ALLERGAN

CHLOROPTIC®

(chloramphenicol ophthalmic solution, USP) 0.5%

sterile

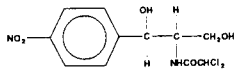
WARNING

Bone marrow hypoplasia including aplastic anemia and death has been reported following topical application of chloramphenicol. Chloramphenicol should not be used when less potentially dangerous agents would be expected to provide effective treatment.

DESCRIPTION

CHLOROPTIC® (chloramphenicol ophthalmic solution, USP) is a topical anti-infective product for ophthalmic use.

CHEMICAL NAME:
D-threo-(-)-2,2-Dichloro-N-[β-hydroxy-α-(hydroxymethyl)-p-nitrophenethyl] acetamide



chlorampenicol
$C_{11}H_{12}Cl_2N_2O_5$
Molecular weight: 323.14

CONTAINS:
Active: chloramphenicol 0.5% (5mg/mL)
Preservative: chlorobutanol(chloral deriv.)..... 0.5% (5 mg/mL)
Inactives: polyethylene glycol 300; polyoxyl 40 stearate; sodium hydroxide or hydrochloric acid to adjust pH; and purified water.

CLINICAL PHARMACOLOGY

Microbiology: 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.

Chloramphenicol has been shown to be active against the following organisms:

Aerobic gram-positive microorganisms: *Staphylococcus aureus*, streptococci, including *Streptococcus pneumoniae*

Aerobic gram-negative microorganisms: *Enterobacter sp., Escherichia coli, Haemophilus influenzae, Klebsiella sp., Moraxella lacunata* (Morax-Axenfeld bacillus), *Neisseria sp.*

This product does not provide adequate coverage against *Pseudomonas aeruginosa or Serratia marcescens.*

Bacteriological studies should be performed to determine the causative organisms and their susceptibilities to chloramphenicol.

INDICATIONS AND USAGE

Chloramphenicol should be used only in those serious infections for which less potentially dangerous drugs are ineffective or contraindicated. (See Boxed Warning)

Chloroptic is indicated for the treatment of surface ocular infections involving the conjunctiva and/or cornea caused by chloramphenicol-susceptible organisms. Chloramphenicol is active against the following common bacterial eye pathogens: *Staphylococcus aureus*; streptococci, including *Streptococcus pneumoniae, Escherichia coli; Haemophilus influenzea; Klebsiella/Enterobacter* species; *Moraxella lacunata* (Morax-Axenfeld bacillus); and *Neisseria species.* Chloramphenicol does not provide adequate coverage against: *Pseudomonas aeruginosa* or *Serratia marcescens.*

CONTRAINDICATIONS

This product is contraindicated in persons sensitive to any of its components.

WARNINGS

SEE BOXED WARNING

Occasionally one sees hematopoietic toxicity with the use of systemic chloramphenicol, and rarely with topical administration. This type of blood dyscrasia is generally a dose-related toxic effect on bone marrow and is usually reversible on cessation of the drug. Rare cases of aplastic anemia have been reported with prolonged (months to years) or frequent intermittent (over months and years) use of topical chloramphenicol.

PRECAUTIONS

General: The prolonged use of antibiotics may occasionally result in overgrowth of nonsusceptible organisms, including fungi. If new infections appear during medication or clinical improvement is not observed within 1 week, the drug should be discontinued and appropriate measures should be taken.

Information for Patients: Do not touch bottle tip to any surface as this may contaminate the solution.

Carcinogenesis, Mutagenesis and Impairment of Fertility: No long-term studies have been conducted in animals or in humans to evaluate the carcinogenic potential or effects on fertility with chloramphenicol. However, there is some clinical evidence that aplastic anemia due to chloramphenicol may be associated with subsequent development of leukemia.

Pregnancy: Pregnancy Category C. Chloramphenicol has been shown to be embryocidal and teratogenic in rat, mouse, rabbit and chicken embryos/fetuses (see below). There are no adequate and well-controlled studies in pregnant women. Chloramphenicol has been shown to cross the placental barrier, but it is not known whether chloramphenicol can cause fetal harm when administered to a pregnant woman. Chloramphenicol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Embryotoxic effects: Significantly lower numbers of live fetuses and an increase in the number of early embryonic resorptions occurred after pregnant **rats** were treated orally with 500 mg/kg (equivalent to 5800 times the recommended maximum daily adult topical ophthalmic dose) from days 5 to 15 of their pregnancy. Similar findings were seen with groups receiving higher oral doses (1000 mg/kg or 2000 mg/kg) at various dosing intervals. Female **mice** receiving 1000 mg/kg orally from days 6 to 12 of their pregnancy showed a significant increase in the number of resorptions. Female **rabbits** receiving the same oral dosing (1000 mg/kg) from days 8 to 11 had an increase in the number of resorptions of embryos without placentation. Chloramphenicol (2.5 mg) injected into **chicken eggs** resulted in a 20% embryo mortality rate one day after administration, which increased to 100% embryo mortality on the 11th day of incubation.

Teratogenicity: When given to female **rats** orally at 2000 mg/kg from days 6 to 8 of pregnancy, 36% of the fetuses exhibited either an omphalocele or an umbilical hernia, with costal fusions. Fetuses of the **rats** treated with 1000 mg/kg orally from days 7 to 12 of pregnancy or 2000 mg/kg from days 11 to 13, and of **mice** treated with 1000 mg/kg from days 6 to 12, had a higher incidence of missing ossification of the phalangeal nuclei of the forelegs and hindlegs and of the 5th sternebra. This correlated with a decrease in the average weight of the fetuses. **Rabbit** fetuses displayed more frequent absence of the phalangeal nuclei of the forelegs than control when pregnant rabbits received 500 mg/kg orally on days 6 to 15 of pregnancy. More frequent missing ossification of the phalangeal nuclei of the forelegs and hindlegs and an increase in the number of unevenly ossified vertebrae was seen in the fetuses of rabbits when pregnant females were given 1000 mg/kg from days 6 to 9 of pregnancy.

Teratogenic effects of chloramphenicol (0.5 mg) when injected into **chicken eggs**, included malformations of the beak, eyes and legs.

Nursing Mothers: Chloramphenicol appears in human milk following oral administration of the drug. Systemic absorption of chloramphenicol may occur when applied topically. Because of the potential for serious, adverse reactions in nursing infants from chloramphenicol, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: The safety and efficacy in pediatric patients below 1 year of age have not been established.

Geriatric Use: No overall difference in safety or effectiveness have been observed between elderly and younger, adult patients.

ADVERSE REACTIONS

Exact incidence figures are not available since no denominator of treated patients is available.

The most serious reaction following prolonged or frequent intermittent use of topical chloramphenicol is bone marrow aplasia.

The most frequently reported adverse reactions have been burning, stinging, ocular irritation, and conjunctival hyperemia. Blood dyscrasia, allergic or inflammatory reactions due to individual hypersensitivity, angioneurotic edema, urticaria, vesicular and maculopapular dermatitis have also been reported. (See Warnings and Box Warning).

DOSAGE AND ADMINISTRATION

One or two drops 4 to 6 times a day for the first 72 hours should be placed in the lower conjunctival sac. Treatment should be continued for approximately 7 days but should not be continued for more than three weeks without re-evaluation by the prescribing physician.

HOW SUPPLIED

CHLOROPTIC®: (chloramphenicol ophthalmic solution, USP) is supplied in the following sizes:
2.5 mL -NDC-11980-109-03
7.5 mL -NDC-11980-109-08

Note: Refrigerate until dispensed. Then store below 30°C (86°F). Discard solution within 21 days from date dispensed.
Rx Only

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/s/

Linda Ng

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