METAPHARMACEUTICAL IND SL
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TECHNICAL DATA SHEET

412-TDS-ENG-2023

CLORANFENICOL (PH.EUR)		
DESCRIPTION DCI: CHLORAMPHENICOL	DESCRIPTION DOE: CLORANFENICOL	
CAS Nº: 56-75-7	EC Nº: 200-287-4	AEMPS CODE: 44A
MOL. WEIGHT: 323.10	MOL. FORMULA: C11H12Cl2N2O5	ARTICLE CODE: 412

ATTRIBUTES	SHOULD BE
Appearance	White, greyish-white or yellowish-white, fine, crystalline powder or fine crystals, needles or elongates plates
Solubility	Slightly soluble in water, freely soluble in alcohol and in propylene glycol
Identification A	Complies
Acidity or alcalinity	=< 0.1 mL of 0.02 M HCl or NaOH
Specific optical rotation	+18.5 / +20.0
Related substances	
Impurity A	=< 0.2 %
Unspecified impurities	=< 0.10 %
Total impurities	=< 0.5 %
Chlorides	=< 100 ppm
Loss on drying	=< 0.5 %
Sulfated ash	=< 0.1 %
Assay	97.5 - 102.0 %

COMPLIES WITH

European Pharmacopoeia 11.0

STORAGE

Keep the container tightly closed, in a cool and dry place. Protect from light.

REMARKS

CHLORAMPHENICOL is subjected to the requirements of the ICH Q3D "Elemental Impurities" guideline and the requirements of guides EMA/CHMP/ICH/82260/2006.

Absence of N-nitrosamines impurities has been ensured after a risk evaluation according to ICH Q9, ICH M7 and in accordance with guidelines EMA/428592/2019 Rev 2 and EMA/189634/2019.

Certificates of residual solvents, allergens, non-GMO and BSE-TSE, among others, are available upon request.

All methods of analysis are validated by official pharmacopoeias or are validated by internal methods of the manufacturer, which can be obtained at specific request. The above information does not exempt from the obligation to identify the product before use.

Properties and uses
It is easily absorbed orally, reaching a blood concentration of 10 µg / ml or more approximately in 1 or 2 hours after a single dose of 1 g orally. Likewise, plasma concentrations of almost 18.5 µg / mL have been described after multiple doses of 1 g. CHLORAMPHENICOL is widely distributed in body tissues and fluids; enters the CSF, where concentrations of approximately 50% of those existing in blood are reached, even in the absence of inflamed meninges; it crosses the placental barrier and passes into the fetal circulation, breast milk and the aqueous and vitreous humors of the eye. Approximately 60% of the circulating drug binds to plasma proteins. The half-life of CHLORAMPHENICOL ranges between 1.5 and 4 hours. The half-life is prolonged in the case of patients with severe liver disease and in newborns. CHLORAMPHENICOL is excreted mostly in the urine, but only 5 to 10% of an oral dose appears unchanged; the rest is

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inactivated in the liver, mostly by conjugation with glucuronic acid. About 3% is excreted by the bile, and 1% through the faeces.
It acts by interference of bacterial protein synthesis. It has an especially marked action on aerobic and anaerobic Gram-negative bacteria and on aerobic Gram +, particularly Salmonella thyphi, Haemophilus influenzae, and Bordatella pertussis. It is also active against spirochetes, rickettsiae, chlamydiae and mycoplasmas.
The possibility of the appearance of serious adverse reactions due to CHLORAMPHENICOL, such as medullar aplasia, has limited its clinical uses, although it is still frequently used in many countries, and blood tests must be carried out regularly during treatment.
It is used in the treatment of very diverse pathologies, although normally nowadays it is a second choice antibiotic

Meningitis and epiglottitis due to Haemophlus influenzae.
Brain or subdiaphragmatic abscess due to Bacteroides fragilis.
Infections due to rickettsiae such as endemic typhus, spotted fever, etc ...
Other infections such as anthrax, severe gastroenteritis (including enteritis due to Salmonella or Yersinia), gas gangrene, severe systemic infections due to Campylobacter fetus, erlichiosis, inguinal granuloma, listerioris, severe melioidosis, plague, psittacosis, Q fever, tularemia, and Whipple's disease .

It is also used in cases of eye infections, applied locally in the form of eye drops and eye ointments, and topically in the form of ointments, ointments, or solutions. Rectally it is irritating and its absorption is irregular.

Dosage
Topical route in salves and ointments at 1% or in 0.5% solutions.
Ophthalmic route in 0.5% eye drops or in 1% ointments.
Oral route, in adults and children older than 2 weeks: usual dose of 50 mg / kg / day, administered every 6 h. They can be administered up to 100 mg / kg / day in case of meningitis or in serious infections caused by moderately resistant microorganisms, although they should be reduced as soon as possible. When there is no alternative to the use of CHLORAMPHENICOL, premature babies and newborns under 2 weeks, the dose is 25 mg / kg / day, divided into four doses.
In renal failure it is advisable to reduce the doses by half, when administered parenterally. Given that the plasma half-life of CLORAMPHENICOL increases considerably in patients with combined renal and hepatic impairment, the dose should be adjusted.

Side effects
It can lead to serious and even deadly effects such as leukopenia, agranulocytosis, aplastic anemia, thrombocytopenia, and medullary aplasia.
Occasionally there may be accidents of the nervous type, with delirium, mental confusion, hallucinations, etc.
In long-term therapies can occur neuritis with blindness but are not frequent
At the dermal level, accidents have been observed, especially in pregnant women, malnourished patients and people treated with corticosteroids and cytostatics. Allergic sensitization is very rare.

Precautions
It should be used with caution in pregnant women since CHLORAMPHENICOL crosses the placental barrier appearing in breast milk, which is potentially toxic to the fetus or infant.

Interactions
Its association with leucopemiant assets such as sulfonamides, gold salts, anti-inflammatories, pyrazolones, paracetamol, and barbiturates should be avoided.
CHLORAMPHENICOL can potentiate the action and / or toxicity of oral anticoagulants (acenocoumarol), antidiabetics (chlorpropamide, tolbutamide), antiepileptics such as phenytoin, and cyclosporine.
It can reduce the metabolism of tacrolimus and cyclophosphamide to its active form.
CLORAMPHENICOL and cimetidine mutually enhance the toxicity.

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The administration of CHLORAMPHENICOL together with phenobarbital or rifampicin inhibits the effect of the former and increases the toxicity of the latter.
Cross-resistance with lincomycin, cyclophosphamide, and penicillins may appear, thus decreasing their action. Paracetamol increases the action and / or toxicity of CHLORANPHENICOL.
CHLORAMPHENICOL can decrease the effect of iron and vitamin B12, and interfere with the action of oral contraceptives.
Incompatibilities
Ascorbic acid, carbenicillin, erythromycin, hydroxyzine, methicillin, metoclopramide, phenothiazine derivatives (such as chlorpromazine, prochlorperazine, and promethazine), phenytoin sodium, polymyxin B, several tetracyclines, vancomycin, and vitamin B complex.

Formulation examples

Topical lotion for dermatological infections
CHLORAMPHENICOL - **2 g**
Calamine lotion - **200 g**
Bio-sulfur - **4 g**
Trans-retinoic acid - **0.05 g**
Camphor - **1 g**
Triamcinolone acetonide -**0.2 g**
Resorcin - **5 g**

Modus operandi
Dissolve all components of the formula except the calamine lotion in a little alcohol. Add this mixture to the calamine lotion along with 0.05% Vitamin E acetate and shake.

CLORAMPHENICOL and mucolytic capsules
CHLORAMPHENICOL - **300 mg**
Carbocysteine - **200 mg**
for 1 capsule No. 50

CHLORAMPHENICOL - **300 mg**
Dextromethorphan - **30 mg**
for 1 capsule No. 50

Modus operandi: See the volume occupied by the powders and compare with the table of volumes to know the number of capsules to be used.