SHINADEX® EYE DROPS

Ingredient(s):
Each ml contains:
Chloramphenicol 5mg
Dexamethasone Sodium Phosphate 1mg
Phenylmercuric Nitrate (as preservative) 0.02mg

Pharmacology (Summary of Pharmacodynamic and Pharmacokinetic):
Pharmacodynamic :
The anti-inflammatory effect of dexamethasone is approximately 25 times stronger than that of hydrocortisone. As an anti-inflammatory glucocorticoid, one of the actions of dexamethasone is to inhibit the phospholipase A2, the first step in prostaglandin synthesis. Also, dexamethasone inhibits the chemotactic infiltration of neutrophils into the site of inflammation.
Chloramphenicol is a low-molecular weight, predominantly lipophilic, antibiotic, and is effective against gram-positive and gram negative bacteria, and also against spirochete, salmonella, rickettsiae and chlamydiae (trachoma). The mechanism of action has been shown to be by selective inhibition of bacterial protein synthesis.

Pharmacokinetic :
Dexamethasone Sodium Phosphate:
Its biological half life in plasma is about 190 minutes. Binding of dexamethasone to plasma proteins is less than for most other corticosteroids. Corticosteroids in the circulation are extensively bound to plasma proteins, mainly to globulin and less so to albumin. The corticosteroid-binding globulin has high affinity but low binding capacity, while the albumin has low affinity but large binding capacity. Only unbound corticosteroid has pharmacological effects or is metabolized. The synthetic corticosteroids are less extensively protein bound than hydrocortisone (cortisol). They also tend to have longer half lives.
Corticosteroids are metabolized mainly in the liver but also in the kidney, and are excreted in the urine. Urinary excretion of 17-hydroxy-corticoids is used as an index of adrenal function. The slower metabolism of the synthetic corticosteroids with their lower protein-binding affinity may account for their increased potency compared with the natural corticosteroids.
Chloramphenicol:
Protein binding
At peak blood levels, about 60% of the chloramphenicol is bound by plasma albumin and the binding is probably readily reversible.
Metabolism
Under conditions of normal hepatic function about 92% of administered chloramphenicol is metabolized in the liver, about 90% undergoes conjugation to the glucuronide by glycuronyl transferase and 2% undergoes reduction to arylamines or undergoes deacetylation and dehalogenation.
Excretion
Chloramphenicol is excreted in the urine and bile. Nearly 90% of the administered chloramphenicol is excreted in the urine during the first six hours after ingestion. Most of this is eliminated by tubular secretion as inactive glucuronide conjugates and arylamines. 5-10% of the chloramphenicol excreted in the urine is eliminated as the active compound and this is largely by glomerular filtration. Approximately 3% of a dose of chloramphenicol is excreted in the bile in the active form but most of this is reabsorbed from the intestine so that only about 1% is excreted in the faeces and this is an inactive form.
Half life
The biological half-life of chloramphenicol is 1.05 to 3.5 hours and there is virtually no drug detectable in the blood after 12 to 18 hours. The half-life of chloramphenicol correlates well with the plasma bilirubin concentration.

Indication(s):
1. Acute and chronic keratitis and conjunctivitis of an infectious, allergic but nonviral nature.
2. Infections of the anterior uvea (iritis, iridocyclitis).
3. Scleritis, episcleritis and myositis.
4. Sympathetic ophthalmia.
5. Post-operative management of cataract, glaucoma, and strabismus.

Dosage and Administration:
1 drop, instilled into the conjunctival sac 3 to 5 times daily for up to 10 days.
In acute cases: up to 1 drop per hour.
Elderly: There is no indication that dosage needs to be modified for the elderly.
Paediatric use: Studies in the paediatric population have not been performed.
Following instillation of the eye drops nasolacrimal occlusion or closing the eyelids for 3 minutes may reduce systemic absorption. This may result in a decrease in systemic side effects and an increase in local activity.
The dispenser remains sterile until the original closure is broken.
Patients must be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures as this may contaminate the solution.
If more than one medication needs to be instilled in the eye an interval of at least 5 minutes between applications of the different medicinal products must be allowed.

Contraindication(s):
1. Known hypersensitivity to the active substances or to any of the excipients.
2. Corneal lesions due to non-bacterial infections and ulcerative processes. Herpes simplex and other viral infections. Mycosis and other fungal infections.
3. Severe blood disorders due to bone marrow depression and hepatic dysfunction.
4. Family history of bone marrow depression.

Precaution(s) / Warning(s):
1. Corticosteroids may mask, activate or aggravate an eye infection.
2. The local use of dexamethasone over a prolonged period may lead in some cases to secondary glaucoma and the development of complicated cataract. To be used, therefore, under stric medical supervision.
3. Because of the possibility of inducing corneal abscess, fungal keratopathy or glaucoma, the patient should be referred to an ophthalmologist if the eye has not responded within 48 hours.
4. Children: Safety and effectiveness in paediatrics have not been established.

Interaction with Other Medicaments:
Chloramphenicol should not be administered simultaneously with anti-bacterial substances (penicillins, cephalosporins, gentamicin, tetracyclines, polymyxin B, vancomycin or sulfadiazine) and furthermore, should not be administered at the same time as systemic treatment with drugs which have an adverse effect on hematopoiesis, nor simultaneously with sulfonylureas, coumarin derivatives, hydantoins and methotrexate.
Interactions known from systemic application of corticosteroids, although of minor importance, have to be considered.
Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. 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 side-effects.

Pregnancy and Lactation:
Chloramphenicol readily traverses the placental barrier and is excreted in the milk. Therefore, it must not be administered in the last trimester of the pregnancy or to a nursing mother, since severe defects in the neonate and in the nursing infant may result (Grey syndrome, dyshematopoiesis) .

Side Effect(s):
Blood and lymphatic system disorders
Rare cases of sometimes irreversible blood dyscrasias (aplastic anaemia, pancytopenia, leucopenia, thrombocytopenia and agranulocytosis) with a fatal outcome have been reported in the literature following the use of ophthalmic preparations containing chloramphenicol.

Immune system disorders
Anaphylactic reactions to topical chloramphenicol have been published in the literature. Rarely, allergic reactions in the form of eczema of the lid margins have been reported.

Nervous system disorder
In rare cases, reversible optic neuritis has been observed following administration of chloramphenicol.

Eye disorders
The most frequently reported adverse reactions are those indicative of irritation or hypersensitivity reactions (itching, redness, swelling, foreign body sensation, or other sign of irritation not present before therapy). Ocular burning or stinging upon drug instillation and blurred vision have also been reported. Adverse reactions associated with topical steroid therapy include elevation of intraocular pressure with possible development of glaucoma (optic nerve damage; visual acuity and field defects), posterior subcapsular cataract formation, secondary ocular infection following suppression of host response; delayed wound healing and corneal thinning and/or perforation of the globe may occur. Ptosis and mydriasis have also been related to the use of ophthalmic steroids.

Gastrointestinal disorder
The patient may experience a bitter taste (dysgeusia) shortly after application of chloramphenicol. Although systemic effects are uncommon, there have been some cases of systemic corticosteroid effects after topical administration of corticosteroids.

Symptoms and Treatment for Overdosage, and Antidote(s):
Accidental ingestion of the drug is unlikely to cause any toxicity due to low content of antibiotic.

Treatment: If irritation, pain, swelling, lacrimation or photophobia occurs after undesired eye contact, the exposed eye(s) should be irrigated with copious amounts of room temperature water for at least 15 minutes. If symptoms persist after 15 minutes of irrigation, an ophthalmological examination should be considered.

Shelf-Life:
2 years from the date of manufacture.

Storage Condition(s):
Before and after opening :
Store at temperature between 2-8°C.
Discard one month after opening.

Product Description & Packing(s):
A clear and colorless solution.
Plastic bottle of 5ml, 5ml x 10, 5ml x 12 , 5ml x 20 & 5ml x 24.

Y. S. P.®
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