Ocupol®

1. Generic Name

Polymyxin-B sulfate

Chloramphenicol

2. Qualitative and Quantitative composition

Each ml of OCUPOL Eye Drops contains:

Polymyxin-B sulfate 5000 IU

Chloramphenicol 4 mg

Each gm of OCUPOL Ointment contains:

Polymyxin-B sulfate 10000 IU

Chloramphenicol 10 mg

3. Dosage form and strength

Topical ophthalmic solution of OCUPOL contains Chloramphenicol (4mg) and Polymyxin- B sulfate (5000IU).

Topical ophthalmic ointment of OCUPOL contains Chloramphenicol (10mg) and Polymyxin-B sulfate (10000IU).

4. Clinical particulars

4.1 Therapeutic indication

For ocular bacterial infection.

4.2 Posology and method of administration

Eye drops: 1-2 drops twice or thrice a day during daytime.

Ointment: half an inch ribbon of “Ocupol ointment” before sleeping.

4.3 Contraindication

The use of OCUPOL is contraindicated in patients:

- With hypersensitivity to any ingredient of the formulations.
- who have experienced bone marrow suppression during previous exposure to chloramphenicol.
- known personal or family history of blood dyscrasias including aplastic anaemia.

4.4 Special warnings and precautions for use

- Chloramphenicol is absorbed systemically from the eye and systemic toxicity has been reported.
- Bone marrow hypoplasia, including aplastic anaemia and death, has been reported following topical use of chloramphenicol. Whilst the hazard is a rare one, it should be borne in mind when assessing the benefits expected from the use of the compound.
- If the eye ointment is to be used on a long-term or intermittent basis, it may be advisable to perform a routine blood profile before therapy and at appropriate intervals thereafter to detect any haemopoietic abnormalities.
- In severe bacterial conjunctivitis and in cases where infection is not confined to the conjunctivae, the topical use of chloramphenicol should be supplemented by appropriate systemic treatment.
- It is recommended that all types of contact lenses be avoided during ocular infections.
- Sensitivity to topically applied aminoglycosides may occur in some patients. Cross-sensitivity to other aminoglycosides may also occur.
- Patients using ophthalmic preparations containing neomycin sulphate should be advised to consult a physician if ocular pain, redness, swelling, or irritation worsens or persists.
- Nephrotoxic and neurotoxic reactions have also occurred with systemic polymyxin B. Although these effects have not been reported following topical ocular use of this product, caution is advised with polymyxin B therapy.
- The prolonged use of antibiotics may occasionally result in overgrowth of non-susceptible organisms, including fungi.
- If new infections appear the drug should be discontinued, and appropriate measures instituted.

4.5 Drug interactions

Concomitant administration of chloramphenicol with other drugs liable to depress bone marrow, hence should be avoided.

4.6 Use in special population

- Pediatric: Safety and efficacy in children has not been established.
- Geriatric: Safety and efficacy in children has not been established.
- Liver impairment: Use with caution.

- Renal failure: Use with caution.
- 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.

4.7 Effects on ability to drive and use machine

Patients should be cautioned against engaging in activities requiring complete mental alertness, and motor coordination such as operating machinery until their response to Ocupol is known.

4.8 Undesirable effects

The adverse reactions reported with Ocupol eye drops/ointment – Periorbital oedema, Ocular hyperaemia, Face oedema, Hypersensitivity.

4.9 Overdose

There is limited experience of overdose with Ocupol. Initiate general symptomatic and supportive measures in all cases of overdosages where necessary.

5. Pharmacological properties

5.1 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.

5.2 Pharmacodynamic properties

Polymyxin B sulfate is a mixture of polymyxins B1 and B2, obtained from Bacillus polymyxins 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. gonorrhoea and N. meningitides, are resistant.

Chloramphenicol is a broad-spectrum antibiotic that was derived from the bacterium Streptomyces Venezuela 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 anaemia) 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.

5.3 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 antibacterial, 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.

6. Nonclinical properties

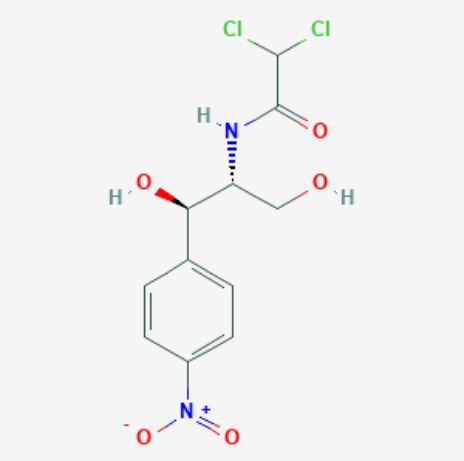
6.1 Animal Toxicology or Pharmacology

Not required.

7. Description

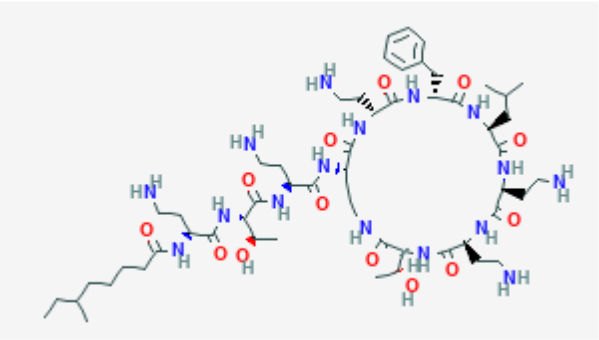
Chloramphenicol

Chloramphenicol is a semisynthetic, broad-spectrum antibiotic derived from Streptomyces venequelae with primarily bacteriostatic activity. The chemical name is 2,2-dichloro-N-[(1R,2R)-1,3-dihydroxy-1-(4-nitrophenyl)propan-2-yl]acetamide. Its empirical formula and molecular weight is $C_{11}H_{12}Cl_2N_2O_5$ and 323.13 g/mol.



Polymyxin-B sulfate

Polymyxin B is a mixture of the polypeptides polymyxins B1 and B2, both obtained from Bacillus polymyxa strains, with antimicrobial activity. The chemical name is N-[(2S)-4- amino-1-[[(2S,3R)-1-[[(2S)-4-amino-1-oxo-1-[[(3S,6S,9S,12S,15R,18R,21S)-6,9,18-tris(2-aminoethyl)-15-benzyl-3-[(1R)-1-hydroxyethyl]-12-(2-methylpropyl)-2,5,8,11,14,17,20-heptaoxo1,4,7,10,13,16,19-heptazacyclotricos-21-yl]amino]butan-2-yl]amino]-3- hydroxy-1-oxobutan-2-yl]amino]-1-oxobutan-2-yl]-6-methyloctanamide . Its empirical formula and molecular weight is $C_{56}H_{98}N_{16}O_{13}$ and 1203.5 g/mol.



8. Pharmaceutical particulars

8.1 Incompatibilities

There are no known incompatibilities.

8.2 Shelf-life

OCUPOL eye drops- 18 months.

OCUPOL eye ointment-24 months.

8.3 Packaging Information

OCUPOL Drops is available in 5 ml lupolen vial

OCUPOL Ointment is available in a tube of 5 g.

8.4 Storage and handling instructions

Store in cool and dry place.

9. Patient Counselling Information

9.1 Adverse reactions

Refer part 4.8

9.2 Drug Interactions

Refer part 4.8

9.3 Dosage

Refer part 4.5

9.4 Storage

Refer part 8.4

9.5 Risk factors

Refer part 4.4

9.6 Self-monitoring information

NA

9.7 Information on when to contact a health care provider or seek emergency help

Patient is advised to be alert for the emergence or worsening of the adverse reactions and contact the prescribing physician.

9.8 Contraindications

Refer part 4.3

10. Manufactured by CENTAUR PHARMACEUTICALS PVT. LTD. and DCI Pharmaceuticals

11. Details of permission or license number with date

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