ROZAKET

Instructions for the medicinal product

Trade name: Rozaket.
International Nonproprietary Name: Ketorolac Tromethamine.
Dosage form: Solution for Injection.
Composition: Each ml contains:
Ketorolac Tromethamine USP 30 mg;
Water for Injection BP q.s.
Pharmacotherapeutic group: Non-steroidal anti-inflammatory drug - a derivative pyrrolysine carboxylic acid.
ATC Classification: M01AB15.
Pharmacologic property:
Pharmacodynamics:
Ketorolac is a potent analgesic agent of the non-steroidal, anti-inflammatory class (NSAID). It is not an opioid and has no known effects on opioid receptors. It's 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.
Pharmacokinetics:
Following intramuscular administration, ketorolac was rapidly and completely absorbed. A mean peak plasma concentration of 2.2 µg/ml occurred an average of 50 minutes after a single 30 mg dose.
Intravenous administration of a single 10mg dose of ketorolac resultes in a mean peak plasma concentration of 2.4µg/ml at an average of 5.4 minutes after dosing. The terminal plasma elimination half-life was 5.1 hours, average volume of distribution 0.15 l/kg, and total plasma clearance 0.35ml/min/kg.
The pharmacokinetics of ketorolac in man following single or multiple doses are linear. Steady-state plasma levels are achieved after dosing every six hours for one day. No changes in clearance occurres with chronic dosing. The primary route of excretion of ketorolac and its metabolites is renal: 91.4% (mean) of a given dose being found in the urine and 6.1% (mean) in the faeces. More than 99% of the ketorolac in plasma is protein-bound over a wide concentration range.
Indications for use:
Ketorolac Injection is indicated for the short-term management of moderate to severe acute post-operative pain (after abdominal, gynecological, orthopedic, urological and other operations), pain injuries (dislocation, fracture, fractures and sprains), osteoarthritis pain, osteochondrosis, rheumatism, myalgia, arthralgia, sciatica, neuralgia, cancer pain, toothache, pain following dental procedures, pericoronitis, pulp, back pain and muscle pain).
Contra-indications:
„ Hypersensitivity to ketorolac or NSAIDS are contraindicated in patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema or urticaria) in response to ibuprofen, aspirin or other non-steroidal anti-inflammatory drugs, patients with complete or partial syndrome of nasal polyps, angioedema or bronchospasm;
„ Active or previous peptic ulcer, or any history of gastrointestinal bleeding, ulceration or perforation (two or more distinct episodes of proven ulceration or bleeding);
„ Active or history of gastrointestinal bleeding or perforation, related to previous NSAID therapy;
„ Inhibits platelet function and contraindicated in patients with suspected or confirmed cerebrovascular bleeding;
„ patients who have had operations with a high risk of haemorrhage or incomplete haemostasis and those at high risk of bleeding such as those with haemorrhagic diatheses, including coagulation disorders;
„ Probenecid or lithium salts;
„ Severe heart failure, hepatic failure and renal failure;
„ Patients on anti-coagulants including warfarin and low dose heparin (2500 - 5000 units twelve hourly);
„ During pregnancy and lactation;
„ Children under 16 years of age;
„ Rozaket is contra-indicated as prophylactic analgesia before surgery due to inhibition of platelet aggregation and is contra-indicated intra-operatively because of the increased risk of bleeding;
With caution - asthma, cholecystitis, chronic heart failure, hypertension, impaired renal function (plasma creatinine less than 50 mg / l); cholestasis, active hepatitis, sepsis, systemic lupus erythematosus, elderly (over 65 years), mucous membrane polyps nose and nasopharynx.
Dosage and directions for use:
Rozaket Injection is for intramuscular or intravenous use only. Intravenous doses should be given over at least 15 seconds.
Treatment should only be initiated in hospitals.
Dosage should be adjusted according to the severity of the pain and the patient response. Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms . Opioid analgesics (e.g. morphine, pethidine) may be used concomitantly, and may be required for optimal analgesic effect in the early post-operative period when pain is most severe.
Adults - the recommended initial dose of Rozaket Injection is 10 mg followed by 10 to 30mg every four to six hours as required. In the initial post-operative period, Rozaket may be given as often as every two hours if needed. The lowest effective dose should be given. A total daily dose of 90 mg for non-elderly and 60 mg for the elderly, patients with renal impairment and patients less than 50 kg should not be exceeded. The dosage in patients under 50 kg should be reduced.
Patients receiving Rozaket Injection, and who are converted to oral Rozaket, should receive a total combined daily dose not exceeding 90 mg (60 mg for the elderly, patients with renal impairment and patients less than 50 kg). The oral component should not exceed 40 mg on the day the change of formulation is made. Patients should be converted to oral treatment as soon as possible.
Elderly - for patients over 65 years, the lower end of the dosage range is recommended and a total daily dose of 60 mg should not be exceeded. The elderly are at increased risk of the serious consequences of adverse reactions. If an NSAID is considered necessary, the lowest effective dose should be used for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.
Renal impairment - Rozaket Injection should not be used in moderate to severe renal impairment and a reduced dosage given in lesser impairment (not exceeding 60mg/day IV or IM).
Side-effects:
Gastro-intestinal disorders: peptic ulcers, perforation or GI bleeding Nausea, dyspepsia, gastro-intestinal pain, abdominal pain/discomfort, haematemesis, gastritis, dry mouth, oesophagitis, diarrhoea, eructation, constipation, flatulence, fullness, melaena, non-peptic gastro-intestinal ulceration, rectal bleeding, ulcerative stomatitis, vomiting, haemorrhage, perforation, pancreatitis, exacerbation of colitis and Crohn's disease have been reported following administration.
Renal and urinary disorders: Increased urinary frequency, oliguria, acute renal failure, haemolytic uraemic syndrome, flank pain (with or without haematuria, azotemia), interstitial nephritis, urinary retention, nephrotic syndrome.
Eye disorders: Optic neuritis, abnormal vision, visual disturbances.
Ear disorders: Hearing loss, tinnitus, vertigo.
Respiratory, thoracic and mediastinal disorders: Dyspnoea, asthma, pulmonary oedema, epistaxis.
Nervous system disorders: Dizziness, headache, paraesthesia, convulsions, abnormal taste, hyperkinesia.
Cardiac disorders: Bradycardia, palpitations, cardiac failure.
Blood and Lymphatic system disorders: Thrombocytopenia, purpura, neutropenia, agranulocytosis, aplastic anaemia, haemolytic anaemia.
Metabolic and nutrition disorders: Anorexia, hyponatraemia, hyperkalaemia
Skin and subcutaneous tissue disorders: pruritus, urticaria, purpura, angiodema, exfoliative dermatitis, maculopapular rash, sweating, bullous reactions, skin photosensitivity, Lyell's syndrome including Stevens-Johnson syndrome and Toxic Epidermal Necrolysis (very rare) and erythema multiforme. Skin photosensitivity.
Psychiatric disorders: Abnormal thinking, depression, euphoria, insomnia, anxiety, nervousness, psychotic reactions, abnormal dreams, hallucinations, inability to concentrate, drowsiness, confusion, stimulation.
Vascular disorders: Flushing, pallor, hypertension, oedema, hypotension, postoperative wound haemorrhage, haematoma.
Hepatobiliary disorders: Hepatitis, cholestatic jaundice and liver failure.
Musculoskeletal and connective tissue disorders: Myalgia, functional disorders.
General disorders and administration site condition: Excessive thirst, asthenia, weight gain, fever, injection site reactions and pain, chest pain, malaise, fatigue.
Overdose:
Symptoms (Single dose): abdominal pain, nausea, vomiting, erosive and ulcerative lesions of the gastrointestinal tract, renal failure, metabolic acidosis.
Treatment: symptomatic (maintenance of the vital functions of the body.) Dialysis is ineffective.
Drug interactive:
The following medicinal products are NOT to be co-administered with Ketorolac Tromethamine Injection:
Ketorolac should not be used with other NSAIDs including cyclooxygenase-2 selective inhibitors or in patients receiving aspirin because of the increased risk of inducing serious NSAID-related adverse effects.
Ketorolac inhibits platelet aggregation, reduces thromboxane concentrations and prolongs bleeding time. Unlike the prolonged effects from aspirin, platelet function returns to normal within 24-48 hours after ketorolac is discontinued.
Ketorolac injection is contraindicated in combination with anti-coagulants, such as warfarin since co-administration may cause an enhanced anti-coagulant effect.
Although studies do not indicate a significant interaction between ketorolac and warfarin or heparin the concurrent use of ketorolac and therapy that affects haemostasis, including therapeutic doses of anticoagulation therapy (warfarin) prophylactic low-dose heparin (2500-5000 units 12-hourly) and dextrans may be associated with an increased risk of bleeding.
In patients receiving lithium, there is a possible inhibition of renal lithium clearance, leading to an increased plasma lithium concentration with some prostaglandin synthesis-inhibiting drugs, and potential lithium toxicity.
Probenecid should not be administered concurrently with ketorolac because of decreased plasma clearance and volume of distribution of ketorolac leading to increases in ketorolac plasma level and half-life.
NSAIDs should not be used for eight to twelve days after mifepristone administration as NSAIDs can reduce the effects of mifepristone.
When ketorolac is administered concurrently with oxpentifylline, there is an increased tendency to bleeding.
The following medicinal products in combination with Rozaket, are to be co-administered with caution:
Diuretics: Ketorolac Solution for injection reduced the diuretic response to furosemide, in normovolaemic healthy subjects by approximately 20%, so particular care should be taken in patients with cardiac decompensation. Co-administration with diuretics can lead to a reduced diuretic effect, and increase the risk of nephrotoxicity of NSAIDs.
Diuretics and Antihypertensives: NSAIDs may reduce the effect of diuretics and antihypertensive medicinal products. The risk of acute renal insufficiency, which is usually reversible, may be increased in some patients with compromised renal function (e.g. dehydrated patients or elderly patients) when ACE inhibitors and/or angiotensin II receptor antagonists are combined with NSAIDs. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately titrated and consideration should be given to monitoring renal function after initiation of concomitant therapy, and periodically thereafter.
Ketorolac and other non-steroidal anti-inflammatory drugs can reduce the anti-hypertensive effect of beta-blockers and may increase the risk of renal impairment when administered concurrently with ACE inhibitors, particularly in volume depleted patients.
Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma cardiac glycoside levels when co-administered with cardiac glycosides.
Methotrexate: Caution is advised when methotrexate is administered concurrently, since some prostaglandin synthesis inhibiting drugs have been reported to reduce the clearance of methotrexate, and thus possibly enhance its toxicity.
Ciclosporin: As with all NSAIDs caution is advised when ciclosporin is co-administered because of the increased risk of nephrotoxicity.
Corticosteroids: As with all NSAIDs, caution should be taken when co-administering with cortico-steroids because of the increased risk of gastro-intestinal ulceration or bleeding.
Quinolone antibiotics: Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.
Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): There is an increased risk of gastrointestinal bleeding when anti-platelet agents and SSRIs are combined with NSAIDs.
*Tacrolimus:*There is a possible risk of nephrotoxicity when NSAIDS are given with tacrolimus.
Zidovudine: NSAIDs given with zidovudine increase the risk of haematological toxicity. There is evidence of an increased risk of haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.
Antacids: did not affect the extent of absorption.
Cautions:
Unlike the prolonged effects from aspirin, platelet function returns to normal within 24 to 48 hours after ketorolac is discontinued. Patients with coagulation disorders should not receive ketorolac. Patients on anti-coagulation therapy may be at increased risk of bleeding if given ketorolac concurrently.
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 dysfunction, the elderly and those taking diuretics.
Discontinuation of NSAID therapy is typically followed by recovery to the pre-treatment state. Inadequate fluid/blood replacement during surgery, leading to hypovolaemia, may lead to renal dysfunction, which could be exacerbated when ketorolac is administered.
Some patients may experience dizziness, drowsiness, visual disturbances, headaches, vertigo, insomnia or depression with the use of Rozaket. If patients experience these, or other similar undesirable effects, they should not drive or operate machinery.
Presentation:
2x5, 1 ml Glass Ampoule in blister pack with the instructions for use in carton box.
Storage:
Keep in dry place, protected from light at a temperature below 25°C. Keep out of reach of children.
Shelf life:
Labeled. Do not use after expiry date.
Distribution Condition:
Prescribed medicine.

VEGAPHARM

Manufactured for:
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