TAMEKRAZ

Instructions for the medicinal product

Trade name: Tamekraz.
International Nonproprietary Name: Tobramycin + Dexamethasone.
Dosage form: Eye Drops.
Composition:
Tobramycin Sulphate USP equivalent to Tobramycin 0.3% w/v;
Dexamethasone Sodium Phosphate USP equivalent to Dexamethasone Phosphate 0.1% w/v;
Benzalkonium Chloride Solution BP 0.02% w/v; (Preservative)
Sterile aqueous vehicle q.s.
Pharmacotherapeutic group: Anti-inflammatory agents and anti-infectives in combination, corticosteroids and anti-infectives in combination.
ATC Classification: S01CA01.
Pharmacologic property:
Pharmacodynamics:
Tobramycin, an aminoglycoside antibiotic obtained from cultures of *Streptomyces tenebrarius*, has a broad spectrum of activity against *Gram-positive and Gram-negative microorganisms:* Staphylococcus (including Staphylococcus aureus, Staphylococcus epidermidis), including strains resistant to penicillin; streptococci, including some types of beta-hemolytic group A, and some types of non-hemolytic Streptococcus pneumoniae. Pseudomonas aeruginosa, Escherichia coil, Klebsiella pneumoniae, Enterobacter aerogenes, Proteus mirabilis, Mnrqanella mornanii. most of the species Proteus vilgaris, Haemophilus influenzae, Haemophilus aegyptius, Moraxella lacunata, Acinetobacter calcoaceticus, and some types of Neisseria.
It exerts its primary effect on bacterial cells by inhibiting polypeptide assembly and synthesis on the ribosome. Tobramycin in this combination provides antibacterial protection against susceptible bacteria.
Dexamethasone:
The efficacy of corticosteroids for the treatment of inflammatory conditions of the eye is well established. Corticosteroids achieve their anti-inflammatory effects through suppression of vascular endothelial cell adhesion molecules, cyclooxygenase I or II, and cytokine expression. This action culminates in a reduced expression of pro-inflammatory mediators and the suppression of adhesion of circulating leukocytes to the vascular endothelium, thereby preventing their migration into inflamed ocular tissue. Dexamethasone has marked anti-inflammatory activity with reduced mineralo-corticoid activity compared with some other steroids, and is one of the most potent anti-inflammatory agents.
Pharmacokinetics:
Tobramycin:
Tobramycin is absorbed into the cornea following ocular administration. Following systemic administration to patients with normal renal function, a plasma half-life of approximately 2 hours has been observed. Tobramycin is eliminated almost exclusively by glomerular filtration with little if any biotransformation.
Dexamethasone:
Following ocular administration, dexamethasone is absorbed into the eye with maximum concentrations in the cornea and aqueous humour attained within 1-2 hours. The plasma half-life of dexamethasone is approximately 3 hours. Dexamethasone is eliminated extensively as metabolites. Systemic exposure to dexamethasone is low following topical ocular administration.
Indications for use:
Prevention and treatment of inflammation and prevention of infection associated with cataract surgery in adults and children aged 2 years and older.
Contraindications:
• Hypersensitivity to tobramycin or dexamethasone or to any of the excipients;
• Herpes simplex keratitis;
• Vaccinia, varicella and other viral disease of the cornea and conjunctiva;
• Mycobacterial infections of the eye caused by, but not limited to, acid-fast bacilli such as Mycobacterium tuberculosis, Mycobacterium leprae, or Mycobacterium avium;
• Fungal diseases of ocular structures;
• Untreated purulent infection of the eye;
• Children under 2 years.
Pregnancy and Lactation:
There are no adequate data for the use of Tamekraz in pregnant women. Tamekraz should not be used during pregnancy unless clearly necessary. Tamekraz should not be used during breast-feeding unless the potential benefit outweighs the potential risk.
Dosage and directions for use:
Adults:
One drop instilled into the conjunctival sac(s) every 4 to 6 hours while the patient is awake. During the initial 24 to 48 hours, the dosage may be increased to one drop every two hours while the patient is awake. Dosing should continue for 14 days not to exceed a maximum of 24 days. Frequency should be decreased gradually as warranted by improvement in clinical signs. Care should be taken not to discontinue therapy prematurely.
Use in the Elderly:
Clinical studies have indicated dosage modifications are not required for use in the elderly.
Paediatric population:
Tamekraz may be used in children 2 years of age and older at the same dose as in adults.
The safety and efficacy in children younger than 2 years of age have not been established, and no data is available.
Shake the vial well before use. To prevent contamination of the dropper tip, care should be taken not to touch the eyelids, surrounding areas, or other surfaces with the dropper tip of the vial. Keep the vial tightly closed when not in use.
In case of concomitant therapy with other topical ophthalmic medicinal products, an interval of 5 minutes should be allowed between successive applications.
Eye ointments should be administered last.
Side-effects:
Immune system disorders: hypersensitivity.
Nervous system disorders: Uncommon – headache. Not known – dizziness.
Eye disorders: Uncommon - eye pain, eye pruritus, ocular discomfort, ocular hypertension, conjunctival oedema, increased intraocular pressure, eye irritation. Rare - keratitis, eye allergy, blurred vision, dry eye, ocular hyperaemia. Not known - eyelid oedema, erythema of the eyelid, mydriasis, lacrimation increased.
Respiratory, thoracic, and mediastinal disorders: Uncommon - Rhinorrhoea, laryngospasm.
Gastrointestinal disorders: Rare – dysgeusia. Not known - nausea, abdominal discomfort.
Skin and subcutaneous tissue disorders: Not known - rash, swelling face, pruritus.
Overdose:
Due to the characteristics of this preparation, no toxic effects are to be expected with an ocular overdose of this product, or in the event of accidental ingestion of the contents of one vial.
A topical overdose of Tamekraz may be flushed from the eye(s) with lukewarm tap water.

Drug interaction:
No clinically relevant interactions have been described with topical ocular dosing.
Concomitant use of topical steroids and topical NSAIDs may increase the potential for corneal healing problems.

Antiplatelet agents and selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal
Cautions:
Prolonged use of topical ophthalmic corticosteroids (i.e., longer than the maximum duration used in clinical trials [24 days]) may result in ocular hypertension/glaucoma with resultant damage to the optic nerve and reduced visual acuity and visual fields defects and may also result in posterior subcapsular cataract formation.
It is advisable that the intraocular pressure be checked frequently. This is especially important in paediatric patients receiving dexamethasone-containing products, as the risk of steroid-induced ocular hypertension may be greater in children below 6 years of age and may occur earlier than a steroid response in adults. The frequency and duration of treatment should be carefully considered, and the intraocular pressure should be monitored from the outset of treatment, recognizing the risk for earlier and greater steroid-induced intraocular pressure increases in the paediatric patients.
The risk of corticosteroid-induced raised intraocular pressure and/or cataract formation is increased in predisposed patients (e.g. diabetes).
Prolonged use may also result in secondary ocular infections due to suppression of host response. Corticosteroids may reduce resistance to and aid in the establishment of bacterial, viral or fungal infections and mask the clinical signs of infection.
Sensitivity to topically administered aminoglycosides may occur in some patients. If hypersensitivity develops during use of this medicine, treatment should be discontinued.
Cross-hypersensitivity to other aminoglycosides can occur, and the possibility that patients who become sensitized to topical tobramycin may also be sensitive to other topical and/or systemic aminoglycosides should be considered.
Serious adverse reactions including neurotoxicity, ototoxicity and nephrotoxicity have occurred in patients receiving systemic aminoglycoside therapy. Caution is advised when used concomitantly.
Fungal infection should be suspected in patients with persistent corneal ulceration. If fungal infection occurs, corticosteroids therapy should be discontinued.
Prolonged use of antibiotics such as tobramycin may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, appropriate therapy should be initiated.
Topical ophthalmic corticosteroids may slow corneal wound healing. Topical NSAIDs are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems.
In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical corticosteroids.
Benzalkonium chloride, used as a preservative in this product, has been reported to cause punctate keratopathy and/or toxic ulcerative keratopathy. Benzalkonium chloride may cause eye irritation and discolour soft contact lenses.
Avoid contact with soft contact lenses. Contact lens wear is not recommended during treatment of an ocular infection or inflammation. If patients are allowed to wear contact lenses, they must be instructed to remove lenses prior to application of Tamekraz and wait at least 15 minutes before reinsertion.
Effects on ability to drive and use machines
Tamekraz has no or negligible influence on the ability to drive and use machines.
No studies on the effects on the ability to drive and use machines have been performed. As with any eye drop, temporarily blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs, the patient must wait until the vision is clear before driving or using machines.
Presentation:
10 ml HDPE Opaque vial in a monocarton, with instruction for use.
Storage:
Keep in dry place protected from light at a temperature below 30°C. Keep out of reach of children.
Shelf life:
Labeled. Do not use after expiry date.
Distribution Condition:
Prescription only medicine (POM).