SUMMARY OF PRODUCT CHARACTERISTICS

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1. NAME OF THE MEDICINAL PRODUCT

Clorocil 8 mg/ml eye drops, solution
Clorocil 10 mg/g eye ointment

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Clorocil 8 mg/ml eye drops, solution (0.8%)
Chloramphenicol 8 mg/ml
Excipient(s):
Benzalkonium chloride (solution at 50%) - 0.2 mg/ml
Boric acid (and borates) – 7.7 mg/ml (and borax 1 mg/ml)

For the full list of excipients, see section 6.1.

Clorocil 10 mg/g eye ointment (1%)
Chloramphenicol 10 mg/g
Excipient(s):
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution.
Colourless, clear and odourless solution.

Eye ointment.
Yellow ointment, odourless or almost odourless, with soft consistency.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Clorocil is indicated in conjunctivitis, blepharitis, dacryocystitis, corneal ulcers, trachoma and keratitis.

4.2 Posology and method of administration

According to medical indication. In a general way the eye drops, solution should be administered one or two drops every 2 hours and the eye ointment up to 6 times a day. The ointment is usually applied in the evening and the eye drops during the day.
Considering the mainly bacteriostatic antibiotic's activity, the treatment should be extended until 48 hours after healing.
Apply the eye drops, solution or the eye ointment in the conjunctival sac (the space between the eye and the lower eyelid).

4.3 Contraindications

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

In patients with medical history of bone marrow impairment.
In newborns.

4.4 Special warnings and precautions for use

Clorocil must not be used in a prolonged way or in repeated and frequent treatments because, in those conditions, it may cause bone marrow aplasia.

The administration of chloramphenicol may cause blood dyscrasias (aplastic anemia, hypoplastic anemia, thrombocytopenia and granulocytopenia). Chloramphenicol should not be used in mild situations and should only be used if there is no alternative treatment that is less risky.

The newborns have a reduced capacity for glucuronidation in the process of degradation and detoxification of chloramphenicol. Consequently, high systemic concentrations of chloramphenicol may originate the "grey baby syndrome" that can lead to the newborn's death. Due to the risk of development of this syndrome, the administration of chloramphenicol in children should not be systemical and the dosages should be suitable to the age and state of maturity of the metabolic processes.
Due to the low amount of chloramphenicol administered and to the low systemic absorption, it is unlikely that Clorocil is associated with the development of "gray baby syndrome".

Like any other antibiotics the development of superinfections should be monitored.

Clorocil, eye drops, solution contains 0.1 mg benzalkonium chloride in each ml of solution.
Benzalkonium chloride may be absorbed by soft contact lenses and may change the colour of the contact lenses. Remove contact lenses before using this medicine and put them back 15 minutes afterwards. Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface. Should be used with caution in dry eye patients and in patients where the cornea may be compromised.
Patients should be monitored in case of prolonged use.

Clorocil eye drops, solution contains boric acid (and borates)
Do not give to a child less than 2 years old as this medicine contains boron and may impair fertility in the future.

4.5 Interaction with other medicinal products and other forms of interaction

Several interactions with other antibiotics have been described, for example, with tetracyclines, with the occurrence of antagonistic effects. The concomitant therapy with other medical products causing bone narrow depression must be avoided.

4.6 Fertility, pregnancy and lactation

Clorocil must not be applied during pregnancy and lactation.

4.7 Effects on ability to drive and use machines

In case of vision disturbances after the administration of the eye drops or the eye ointment, patients should not drive or use machinery.

4.8 Undesirable effects

The prolonged use of Clorocil is a risk factor for the development of myelodysplasia, although this risk is maximized when the administration is systemic.

Certain patients may suffer from sensitivity reactions, such as irritation, burning, urticaria, maculopapular and vesicular dermatitis and angioneurotic edema. In such cases, it is advisable to stop the treatment.

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
Not applicable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: 15.1.1 – Medicinal products used in ocular afections. Topical anti-infectives. Antibacterials.

ATC code: S01AA01

Chloramphenicol is used topically in the treatment of ocular infections by its broad spectrum of action and the capacity of penetration in the ocular tissue and aqueous humour.
Chloramphenicol is a bacteriostatic antibiotic with a broad spectrum of action and marked activity against both aerobic and Gram-positive and Gram-negative anaerobic bacteria as well as against rickettsia but not chlamydia. The majority of Gram-positive bacteria are inhibited in concentrations of 1-10 µg/ml and many Gram-negative bacteria are inhibited in concentrations of 0.2-5 µg/ml. *Haemophillus influenzae*, *Neisseria meningitidis* and some bacterial strains are highly sensitive to chloramphenicol, having a bactericidal action against these microorganisms.
Chloramphenicol acts as a powerful inhibitor of the synthesis of bacterial proteins by binding reversibly to the 50S subunit of the bacterial ribosome and inhibiting the peptide bond formation by peptidyl transferase of the protein synthesis.
In some populations sensitive to chloramphenicol may appear the resistance in low levels through the selection of mutants with low permeability. The clinical significant resistances are associated to production of a chloramphenicol acetyltransferase, a plasmid-mediated enzyme that inactivates the drug.

5.2 Pharmacokinetic properties

The usual dose is of 50-100 mg/kd/d. After oral administration, the absorption of crystalline chloramphenicol is fast and total. One dose of 1 g given by oral administration produces serum levels of 10 to 15 µg/ml.
After absorption, chloramphenicol is widely distributed by practically all body tissues and fluids, it enters the central nervous system and the cerebrospinal fluid and may reach concentrations in the cerebral tissue equivalents to the serum concentrations. The molecule penetrates easily the cell membranes.
A large percentage of chloramphenicol is inactivated, by conjugation with glucuronic acid (mainly in the liver) or by the reduction to inactivated aryl amines.
The excretion of active chloramphenicol (about 10% of the administered total dose) and the inactivated products of degradation (about 90% of the total) occurs by renal pathway.
A small quantity of active chloramphenicol is excreted in the bile or in the faeces.
The systemic posology of chloramphenicol does not need to be adjusted in cases of renal impairment but must be considerably decreased in patients with hepatic impairment.

Premature newborns or newborns with less than one week of life possess an immature metabolism of degradation and detoxification of chloramphenicol, by this the dosage must be reduced to 25 mg/kg/d.

5.3 Preclinical safety data

There are not additional preclinical data relevant for the doctor.

6. PHARMACEUTICAL PROPERTIES

6.1 List of excipients

Clorocil 8 mg/ml eye drops, solution
Boric acid
Borax
Sodium chloride
Benzalkonium chloride (50% solution)
Dimethyl-β-cyclodextrin
Highly purified water
Hydrochloric acid and/or sodium hydroxide (for pH adjustment)

Clorocil 10 mg/g eye ointment
Wool fat
White soft paraffin

6.2 Incompatibilities

Not applicable.

6.3. Shelf life

Clorocil 8 mg/ml eye drops, solution
Closed container: 36 months.
After first opening the bottle: 28 days.

Clorocil 10 mg/g eye ointment
Closed container: 36 months.
After first opening the tube: 28 days.

6.4. Special precautions for storage

Clorocil 8 mg/ml eye drops, solution: Store in a refrigerator (2°C – 8°C) until first opening the bottle.

Clorocil 10 mg/g eye ointment: Do not store above 30°C.

6.5 Nature and contents of container

Clorocil 8 mg/ml eye drops, solution
Clorocil eye drops, solution is supplied in a sterile 10 ml opaque LDPE bottles with dropper insert and HDPE caps, filled with 5 ml of Clorocil eye drops, solution, previously sterilized with gamma radiation. After filled, the bottles are packed in printed cartoons with a package leaflet inside.

Clorocil 10 mg/g eye ointment
Clorocil eye ointment is supplied in 5 g lacquered aluminium tubes with High Density Polyethylene screw cap.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

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10. DATE OF REVISION OF THE TEXT

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