

Attachment 2

AUSTRALIAN PRODUCT INFORMATION – OCUZO (CHLORAMPHENICOL)

1. NAME OF THE MEDICINE

Chloramphenicol

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

OCUZO eye drops contain chloramphenicol 5 mg per 1 mL of water with boric acid and borax.

For the full list of excipients, see [Section 6.1 List of excipients](#).

3. PHARMACEUTICAL FORM

Chloramphenicol is a white to greyish-white or yellowish-white, fine crystalline powder or fine crystals, needles or elongated plates. Soluble 1 in 400 of water, 1 in 2.5 of alcohol, and 1 in 7 of propylene glycol; freely soluble in acetone and ethyl acetate; slightly soluble in ether. A 2.5% suspension in water has a pH of 4.5 to 7.5.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Indicated for ocular bacterial infections caused by organisms susceptible to chloramphenicol.

4.2 Dose and method of administration

Instil one or two drops in the affected eye(s) two to six-hourly for two to three days. The interval between applications may then be increased. Discard the solution within 4 weeks of opening the container.

Instructions to Patients

- If symptoms worsen at any time or if the eye infection does not improve within 48 hours, seek prompt medical advice.
- Do not use in children under 2 years of age except on medical advice.
- Patients who wear contact lenses should be advised to seek medical advice from their doctor or optometrist before using Chloromycetin. Contact lenses should not be worn during the course of Chloromycetin treatment. If wearing hard or disposable contact lenses, patients can start using their contact lenses again after successfully completing the course of treatment. If wearing soft contact lenses, patients should wait 24 hours after successfully completing the course of treatment before starting to use their lenses again.

- Treatment should be continued for at least 2 days after the eye appears normal but do not use for longer than 5 days except on medical advice.

4.3 Contraindications

OCUZO eye drops are contraindicated in individuals with a history of hypersensitivity and/or toxic reaction to chloramphenicol or any other component of the medication.

4.4 Special warnings and precautions for use

Discontinue promptly if sensitisation or irritation occurs.

Bone marrow hypoplasia, including aplastic anaemia and death, has been rarely reported following local application of chloramphenicol. Chloramphenicol should not be used when less potentially dangerous agents would be expected to provide effective treatment. Ophthalmic agents may retard corneal wound healing.

The use of this antibiotic, 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 all serious infections, the topical use of chloramphenicol should be supplemented by appropriate systemic medication.

Chloramphenicol eye preparations should not be recommended for OTC use under the following circumstances:

- Photophobia
- Severe pain in the eye or pain and swelling around the eye
- Loss of, reduced or blurred vision
- Restriction of eye movement
- Cloudy cornea
- Copious yellow-green purulent discharge that accumulates after being wiped away
- Abnormal pupils
- Injury to the eye or suspicion of a foreign body in the eye
- History of welding without eye protection immediately prior to onset of symptoms
- Glaucoma
- Dry eye syndrome
- Individuals who wear contact lenses except on medical advice
- Patient is using other eye preparations at the time of presentation
- Patient has had eye surgery or laser treatment in the past six months
- Individual or family history of bone marrow problems
- Recent overseas travel
- Patient has had similar symptoms in the past
- Patient feels unwell

- Children under the age of 2 years except on medical advice
- Use for longer than 5 days unless on medical advice.

In these cases, referral to a doctor or optometrist is required.

Use in the elderly

No data available.

Paediatric Use

Do not use in children under 2 years of age except on medical advice.

Effects on laboratory tests

No data available.

4.5 Interactions with other medicines and other forms of interactions

No data available.

4.6 Fertility, pregnancy and lactation

Effects on fertility

Excipients containing boron such as boric acid or borate compounds have been shown to cause reduced fertility and effects on embryofetal development in animal studies and this appears to be dose related. The relevance of this to humans is uncertain.

Use in pregnancy and lactation

Category A

There are no studies to establish the safety of this drug in pregnancy.

Systemically absorbed/administered forms of chloramphenicol enter the foetal circulation and are distributed into breast milk. If given systemically to the mother shortly before parturition or whilst breastfeeding, chloramphenicol may cause bone marrow suppression of the neonate or the "grey baby syndrome", characterised by cyanosis and hypothermia, owing to the limited glucuronidating capacity of the neonate's liver. However, limited absorption following ophthalmic use at the recommended dosage is generally not expected to pose a risk to the foetus or neonate.

4.7 Effects on ability to drive and use machines

The effect of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 Adverse effects

Chloramphenicol is absorbed systemically from the eye, and toxicity has been reported following chronic exposure. Dose-related toxicity following a single ocular exposure is unlikely. The following clinical adverse experiences have been observed with the use of chloramphenicol. More serious side effects (indicated by *) have been reported in patients sensitive to chloramphenicol and are causes for discontinuing the medication.

Blood and Lymphatic System Disorders: blood dyscrasias have been reported in association with the use of chloramphenicol.

Immune System Disorders: Anaphylactic reaction*, hypersensitivity, reaction to drug excipient.

Skin and Subcutaneous Tissue Disorders: Angioedema*, urticaria*, rash vesicular and rash maculopapular*, pruritus.

General Disorders and Administration Site Conditions: local irritation may include subjective symptoms of itching or burning, fever*, similar sensitivity reactions to other materials in topical preparations also may occur, pyrexia*.

Interactions with other drugs: Systemically absorbed/administered forms of chloramphenicol have been known to interact with certain drugs.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at <http://www.tga.gov.au/reporting-problems>>

4.9 Overdose

Accidental ingestion of the drug is unlikely to cause any toxicity due to the low content of antibiotic. Each mL of OCUZO eye drops contains 19 mg of borax/boric acid as buffer. It is advisable to keep medication out of reach of children. If accidentally ingested by infants or young children, a local Poisons Information Centre should be contacted. As there is individual variability in the pharmacokinetics of chloramphenicol in infants and children monitor plasma levels. Levels exceeding 25 microgram/mL are frequently considered toxic. 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.

For more information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

Chloramphenicol is a broad-spectrum antibiotic originally isolated from *Streptomyces venezuelae*. It is primarily bacteriostatic and acts by inhibition of protein synthesis by interfering with the transfer of activated amino acids from soluble RNA to ribosomes.

Clinical trials

No data available.

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.

5.3 Preclinical safety data

Genotoxicity

No data available.

Carcinogenicity

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Boric acid

Borax

Sodium hydroxide (may be added to adjust pH) and/or

Hydrochloric acid (may be added to adjust pH)

Water for injections.

6.2 Incompatibilities

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

Once opened, the bottle should be discarded after 4 weeks.

6.4 Special precautions for storage

Unopened bottle: Store at 2 °C to 8 °C (Refrigerate. Do not freeze).

Opened bottle: Store at or below 25 °C.

Protect from light.

6.5 Nature and contents of container

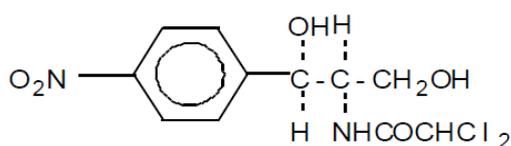
The container closure system for OCUZO eye drops comprises a novel preservative free multidose eye drop device (Novelia® - 11 mL LDPE white bottle with a Nozzle/cap sub assembly) containing the formulation as a bulk sterile solution with a mechanism to dispense individual drops from the bulk.

6.6 Special precautions for disposal

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 Physicochemical properties

Chemical structure



Chemical name:

2,2-Dichloro-N-[(αR,βR)-β-hydroxy-α-hydroxymethyl-4-nitrophenethyl] acetamide

Molecular formula: C₁₁H₁₂Cl₂N₂O₅

Molecular weight: 323.1

CAS number

56-75-7

7. MEDICINE SCHEDULE

Schedule 3 (Pharmacist Only Medicine)

8. SPONSOR

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9. DATE OF FIRST APPROVAL

24 July 2020

10. DATE OF REVISION

30 June 2022

Summary table of changes

| Section changed | Summary of new information |
|-----------------|---|
| 4.6 | Include boron-containing excipients and fertility concerns. |
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