CHLOROMYCETIN® APLICAP®

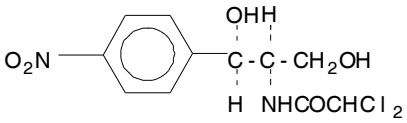
(Chloramphenicol Eye Ointment IP)

1. NAME OF THE MEDICINAL PRODUCT

CHLOROMYCETIN APLICAP.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Chloramphenicol is an antibiotic originally isolated from *Streptomyces venezuelae*. Its chemical name is 2,2-Dichloro-N-[(2R,3R)-3-hydroxy-2-hydroxymethyl-4-nitrophenethyl] acetamide, $C_{11}H_{12}Cl_2N_2O_5$ and its molecular weight = 323.1. The structure for chloramphenicol is:



Chloramphenicol occurs as fine, white to grayish or yellowish white, needle-like crystals, has a solubility of approximately 2.5 mg/mL in water at 25°C, and is freely soluble in alcohol. The pK_a of the drug is 5.5.

Chloromycetin Aplicap is a pliable gelatin capsule containing chloramphenicol ointment for single application. Each Soft Gelatin Aplicap contains 250 mg of Chloramphenicol Eye Ointment I.P. (1% w/w) in an oleaginous ointment base.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Ophthalmic Ointment.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Chloramphenicol should be reserved for serious infections caused by organisms susceptible to its antimicrobial effects when less potentially hazardous therapeutic agents are ineffective or contraindicated. Bacteriological studies should be performed to determine the causative organisms and their sensitivity to chloramphenicol.

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Chloramphenicol ophthalmic ointment is indicated for the treatment of surface ocular infections involving the conjunctiva and/or cornea caused by chloramphenicol-susceptible organisms. They are effective against the following common bacterial eye pathogens:

Staphylococcus aureus
Streptococci, including *Streptococcus pneumoniae*
Escherichia coli
Haemophilus influenzae
Klebsiella/*Enterobacter species*
Moraxella lacunata (Morax-Axenfeld bacillus)
Neisseria species

These products do not provide adequate coverage against:
Pseudomonas aeruginosa
Serratia marcescens

4.2 Posology and Method of Administration

Posology
Each aplicap contains sufficient medication for single application to both eyes. To use the aplicap wipe the tip with alcohol, cut the end with a clean instrument and compress the body to squeeze out the contents (ointment). A small amount of ointment is to be placed in the lower conjunctival sac of the affected eye(s) every 3 hours, or more frequently if deemed necessary by the prescribing physician.

Administration should be continued day and night for the first 48 hours, after which the interval between applications may be increased. Treatment should be continued for at least 48 hours after the eye appears normal. However, the length of treatment should not exceed 7 days.

Systemic absorption is decreased when the nasolacrimal duct is blocked (nasolacrimal occlusion) or the eyes are kept closed for two minutes. This may lead to fewer systemic adverse reactions and an increased local effect.

For external use only.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

4.4 Special Warnings and Special Precautions for Use

Hematologic Effects

Bone marrow hypoplasia, including aplastic anemia and death, has been reported following local application of chloramphenicol. Chloramphenicol should be used with caution in patients with a known history of a bleeding disorder or a family history of bleeding disorders. Chloramphenicol should not be used when less potentially dangerous agents would be expected to provide effective treatment.

Ocular Effects

Just like other eye ointments, Chloromycetin eye ointment may delay the healing process for corneal lesions.

General

The use of chloramphenicol, as with other antibiotics, may result in an overgrowth of non-susceptible organisms, including fungi. If infections caused by non-susceptible organisms appear during therapy, its use should be discontinued and appropriate measures should be taken. In the case of a severe infection, topical treatment with chloramphenicol should be supplemented with appropriate systemic treatment or another topical agent.

4.5 Interactions with Other Medicaments and Other Forms of Interaction

Systemically absorbed forms of chloramphenicol have been known to interact with certain drugs.

As low systemic absorption is achieved after application in the eye the risk for interactions should be low.

4.6 Fertility, Pregnancy and Lactation

The safety, when used during pregnancy and lactation, is not demonstrated as modern clinical documentation is lacking. Chloramphenicol crosses the placental barrier and is distributed into breast milk. As the extent of systemic exposure after topical application is not completely investigated eye ointment including chloramphenicol should be used during pregnancy only when treatment is absolutely necessary. Breast-feeding should be stopped during treatment with Chloromycetin eye ointment.

4.7 Effects on Ability to Drive and Use Machines

The effect of chloramphenicol on the ability to drive or use machinery has not been systematically evaluated. There is no evidence to suggest that this drug may affect these abilities.

4.8 Undesirable Effects

Undesirable effects are listed below in accordance with MedDRA terminology and presented in each frequency interval according to the clinical significance.

System organ class	Very common (≥1/10)	Common (≥1/100, <1/10)	Uncommon (≥1/1,000, <1/100)	Rare (≥1/10,000, <1/1,000)	Not known (cannot be estimated from the available data)
Blood and lymphatic system disorders				Agranulocytosis	Bleeding disorders
Immune system disorders			Hypersensitivity		Anaphylactic reactions, reaction to drug excipients
Nervous system disorders			Burning sensation	Peripheral neuropathy	
Eye disorders		Ocular swelling, ocular hyperaemia	Superinfections	Optic neuritis	
Skin and subcutaneous tissue disorders					Angioedema, urticaria, rash vesicular, rash maculopapular, pruritus
General disorders and administration site conditions			Allergic reactions		Pyrexia

Serious hypersensitivity reactions have been reported in patients who are sensitive to chloramphenicol and are causes for discontinuing the medication.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions.

4.9 Overdose

Accidental ingestion of chloramphenicol ophthalmic ointment is unlikely to cause systemic toxicity due to the low content of antibiotic. However, it should be kept out of the reach of children.

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 ophthalmologic examination should be considered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Ophthalmologicals, antibiotics
ATC code: S01AA01

Chloramphenicol is an aromatic nitro-compound manufactured synthetically. It has a bacteriostatic effect and is acting by inhibiting the protein synthesis in the bacteria. Chloramphenicol is active against most gram-positive and negative aerobic and anaerobic bacteria.

Antibacterial spectrum:
Susceptible: Pneumococci, Meningococci, *Haemophilus influenzae, E coli, Staphylococcus aureus* and coagulase negative staphylcocci
Resistant: *Acinetobacter, Psedomonas, Stenotrophomonas maltophilia*

Resistance occurs (1%-10%) in pneumococci, *Haemophilus influenzae* and gram-negative intestinal bacteria.

The resistance is often plasmid mediated.

The resistance situation varies geographically and information about the local resistance situation should therefore be requested from a local microbiological laboratory.

Chloramphenicol is a small molecule with good lipid solubility. This contributes to a good ability to penetrate ophthalmic tissue.

5.2 Pharmacokinetic Properties

Chloramphenicol is found in measurable amounts in the aqueous humor following local application to the eye.

Chloramphenicol is rapidly absorbed from the gastrointestinal tract when given by mouth and widely distributed throughout most body tissues and fluids. It is inactivated primarily in the liver by glucuronyl transferase and excreted mainly in the urine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

White soft paraffin, Paraffin liquid.

6.2 Incompatibilities*

Incompatibility or loss of activity has been reported between chloramphenicol and many other substances. Other factors, especially drug concentration, may play a part and incompatibilities are often seen mainly with concentrated solutions.

6.3 Shelf-life

24 Months.

6.4 Special Precautions for Storage

Keep bottle securely closed in a cool place.

6.5 Nature and Contents of Container

50 Aplicaps in amber coloured glass bottles sealed with ROPP caps.

6.6 Instructions for Handling

No special instructions applicable.