiratory System: Dyspnea, asthma, epistaxis

Urogenital System: Haematuria, increased urinary frequency, oliguria, polyuria

Haematic & Lymphatic: Anemia, purpura

Abnormal Haematologic and Clinical Chemistry Findings
Elevations of blood urea nitrogen (BUN) and creatinine have been reported in clinical trials with ketorolac.

USE IN PREGNANCY & LACTATION:
There are no adequate and well-controlled studies of TORADOLIN in pregnant women. TORADOLIN should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

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.

USE IN CHILDREN & ADOLESCENTS:
TORADOLIN is not indicated for use in pediatric patients. The safety and effectiveness of TORADOLIN in pediatric patients below the age of 18 have not been established.

DRUG INTERACTIONS:
Drug-Drug Interactions
Acetylsalicylic acid (ASA) or other NSAIDs: The use of TORADOLIN in addition to most NSAIDs, including over-the-counter ones (such as ibuprofen) for analgesic and/or antiinflammatory effects is usually contraindicated because of the absence of any evidence demonstrating synergistic benefits and the potential for additive adverse reactions.

The exception is the use of low dose ASA for cardiovascular protection, when another NSAID is being used for its analgesic/anti-inflammatory effect, keeping in mind that combination NSAID therapy is associated with additive adverse reactions.

Some NSAIDs (e.g. ibuprofen) may interfere with the anti-platelet effects of low dose ASA, possibly by competing with ASA for access to the active site of cyclooxygenase-1. In vitro studies indicated that, at therapeutic concentrations of salicylates (300 µg/mL), the binding of ketorolac tromethamine was reduced from approximately 99.2% to 97.5% representing a potential two-fold increase in unbound TORADOLIN plasma levels.

Antacids: There is no definitive evidence that the concomitant administration of histamine H_2 receptor antagonists and/or antacids will either prevent the occurrence of gastrointestinal side effects or allow the continuation of TORADOLIN therapy when and if these adverse reactions appear.

Anti-hypertensives: NSAIDs may diminish the anti-hypertensive effects of angiotensin converting enzyme (ACE) inhibitors. Combinations of ACE inhibitors, angiotensin-II antagonists, or diuretics with NSAIDs might have an increased risk for acute renal failure and hyperkalemia. Blood pressure and renal function (including electrolytes) should be monitored more closely in this situation, as occasionally there can be a substantial increase in blood pressure.

Anti-platelet Agents (including ASA): There is an increased risk of bleeding, via inhibition of platelet function, when anti-platelet agents are combined with NSAIDs, such as TORADOLIN .

Digoxin: Concomitant administration of an NSAID with digoxin can result in an increase in digoxin concentrations which may result in digitalis toxicity. Increased monitoring and dosage adjustments of digitalis glycosides may be necessary during and following concurrent NSAID therapy. Ketorolac tromethamine does not alter digoxin protein binding.

Diuretics: Clinical studies as well as post-marketing observations have shown that NSAIDs can reduce the effect of diuretics. Ketorolac tromethamine reduces the diuretic response to furosemide by approximately 20% in normovolemic subjects, so particular care should be taken in patients with cardiac decompensation.

Glucocorticoids: Some studies have shown that the concomitant use of NSAIDs and oral glucocorticoids increases the risk of GI adverse events such as ulceration and bleeding. This is especially the case in older (> 65 years of age) individuals.

Lithium: Monitoring of plasma lithium concentrations is advised when stopping or starting a NSAID, as increased lithium concentrations can occur. Some NSAIDs have been reported to inhibit renal lithium clearance, leading to an increase in plasma lithium concentrations and potential lithium toxicity. The effect of ketorolac tromethamine on lithium plasma levels has not been studied. Cases of increased lithium plasma concentrations during therapy with TORADOLIN have been reported.
Methotrexate: Caution is advised in the concomitant administration of methotrexate and NSAIDs, as this has been reported to reduce the clearance of methotrexate, thus enhancing its toxicity. In case combination treatment with methotrexate and NSAIDs is necessary, blood cell count and the renal function should be monitored. Concomitant administration of NSAIDs with a potentially myelotoxic drug, such as methotrexate, appears to be a predisposing factor to the onset of a cytopenia.

Oxpentifylline: When TORADOLIN is administered concurrently with oxpentifylline, there is an increased tendency to bleeding. The concomitant use of TORADOLIN and oxpentifylline is contraindicated.

Probenacid: Concomitant administration of ketorolac tromethamine and probenacid results in the decreased clearance and volume of distribution of ketorolac and a significant increase in ketorolac plasma levels (approximately three-fold increase) and terminal half-life (approximately two-fold increase). The concomitant use of TORADOLIN and probenacid is contraindicated.

Selective Serotonin Reuptake Inhibitors (SSRIs): Concomitant administration of NSAIDs and SSRIs may increase the risk of gastrointestinal ulceration and bleeding.

OVERDOSE:
Signs and Symptoms: Overdoses of TORADOLIN have been variously associated with abdominal pain, nausea, vomiting, hyperventilation, peptic ulcers and/or erosive gastritis, gastrointestinal bleeding, and renal dysfunction which have generally resolved after discontinuation of dosing. Metabolic acidosis has been reported following intentional overdosage. Although rare, hypertension, acute renal failure, respiratory depression, coma and death have been reported after significant overdose of NSAIDs. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs and may occur following an overdose. In a gastroscopic study of healthy subjects, daily doses of 360 mg given over an 8-hour interval for each of five consecutive days (3 times the highest recommended dose) caused pain and peptic ulcers which resolved after discontinuation of dosing.

Treatment:
Patients should be managed by symptomatic and supportive care following overdose. There are no specific antidotes. Dialysis does not significantly clear ketorolac from the bloodstream. For management of a suspected drug overdose contact your regional Poison Control Centre.

Pharmaceutical Precaution:
This medicine must not be used after the expiry date (EXP) shown on the pack.

STORAGE:
Do not store above 30°C, protect from light & moisture.

Medicine: Keep out of reach of children.

PACKING:
Each box contains 2 x 10 tablets in Alu-Alu blister pack.

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PMR 5446 Version: 01

RADIANT PHARMACEUTICALS

Manufactured by
Radiant Pharmaceuticals Limited
B-34 & B-46, BSCIC Industrial Estate
Tongi, Gazipur-1710, Bangladesh

টোরাডলিন® ট্যাবলেট

কিটোরোলাক ট্রোমেথামিন ইউএসপি

উপস্থাপনঃ
প্রতিটি ফিল্ম কোটেড ট্যাবলেটে আছে কিটোরোলাক ট্রোমেথামিন ইউএসপি ১০ মিগ্রা।
টোরাডলিন একটি শক্তিশালী বেদনানাশক যা নন স্টেরয়ডাল এন্টিইনফ্লামেটরী শ্রেনীভুক্ত। ইহা সাইক্লো অক্সিজিনেজ এনজাইম সিস্টেমকে বাধা দিয়ে প্রোস্টাগ্লানডিন সংশ্লেষণ বাধাগ্রস্থ করে।

কার্যপ্রণালীঃ
টোরাডলিন একটি নন-স্টেরয়ডাল এন্টি-ইনফ্লামেন্টরি ওষুধ যা প্রান্তিক/পেরিফেরাল প্রভাব এর মাধ্যমে ব্যথানাশক ক্রিয়া প্রদর্শন করে। কিটোরোলাক এর কার্যপ্রনালী অন্যান্য NSAID এর মতই পুরোপুরি উপলব্ধি করা যায় না। তবে ধারণা করা হয় এটি প্রোস্টাগ্লান্ডিন সিনথেসিস্ সংশ্লেষণ বাধাগ্রস্থ করার সাথে সম্পর্কিত।

শোষণঃ
মুখে গ্রহনের পর কিটোরোলাক ট্রোমেথামিন খুব দ্রুত এবং সম্পূর্ণ পরিশোষিত হয় এবং সর্বোচ্চ ঘনমাত্রায় পৌছানোর সময় ০.২৫ থেকে ১.৫ ঘন্টা।

নির্দেশনাঃ
টোরাডলিন স্বল্পকালিন মাঝারী থেকে তীব্র ব্যথায় নির্দেশিত।

মাত্রা ও প্রয়োগঃ
পূর্ণ বয়স্ক রোগীর ক্ষেত্রে (>১৮ বছর): ব্যথার তীব্রতা অনুযায়ী টোরাডলিন ১০ মিগ্রা ট্যাবলেট প্রতি ৪-৬ ঘন্টা অন্তর নির্দেশিত।
মাত্রা নির্দেশ সুবিন্যস্ত করতে হবে ব্যথার তীব্রতা এবং রোগীর প্রতিক্রিয়া অনুসারে।
টোরাডলিন ট্যাবলেট শুধুমাত্র স্বল্পকালীন ব্যবহারের জন্য পরামর্শ দেওয়া হয় (সাত দিন পর্যন্ত) এবং ইহা দীর্ঘস্থায়ী ব্যবহারের জন্য পরামর্শ দেওয়া হয় না।

বিরূপ ব্যবহারঃ
- রোগীর পাকস্থলীর ক্ষত ও পাকতান্ত্রিক রক্তক্ষরণের পূর্ব বৃত্তান্ত যদি থাকে।
- সন্দেহজনক বা নিশ্চিত মস্তিষ্ক ও সংবহন নালিকার রক্তক্ষরণ।
- রক্ত জমাট বাঁধন বিশৃঙ্খলা সহ রক্তক্ষরণজনিত রোগ প্রবণতা।
- কিটোরোলাক বা অন্যান্য NSAID এর প্রতি অতি সংবেদনশীলতা।
- ন্যাসাল পলিপস্, এনজিও ইডিমা অথবা ব্রোঙ্কোস্পাজমের সম্পূর্ন বা আংশিক লক্ষণযুক্ত রোগী।
- অন্যান্য NSAID, অক্সপেনটিফাইলাইন, প্রোবেনিসিড অথবা লিথিয়াম সল্ট এর সাথে সহ চিকিৎসায়।
- যে কোন কারণে ডিহাইড্রেশন বা হাইপোভোলেমিয়া।
- লঘু বা তীব্র বৃক্ক সম্বন্ধীয় দুর্বলতা (সিরাম ক্রিয়েটিনিন >১৬০ মাইক্রোমোল/ লিটারের নিচে)।
- হাঁপানি রোগের পূর্ববৃত্তান্ত যদি থাকে।
- যাদের অস্ত্রোপচার জনিত রক্তক্ষরণের তীব্র আশংকা আছে।
- রক্ত জমাট বাঁধন রোধী স্বল্পমাত্রার হেপারিন চিকিৎসায় রয়েছে এমন রোগী (১২ ঘন্টায় ২৫০০-৫০০০ ইউনিট)
- গর্ভকালীন সময়ে, প্রসবাবস্থায় এবং প্রসব কালীন সময়ে।
- ১৮ বছরের নিচে শিশুদের ক্ষেত্রে।

সংরক্ষণঃ
আলো থেকে দূরে, ঠাণ্ডা ও শুষ্ক স্থানে ৩০° সেঃ তাপমাত্রার নীচে সংরক্ষণ করুন।
প্যাকেট এর উপর লেখা মেয়াদ উত্তীর্নের তারিখ অতিক্রম করলে ওষুধ ব্যবহার করা উচিত নয়।

সরবরাহঃ
প্রতি বাক্সে আছে ২ X ১০ টি ট্যাবলেট অ্যালু-অ্যালু ব্লিস্টার প্যাকিং এ।

ওষুধ শিশুদের নাগালের বাইরে রাখুন।

বিস্তারিত তথ্যের জন্য ইংরেজী অংশ দেখুন।

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