Package leaflet: Information for the patient

TOB DEX

Tobramycin (0.3%w/v) and Dexamethasone sodium Phosphate 0.1%w/v Eye drops

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.
- Your medicine, Tobramycin and Dexamethasone Eye Drops will be referred to as Tobramycin and Dexamethasone in this leaflet.

What is in this leaflet

1. What Tobramycin and Dexamethasone is and what it is used for

It is an Anti-inflammatory agents and anti-infectives in combination, corticosteroids and anti-infectives in combination.
It is used for the Prevention and treatment of inflammation and prevention of infection associated with cataract surgery in adults and children aged 2 years and older.

2. What you need to know before you use Tobramycin and DexamethasoneDo not use Tobramycin and Dexamethasone if:

Warnings and precautions

TOB - DEX is for topical use only and not for injection or oral use.
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.

Visual disturbance

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

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.
Cushing's syndrome and/or adrenal suppression associated with systemic absorption of ocular dexamethasone may occur after intensive or long-term continuous therapy in predisposed patients, including children and patients treated with CYP3A4 inhibitors (including ritonavir and cobicistat).
In these cases, treatment should be progressively discontinued.

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, fungal or parasitic infections and mask the clinical signs of infection.

Sensitivity to topically administered aminoglycosides may occur in some patients. Severity of hypersensitivity reactions may vary from local effects to generalized reactions such as erythema, itching, urticarial, skin rash, anaphylaxis, anaphylactoid reactions, or bullous reactions. 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 (see section 4.5).

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 TOB-DEX and wait at least 15 minutes before reinsertion.

Other medicines and Tobramycin and Dexamethasone

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.

Dexamethasone is metabolized via cytochrome P450 3A4 (CYP3A4). CYP3A4 inhibitors (including ritonavir and cobicistat); may decrease dexamethasone clearance resulting in increased effects and adrenal suppression/Cushing's syndrome. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid effects.

Ask your doctor for advice before taking any medicine.

Use in pregnancy

There are no or limited amount of data from the topical ocular use of tobramycin and dexamethasone in pregnant women. Tobramycin does cross the placenta into the fetus after intravenous dosing in pregnant women. Tobramycin is not expected to cause ototoxicity from in utero exposure. Prolonged or repeated corticoid use during pregnancy has been associated with an increased risk of intra-uterine growth retardation. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be observed carefully for signs of hypoadrenalism.

Studies in animals have shown reproductive toxicity after systemic administration of tobramycin and dexamethasone. These effects were observed at exposures considered sufficiently in excess of the maximum human ocular dosage delivered from the maternal use of the product.

Tob dex is not recommended during pregnancy.

Use in breast-feeding

Tobramycin is excreted in human milk after systemic administration. No data is available on the passage of dexamethasone into human breast milk. It is unknown whether tobramycin and dexamethasone are excreted in human milk following topical ocular administration. It is not likely that the amount of Tobramycin and Dexamethasone would be detectable in human milk or be capable of producing clinical effects in the infant following topical use of the product.

A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Driving and using machines

Tob dex 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.

Tobramycin and Dexamethasone contains

This medicine contains 0.10 mg/ml benzalkonium chloride as a preservative. Benzalkonium chloride may be absorbed by soft contact lenses and may change the colour of the contact lenses. You should remove contact lenses before using this medicine and put them back 15 minutes afterwards.

Benzalkonium chloride may also cause eye irritation, especially if you have dry eyes or disorders of the cornea (the clear layer at the front of the eye). If you feel abnormal eye sensation, stinging or pain in the eye after using this medicine, talk to your doctor.

3. How to use Tobramycin and Dexamethasone

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:
TOB - DEX 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.

Use in hepatic and renal impairment:
TOB - DEX has not been studied in these patient populations
Method of Administration:
Ocular Use:

Shake the bottle well before use. To prevent contamination of the dropper tip and suspension, care should be taken not to touch the eyelids, surrounding areas, or other surfaces with the dropper tip of the bottle. Keep the bottle tightly closed when not in use. After cap is removed, if tamper evident snap collar is loose, remove before using product.

Duration of treatment:
Your doctor or your child's doctor will decide for how long the eye drops will be needed.

If you use more Tobramycin and Dexamethasone than you should

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 bottle or tube.

A topical overdose of Tob dex may be flushed from the eye(s) with lukewarm tap water.

If this happens, contact your doctor immediately.

If you forget to use Tobramycin and Dexamethasone

It is important to take Tobramycin and Dexamethasone as prescribed by your doctor.

- If you miss the dose, use the drops as soon as possible.
- If it is almost time for the next dose, skip the missed dose and take the next dose at the usual time.
- Do not take a double dose to make up for the forgotten dose.

If you stop using Tobramycin and Dexamethasone

If you want to stop using this medicine talk to your doctor first. If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Tabulated list of adverse reactions

The following adverse reactions have been reported with Tob Dex during clinical trials or during post marketing experience and are classified according to the subsequent convention: very common (≥ 1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000) and very rare (<1/10,000), and not known (cannot be estimated from the available data). Within each frequency-grouping, adverse reactions are presented in order of decreasing seriousness.

System organ classification	**Frequency**	**Adverse reaction**
Immune system disorders	Not known	anaphylactic reaction, hypersensitivity
Endocrine disorders	Not known	Cushing's syndrome, adrenal suppression (see section 4.4)
Nervous system disorders	Uncommon Not known	headache dizziness
Eye disorders	Uncommon Rare Not known	eye pain, eye pruritus, ocular discomfort, ocular hypertension, conjunctival oedema, increased intraocular pressure, eye irritation keratitis, eye allergy, vision blurred (see also section 4.4), dry eye, ocular hyperaemia eyelid oedema, erythema of the eyelid, mydriasis, lacrimation increased
Respiratory, thoracic, and mediastinal disorders	Uncommon	rhinorrhoea, laryngospasm
Gastrointestinal disorders	Rare Not known	dysgeusia nausea, abdominal discomfort
Skin and subcutaneous tissue disorders	Not known	erythema multiforme, rash, swelling face, pruritus

Description of selected adverse reactions

The following adverse reactions have been observed following use with dexamethasone ophthalmic suspension:

System organ classification	**Frequency**	**Adverse reaction**
Nervous system disorders	Common	headache
Eye disorders	Common	eye irritation,* ocular hyperaemia,* erythema of

		eyelid, abnormal sensation in eye*
Respiratory, thoracic, and mediastinal disorders	Common	post nasal drip

The following adverse reactions have been observed following use with Tobramycin ophthalmic solution:

System organ classification	**Frequency**	**Adverse reaction**
Eye disorders	Common Uncommon	ocular hyperaemia,* eye pain* eye pruritus,* ocular discomfort,* eye allergy, eyelid oedema,* conjunctivitis,* glare, increased lacrimation,* keratitis*

∗These adverse reactions were also observed with Tob Dex during post marketing.

Prolonged use of topical ophthalmic corticosteroids may result in increased intraocular pressure with damage to the optic nerve, reduced visual acuity and visual field defects, posterior subcapsular cataract formation and delayed wound healing.

Due to the corticosteroid component, in diseases causing thinning of the cornea or sclera there is a higher risk for perforation especially after long treatments.

The development of secondary infection has occurred after the use of combinations containing corticosteroids and antimicrobials. Fungal infections of the cornea are particularly prone to develop coincidentally with long term applications of steroids.

Serious adverse reactions including neurotoxicity, ototoxicity and nephrotoxicity have occurred in patients receiving systemic tobramycin therapy.

Sensitivity to topically administered aminoglycosides may occur in some patients.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the CDSCO, India. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Tobramycin and Dexamethasone

Keep this medicine out of sight and reach of children.

- Do not store at a temperature above 30^0C.
- Store the bottle in the outer carton in order to protect it from light.
- **Discard the bottle 30 days after opening, even if there is solution remaining.**

Do not use Tobramycin and Dexamethasone after the expiry date which is stated on the carton and the bottle after EXP.
The expiry date refers to the last day of that month. Make sure the container is properly closed.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Tobramycin and Dexamethasone contains
The active ingredients are Tobramycin and Dexamethasone Sodium Phosphate.
This product also contains Borax, Boric acid, Sodium chloride, Sodium metabisulphite, Tween 80,

Disodium edetate, Benzalkonium chloride and Purified water BP

What Tobramycin and Dexamethasone looks like and contents of the pack

Packed in 10ml Low density polyethylene container with HDPE cap and Nozzle. Such 10ml is packed in a monocarton with package insert.

Marketing Authorisation Holder and Manufacturer

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