מאי 2025

רוקח/ת נכבד/ה,רופא/ה נכבד/ה,

חברת פרופארם בע"מ מודיעה על העדכונים הבאים בעלון לרופא של התכשיר:

CHLORAMPHENICOL FISIOPHARMA 1G

כלורמפניקול פיזיופארמה 1 גרם

חומר פעיל: CHLORAMPHENICOL 1 GRAM

צורת מינון: POWDER FOR SOLUTION FOR INJECTION

צורת המתן:I. V

עדכונים בעלון לרופא

התויה כפי שאושרה בתעודת הרישום:

Chloramphenicol is active against several bacteria in the following infections:
- Typhoid fever and salmonellosis (Salmonella typhi);
- Bacterial meningitis (Haemophilus influenzae, Neisseria meningitidis);
- Rickettiosis (Rickettsia);
- Brucellosis (Brucella);
- Psittacosis (Chlamydophila psittaci);
- Lymphogranuloma Venereum (Lymphogranuloma-psittacosis);
- Urinary infection caused by gram-negative bacteria;
- Infections caused by anaerobic bacteria (Cocci gram-positive cocci, Clostridium).

and is indicated when oral administration is contraindicated or not feasible due to vomiting, diarrhea or severe sepsis.

ברצוננו להודיע שהעלון עודכן, בפירוט שלהלן כלולים העדכונים העיקריים בלבד(תוספות /שינויים מסומנים באדום והחמרות/מידע חדש על רקע צהוב):

3. PHARMACUTICLA FORM

Powder for solution for injection for intravenous use.
White or yellowish-white powder.

4. CLINICAL PARTICULARS

[…]

4.2 Posology and method of administration

~~Chloramphenicol Fisiopharma is for~~ The product should be administered via the intravenous ~~use~~. ~~The following~~ route.

Recommended dosages~~dosages are recommended~~:

Adults and adolescents

The recommended dose for the treatment of most infections is 50-100 mg/kg/day divided into 4 daily administrations~~doses~~ (1 administration~~dose~~ every 6 hours).

Infants up to 2 weeks

The recommended dose for the treatment of most infections is 25 mg/kg/day divided into 4 daily administrations~~doses~~ (1 administration~~dose~~ every 6 hours).

For infants under~~up~~ to 1 week or weighing less than 2 kg the recommended dose is 25 mg/kg/day every 24 hours (1 administration~~once~~ daily).

For infants over 1 week and weighing more than 2 kg, the recommended dose is 25 mg/kg/day divided into 2 daily administrations~~doses~~ (1 administration~~dose~~ every 12 hours).

Infants over 2 weeks and children (up to 12 years)
The recommended dose for the treatment of most infections is 50 mg/kg/day divided into 4 daily administrations~~doses~~ (1 administration~~dose~~ every 6 hours).
Impaired renal function
Although chloramphenicol does not accumulate significantly ~~accumulate~~ even in the presence of reduced~~impaired~~ renal function, ~~the affected~~ patients with this condition may find more difficult ~~have reduced ability~~to eliminate the drug and may need~~require~~ a dosage adjustment. To determine ~~Concentration of the drug in the blood should be frequently monitored to establish~~if a~~the~~ dosage adjustment is necessary, blood levels of the drug should be monitored frequently.
Impaired hepatic function
Patients with ~~impairment of hepatic~~a reduced liver function may have a reduced ability to eliminate the drug and, therefore, ~~the~~ dosage adjustment may be necessary~~required~~. To determine if a dosage adjustment is necessary, blood levels ~~Concentration~~ of the drug i~~n the blood~~ should be monitored ~~to establish if the dosage adjustment is necessary~~.
~~In~~ For patients with ~~impaired~~ hepatic impairment it is recommended to use~~function~~, a loading dose of 1 g followed by 500 mg every 6 hours ~~is recommended. Dosage of 500 mg every 6 hours is recommended in~~ For patients with liver cirrhosis the recommended dose is 500 mg every 6 hours.
~~In~~ For patients suffering from ~~with~~ jaundice, the dos~~age~~ of 25 mg/kg/day should~~must~~ not be exceeded.
Dialysis patients ~~on dialysis~~
The amount of drug removed from ~~by~~ haemodialysis ~~cannot~~ is not such as to justify a dosage adjustment in all the cases.
There is no need to change the ~~The~~ dosage ~~should not be adjusted~~ in patients undergoing continuous ambulatory peritoneal dialysis (CAPD) or continuous arterio-venous hemofiltration (CAVH).
The injectable solution ~~for injection should~~ must be prepared extemporaneously by dissolving the powder in water for injectable preparations, saline solution or 5% glucose solution, at the desired concentrations.

4.3 Contraindications

- Hypersensitivity to the active substanceor to any of the excipients;
- Bone marrow depression;
- Breastfeeding ~~(see the section 4.6).~~

Chloramphenicol ~~must~~ should not be administered for ~~used in~~the treatment of minor~~trivial~~ infections or for prophylaxis.
Chloramphenicol may interfere with ~~the~~ immunity mechanisms and should~~must~~ not be administered during the ~~phase of~~ active immunisation phase (see section 4.5).

4.4 Special warnings and precautions for use

Limit the administration of ~~Treatment with~~the antibiotic strictly to~~should not be continued longer than~~ the period indicated by the specific recommendations for each infection, possibly no later~~longer~~ than 2 weeks. ~~Close monitoring of the blood levels during~~ During the treatment ~~is recommended. Administration of~~ with chloramphenicol it is necessary to carefully monitor the haematological parameters.
In fact, the administration of chloramphenicol, in high ~~dosages~~ doses and for prolonged and repeated ~~courses may cause~~ therapies, can incdlucde the onset of aplastic anaemia, ~~that may be detected~~ detectable even weeks or months after ~~the treatment~~ discontinuation of treatment.
~~Chloramphenicol must be~~ In patients with impaired blood flow, chloramphenicol should be used with great caution ~~in patients with blood dyscrasias~~. In prolonged or repeated ~~treatment, the~~ therapies, blood pressure must be ~~frequently~~ monitored frequently, stopping ~~and the~~ treatment ~~should be interrupted~~ immediately if ~~the~~ leukocytes ~~drop~~ decrease below 4000 per mm3 and ~~the~~ granulocytes ~~decrease by~~ of

0% (unless ~~it is an inherent leukopenic infection~~ they are leukopenising infections in themselves such as ~~fever~~ typhoid fever); late complications may occur~~are possible~~.
The use of chloramphenicol may also ~~lead to~~result in a decrease in prothrombin time~~due to the~~ for inhibition of the intestinal bacterial flora that produces ~~producing~~vitamin K.
In patients suffering from~~with~~ hepatic or renal failure~~insufficiency~~, dose adjustment may be necessary (see section 4.2 Posology and method of administration).
Treatment with chloramphenicol, as with other antibiotics, may result in superinfections ~~due to~~with insensitive bacterial agents or fungi.

4.5 Interaction with other medicinal products and other forms of interaction

Chloramphenicol is an inhibitor of ~~P450~~ cytochrome P450 and, therefore, ~~that~~ may result in an increase in the half-life of several~~various~~ drugs with consequent increase in~~of~~ their toxicity. Chloramphenicol decreases the metabolism of the following drugs:
[…]
- hypoglycaemic sulphonamides (tolbutamide, chlorpropamide, glimepiride, etc.): chloramphenicol can~~may~~ cause an excessive hypoglycaemic response;

[…]
Furthermore, chloramphenicol may interfere with immunity mechanisms and should not be administered during the active immunisation phase, for example~~such as~~ with tetanus toxoid or live typhoid vaccine.
Chloramphenicol may result in~~give~~ a false positive result in the test that exploits~~uses~~ the copper reduction method for the determination of glucose in urine. In patients treated with chloramphenicol, urine tests based on glucose oxidase reactions should be used.

4.6 Pregnancy and breastfeeding

Pregnancy
Data on~~obtained with~~ a large number of exposed pregnancies do not indicate~~no~~ particular side~~undesirable~~ effects of chloramphenicol on pregnancy and on the health of the foetus/newborn, with the exception of the late~~final~~ stages of pregnancy, during which "gray baby syndrome"~~may occur~~, sometimes even lethal, may occur (fatal (see section 4.8). Therefore, chloramphenicol should not be used during the pregnancy unless ~~absolutely~~ clearly necessary.
Breastfeeding
Chloramphenicol is excreted in ~~breast~~ human milk. Although chloramphenicol concentrations are probably too low to induce "gray baby syndrome" (see section 4.8), this risk cannot be completely excluded. Furthermore~~In addition~~, the bone marrow depression or other serious adverse effects to~~in~~ the infant may occur. Therefore, chloramphenicol should not be ~~administered~~ used during the breastfeeding period.

4.7 Effects on the ability to drive and use machines

Chloramphenicol Fisiopharma does not alter~~affect~~ the ability to drive and use machines.

4.8 Undesirable effects

Below,~~The following are~~ the undesirable effects of chloramphenicol organized~~categorised~~ according to the MedDRA organic system classification are described.~~organ class. Insufficient~~ There are insufficient data~~are available~~ to establish the frequency of the single listed ~~individual~~effects~~listed~~.
~~*Disorders of the*~~ *Blood and lymphatic system disorders*
Bone marrow depression: it can~~may~~ occur in two different forms: the first, dose-dependent~~form is~~ characterised by agranulocytosis, anaemia, leukopenia, thrombocytopenia and reticulocytopenia; the

second ~~form that is~~ not-dose-related, is a very severe form of aplastic anaemia which~~that~~ develops after a latency period of weeks or even months.
Depression of erythropoiesis is more frequent in patients with hepatic or ~~renal insufficiency~~kidney failure.
Trauma, poisoning and procedure complications.
"Grey baby syndrome": this toxic manifestation is~~has been~~ observed in new-borns ~~who have been~~ who are given high doses of chloramphenicol. It is characterised by abdominal distension, vomiting, ash colour~~y skin~~, hypothermia, progressive cyanosis, circulatory collapse and death within a few hours or days. It appears that the cause may be the lack of glucuronoconjugation~~ide conjugation~~ of chloramphenicol, due to inadequate hepatic glucuronyltransferase activity during the first weeks of the neonatal life, and inadequate renal excretion of the unconjugated drug.
[…]
Infections and infestations
Jarisch-Herxheimer reaction, characterised by shivers~~chills~~, headache, fever and mucocutaneous lesions.

4.9 Overdose
An overdose increases the risk of mainly~~complications especially~~ haematological complications related to the direct toxicity of chloramphenicol (see section 4.8 Undesirable effects).
Chloramphenicol is only partially removed from the blood through ~~the~~~~by~~ peritoneal dialysis or haemodialysis. ~~In infants, both full~~ Both complete blood transfusions and charcoal haemoperfusion ~~were used~~ for chloramphenicol overdoses were used in newborns.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacoynamic properties
Pharmacotherapeutic group: Antibacterials for systemic use, carbapenems, ATC code: J01BA01.
Chloramphenicol is a broad-spectrum antibiotic with a bacteriostatic action...
Generally susceptible~~The generally sensitive~~ microbial species (mic ≤ ~~CMI~~ 5 µg~~g~~/ml) are: ...
The microbial species which~~that~~ are not always sensitive: Staphylococci, Enterococci, Colibacilli, Klebsiella, Proteus.
~~On the other hand, t~~The following species are resistant (mic ≥ ~~CMI~~ 25 µg~~g~~/ml): Serratia, Acinetobacter, Pseudomonas.
[…]
You may have cross-resistance to thiamphenicol ~~may occur~~. Pseudomonas aeruginosa and certain~~some~~ strains of Proteus and Klebsiella resist chloramphenicol by~~with~~ a non-enzymatic mechanism comprising~~which includes~~ an inducible block of permeability.

5.2 Pharmacokinetic properties
[…]
<u>Distribution</u>
Chloramphenicol spreads rapidly, but~~however~~ its distribution is not uniform. The highest concentrations are in the liver and kidney; the lowest concentrations are in the brain and cerebrospinal fluid.
Chloramphenicol penetrates into the cerebrospinal fluid even in the absence of ~~the meninx~~ inflammatory state of the meninge and reaches concentrations equal to about half those offound in the blood.
Measurable levels are also found~~detected~~ in pleural and ascitic fluids, saliva, milk, and aqueous and vitreous humours. In addition~~Furthermore~~, chloramphenicol crosses the placental barrier.
The volume of distribution is about 0.5~~1~~ l/kg.
50%-80% of the dose is bound to plasma proteins.
<u>Metabolism</u>

Chloramphenicol is rapidly metabolised at the hepatic level~~, mostly~~ especially in derivatives with glucuronic acid, microbiologically inactive, which are rapidly excreted by the kidney. It should be necessary to consider ~~taken into consideration~~ that in newborns~~neonates~~ the capacity for glucuronidation and renal elimination is very limited.

Elimination

Chloramphenicol is~~ mainly~~ excreted mainly through the kidney~~in the urine~~ (90%) as a~~ conjugate of~~ glucuronic acid conjugate and, to a small extent, also~~amount,~~ in unchanged form. Small amounts are excreted in bile (2-3%) and faeces (1%).

The plasma half-life varies ~~from~~ between 1.5 and 5 hours.

In patients suffering from renal failure, ~~with kidney impairment,~~ the half-life varies from 3 to 7 hours.

In patients ~~with~~ suffering from reduced renal function, the half-life is generally prolonged, especially in patients with cirrhosis and jaundice.

The half-life of chloramphenicol reaches up to 28 hours in infants~~newborns~~ with very few days of life.

5.3 Preclinical safety data

~~In~~ Effects in non-clinical studies~~ effects at exposure~~ were~~ only~~ observed~~ since~~ only at exposures considered sufficiently in excess of ~~significantly higher than~~ the maximum human exposure indicating little relevance to ~~however, this has insignificant~~ clinical ~~relevance~~use. In fact, chloramphenicol was~~has been~~ shown to be genotoxic in human and murine~~ mouse~~ cells only at concentrations 25 times higher than the maximum dose used in humans.

In chicken embryos, chloramphenicol inhibits growth and rarely ~~leads to splanchnopleural~~ causes splanchnopleure and neural tube defects. In rat experiments~~ with rats~~, exposure to a diet containing 2-4% chloramphenicol during the last stage~~phase~~ of gestation~~ only~~ caused only oedema in foetuses. No other congenital anomalies were detected in further teratogenicity~~ additional teratogenic~~ studies conducted in rats, rabbits and monkeys.

6. PHARMACEUTICAL PARTICULARS

6.5 Nature and contents of container

Package of Chloramphenicol Fisiopharma 1 g powder for solution for injection is packaged in transparent glass vials, with chlorobutyl rubber stoppers and closed with flip-off caps. The package contains 10 vials with 1 g of chloramphenicol ~~powder~~ each.

6.6 Special precautions for disposal and handling

The unused drug~~medicine~~ and waste material derived from this drug should~~medicine must~~ be disposed of according to the~~in accordance with~~ local rules in force~~regulations~~.

העלון לרופא מצורף להודעה זו וכן נשלח לפרסום במאגר התרופות שבאתר האינטרנט של משרד הבריאות.
ניתן לקבל את העלון מודפס ע"י פניה לבעל הרישום, חברת פרופארם בע"מ, טל 04-6294242.

בברכה,
מירי חזן
רוקחת ממונה