Ocupol® Dx

Composition:

Each ml of OCUPOL DX Eye Drops contains:

Polymyxin-B sulfate	5000 IU
Chloramphenicol	4 mg
Dexamethasone	1mg

Each gm of OCUPOL DX Ointment contains:

Polymyxin-B sulfate	10000 IU
Chloramphenicol	10 mg
Dexamethasone	1mg

Pharmacokinetic properties:

Polymyxin B sulfate is not absorbed from the gastrointestinal tract, except in infants who may absorb up to 10% of a dose. It is not absorbed through mucous membranes, or intact or denuded skin. Peak plasma concentrations after intramuscular injection usually occur within 2 hours, but are variable and Polymyxin B sulfate is partially inactivated by serum. It is widely distributed and extensively bound to cell membranes in the tissues; it does not appear to be highly bound to serum proteins. Accumulation may occur after repeated doses. There is no diffusion into the CSF and it does not cross the placenta. Polymyxin B is reported to have a serum half-life of about 6 hours but this is prolonged in renal impairment; values of 2 to 3 days have been reported in patients with a creatinine clearance of less than 10 mL/minute. Polymyxin B sulfate is excreted mainly by the kidneys by glomerular filtration, about 60% of a dose being recovered unchanged in the urine, but there is a time lag of 12 to 24 hours before Polymyxin B is recovered in the urine. Polymyxin B is not removed to an appreciable extent by peritoneal dialysis or haemodialysis.

Chloramphenicol is active when given orally and, unlike most other antibacterials, it diffuses into the CSF even when the meninges are not inflamed. The majority of a dose is inactivated in the liver, only a small proportion appearing unchanged in the urine.

Dexamethasone is readily absorbed from the gastrointestinal tract. Its biological half-life in plasma is about 190 minutes. Binding of dexamethasone to plasma proteins is about 77%, which is less than for most other corticosteroids. Up to 65% of a dose is excreted in urine within 24 hours. Clearance in premature neonates is reported to be proportional to gestational age, with a reduced elimination rate in the most premature. It readily crosses the placenta with minimal inactivation.

Mechanism of Action

Polymyxin B sulfate has a bactericidal action against almost all gram-negative bacilli except the Proteus group. Polymyxin B sulfate interacts with the lipopolysaccharide of the cytoplasmic outer membrane of Gram-negative bacteria, altering membrane permeability and causing cell death. It does not need to enter the cell.

Chloramphenicol is lipid-soluble, allowing it to diffuse through the bacterial cell membrane. It then reversibly binds to the L16 protein of the 50S subunit of bacterial ribosomes, where transfer of amino acids to growing peptide chains is prevented (perhaps by suppression of peptidyl transferase activity), thus inhibiting peptide bond formation and subsequent protein synthesis.

Dexamethasone is a glucocorticoid agonist. Unbound dexamethasone crosses cell membranes and binds with high affinity to specific cytoplasmic glucocorticoid receptors. This complex binds to DNA elements (glucocorticoid response elements) which results in a modification of transcription and, hence, protein synthesis in order to achieve inhibition of leukocyte infiltration at the site of inflammation, interference in the function of mediators of inflammatory response, suppression of humoral immune responses, and reduction in edema or scar tissue. The anti-inflammatory actions of dexamethasone are thought to involve phospholipase A_2 inhibitory proteins, lipocortins, which control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes.

Other pharmacodynamic properties:

Polymyxin B sulfate is a mixture of polymyxins B1 and B2, obtained from *Bacillus polymyxa* strains. They are basic polypeptides of about eight amino acids and have cationic detergent action on cell membranes. Polymyxin B is used for infections with gram-negative organisms, but may be neurotoxic and nephrotoxic. All gram-positive bacteria, fungi, and the gram-negative cocci, *N. gonorrhea* and *N. menigitidis*, are resistant.

Chloramphenicol is a broad-spectrum antibiotic that was derived from the bacterium Streptomyces venezuelae and is now produced synthetically. Chloramphenicol is effective against a wide variety of microorganisms, but due to serious side-effects (e.g., damage to the bone marrow, including aplastic anemia) in humans, it is usually reserved for the treatment of serious and life-threatening infections (e.g., typhoid fever). Chloramphenicol is bacteriostatic but may be bactericidal in high concentrations or when used against highly susceptible organisms. Chloramphenicol stops bacterial growth by binding to the bacterial ribosome (blocking peptidyl transferase) and inhibiting protein synthesis.

Dexamethasone and its derivatives, dexamethasone sodium phosphate and dexamethasone acetate, are synthetic glucocorticoids. Used for its anti-inflammatory or immunosuppressive properties and ability to penetrate the CNS, dexamethasone is used alone to manage cerebral edema and with tobramycin to treat corticosteroid-responsive inflammatory ocular conditions.

Indication:

OCUPOL DX is indicated for, ·

- The treatment of, surface ocular infections involving the conjunctiva and/or cornea caused by susceptible organisms. ·
- For the treatment of superficial bacterial infections of the external auditory canal caused by organisms susceptible to the action of the antibiotics, and
- For the treatment of infections of mastoidectomy and fenestration cavities caused by organisms susceptible to the antibiotics.
- For steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where bacterial infection or a risk of bacterial ocular infection exists. Ocular steroids are indicated in inflammatory conditions of the palpebral and bulbar conjunctiva, cornea and anterior segment of the globe to obtain a diminution in edema and inflammation. They are also indicated in chronic anterior uveitis and corneal injury from chemical, radiation or thermal burns, or penetration of foreign bodies

Contraindication:

- The use of OCUPOL DX is contraindicated in patients with hypersensitivity to any ingredient of the formulations.
- The use of OCUPOL DX is also contraindicated in epithelial herpes keratitis (dendritic keratitis), vaccinia, varicella other viral diseases of the cornea and conjunctiva, mycobacterial infections of the eye and fungal diseases of ocular structures.

Drug Interaction:

The risk of increased intraocular pressure associated with prolonged corticosteroid therapy may be more likely to occur with concomitant use of anti-cholinergic, especially atropine and related compounds, in patients predisposed to acute angle closure. The risk of corneal deposits or corneal opacity may be more likely to occur in patients presenting with compromised cornea and receiving polypharmacy with other phosphate containing eye medications. The following drug interactions are possible, but are unlikely to be of clinical significance, following the use of Dexamethasone: The therapeutic efficacy of dexamethasone may be reduced by phenytoin, phenobarbitone, ephedrine and rifampicin. Glucocorticoids may increase the need for salicylates as plasma salicylate clearance is increased. If more than one topical ophthalmic medicinal product is being used, the medicines must be administered at least 5 minutes apart. Eye ointments should be administered last.

Adverse effects:

- The adverse reactions reported with topical corticosteroids especially under occlusive dressings include burning sensation, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae and miliaria.
- Blood dyscrasias have been reported in association with the use of chloramphenicol.
- Chloramphenicol is absorbed systemically from the eye and toxicity has been reported following chronic exposure.

- Bone marrow hypoplasia, including aplastic anaemia and death, has been reported following topical use of chloramphenicol.
- Whilst the hazard is rare, it should be borne in mind when assessing the benefits expected from the use of the compound.
- More serious side effects include hypersensitivity reactions that may present as angioneurotic oedema, urticaria, anaphylaxis, fever, and vesicular and maculopapular dermatitis. If this happens treatment must be discontinued immediately

Warnings and Precautions:

- The prolonged use of antibiotics may occasionally result in overgrowth of nonsusceptible organisms, including fungi.
- If new infections appear the drug should be discontinued and appropriate measures instituted.
- In all serious infections the topical use of OCUPOL DX should be supplemented by appropriate systemic medication.
- Prolonged use of OCUPOL-DX may result in glaucoma and posterior subcapsular cataract formation. If these products are used for 10 days or longer, intra-ocular pressure should be routinely monitored even though it may be difficult in children and uncooperative patients.

Use in special population:

1. **Pediatric:** Safety and efficacy in children has not been established.
2. **Geriatric:** Safety and efficacy in elderly patient has not been established.
3. **Liver impairment:** Use with caution.
4. **Renal failure:** Use with caution.
5. **Pregnancy and lactation:** The safety of topical chloramphenicol in pregnancy and lactation has not been established. Chloramphenicol may be absorbed systemically following the use of eye ointment and may cross the placenta and appear in breast milk. Therefore this product is not recommended for use during pregnancy and lactation.

Dosage:

As directed by physician.

Presentation:

OCUPOL DX Drops is available in 5 ml lupolen vial

OCUPOL DX Ointment is available in a tube of 5 g.

Storage and handling:

Store in cool and dry place.