Drugfield PHARMACEUTICALS LIMITED

SUMMARY OF PRODUCT CHARACTERISTICS

(SmPC) of

Chloramphenicol® Capsules (chloramphenicol 250mg)

1. NAME OF THE MEDICINALPRODUCT

Chloramphenicol® Capsules (chloramphenicol 250mg)

2. QUALITATIVE AND QUANTITATIVECOMPOSITION

Each capsule contains chloramphenicol 250mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solid - Capsule

4. Clinical particulars

4.1 Therapeutic indications

Chloramphenicol is indicated in the following:
1. Typhoid fever and other types of systemic salmonella infections. The carrier state will not be eliminated.
2. Bacterial meningitis due to Haemophilus influenzae.
3. Anaerobic infections originating from foci in the bowel or pelvis.
4. Rickettsial diseases such as epidemic, murine, scrub and recrudescent typhus, Rocky Mountain spotted fever and Q. fever when tetracyclines are not indicated.
5. Brucellosis when tetracyclines are contra-indicated.
The use of chloramphenicol should be limited to serious infections where positive bacteriological evidence and clinical judgement indicates that chloramphenicol is an appropriate antibiotic.

4.2 Posology and method of administration

Posology

Important Dosage and Administration Instructions

Dosage should be determined on an individual basis and the lowest dosage necessary to achieve the desired result should be used.

Adults: –500 mg every 6 hours or 50 mg/kg body mass daily in divided doses every 6 hours.

The dose of chloramphenicol should be reduced in the presence of hepatic disease or in patients with renal insufficiency.

Children: –25 to 50 mg/kg body mass daily, given in divided doses at intervals of 6 hours.

Method of administration

Oral administration

4.3 Contraindications

Chloramphenicol is contra-indicated in the following conditions:

1. Patients with a history of hypersensitivity or toxic reactions.

2. Contraindicated in minor infections or for prophylaxis.

2. Aplastic anaemia.

3. During active immunization.

4.4 Special warnings and precautions foruse

Chloramphenicol should not be used in the treatment of any infection for which a less toxic antibiotic is available. It is also advisable to perform blood tests in the case of prolonged or repeated administration. Evidence of any detrimental effect on blood elements is an indication to discontinue therapy immediately.

The dosage of chloramphenicol should be reduced in patients with impairment of hepatic or renal function. Because of its toxic nature it is important to monitor serum levels of this antibiotic particularly in new-born and premature infants, in the elderly, in patients with renal or hepatic disease and in those receiving other drugs with which chloramphenicol may interact.

4.5 Interaction with other medicinal products and other forms of interaction

Administration of chloramphenicol concomitantly with bone marrow depressant drugs is contraindicated, although concerns over aplastic anaemia associated with ocular chloramphenicol have largely been discounted.

Chloramphenicol has been shown to interact with, and enhance the effects of coumarin anticoagulants, some hypoglycaemic agents (e.g. tolbutamide) and phenytoin. When given concurrently, a dose reduction of these agents may be necessary. Plasma concentrations of chloramphenicol may be reduced with concomitant usage of phenobarbital and rifampicin.

4.6 Pregnancy and Lactation

Pregnancy

Risk Summary

When deciding whether to use chloramphenicol during pregnancy it is important to weigh up how necessary chloramphenicol is to your health against any possible risks to you or your baby, some of which might depend on how many weeks pregnant you are.

Lactation

Risk Summary

Milk levels are not enough to induce grey baby syndrome, but since drug-induced aplastic anemia is not dose-related, this might occur (but has not been reported). There is a theoretical risk of bone marrow depression, but this has not been reported.

In 10 breastfeeding women, peak milk levels were 1.7 to 2.8 mg/L during therapy with 250 mg orally 4 times a day and 3.6 to 6.1 mg/L during therapy with 500 mg orally 4 times a day.

Females and Males of Reproductive Potential

Infertility

No report from any studies that chloramphenicol reduced male and female reproductive potential.

Pediatric Use

The 'Grey syndrome' may occur after administration in patients with immature hepatic metabolic capacity, i.e. infants and neonates, usually in those treated with doses substantially in excess of those recommended.

Geriatric Use

Chloramphenicol is metabolized by the liver to chloramphenicol glucuronate (which is inactive). In liver impairment, the dose of chloramphenicol must therefore be reduced. No standard dose reduction exists for chloramphenicol in liver impairment, and the dose should be adjusted according to measured plasma concentrations.

The majority of the chloramphenicol dose is excreted by the kidneys as the inactive metabolite, chloramphenicol glucuronate. Only a tiny fraction of the chloramphenicol is excreted by the kidneys unchanged. Plasma levels should be monitored in patients with renal impairment, but this is not mandatory.

4.7 Effects on ability to drive and use machines

None stated

4.8 Undesirable effects

The following may become apparent after chloramphenicol treatment: dryness of the mouth, nausea and vomiting, diarrhoea,urticaria, optic neuritis with blurring or temporary loss of vision, peripheral neuritis, headache and depression. Superinfection by fungi e.g. C. albicans in the gastro-intestinal tract or vagina, may also occur due to the disturbance of normal bacterial flora.

Aplastic Aneamia

The most serious side effect of chloramphenicol treatment is aplastic anaemia. This effect is rare and sometimes fatal. The risk of AA is high enough that alternatives should be strongly considered. Treatments are available but expensive. No way exists to predict who may or may not get this side effect. The effect usually occurs weeks or months after treatment has been stopped, and a genetic predisposition may be involved. It is not known whether monitoring the blood counts of patients can prevent the development of aplastic anaemia, but patients are recommended to have a baseline blood count with a repeat blood count every few days while on treatment. Chloramphenicol should be discontinued if the complete blood count drops.

Bone marrow suppression

Chloramphenicol may cause bone marrow suppression during treatment; this is a direct toxic effect of the drug on human mitochondria. This effect manifests first as a fall in hemoglobin levels, which occurs quite predictably once a cumulative dose of 20 g has been given. The anaemia is fully reversible once the drug is stopped and does not predict future development of aplastic anaemia. Studies in mice have suggested existing marrow damage may compound any marrow damage resulting from the toxic effects of chloramphenicol.

Leukemia

Leukemia, a cancer of the blood or bone marrow, is characterized by an abnormal increase of immature white blood cells. The risk of childhood leukemia is increased, as demonstrated in a Chinese case–control study, and the risk increases with length of treatment.

Hypersensitivity reactions

Fever, macular and vesicular rashes, angioedema, urticaria, and anaphylaxis may occur. Herxheimer's reactions have occurred during therapy for typhoid fever.

Neurotoxic reactions

Headache, mild depression, mental confusion, and delirium have been described in patients receiving chloramphenicol. Optic and peripheral neuritis have been reported, usually following long-term therapy. If this occurs, the drug should be promptly withdrawn.

4.9 Overdose

Toxic manifestations include aplastic anaemia, blurring of vision, digital paresthesias, optic neuritis, allergic skin rashes, and gastro-intestinal haemorrhage. Chloramphenicol should be discontinued immediately on the appearance of toxic symptoms. Treatment is symptomatic and general supportive therapy.

5. PHARMACOLOGICALPROPERTIES

5.1 Pharmacodynamics properties

Mechanism of Action

Chloramphenicol is a bacteriostatic by inhibiting protein synthesis. It prevents protein chain elongation by inhibiting the peptidyltransferase activity of the bacterial ribosome. It specifically binds to A2451 and A2452 residues in the 23S rRNA of the 50S ribosomal subunit, preventing peptide bond formation.[36] Chloramphenicol directly interferes with substrate binding in the ribosome, as compared to macrolides, which sterically block the progression of the growing peptide.

5.2 Pharmacodynamic

Chloramphenicol is a broad-spectrum antibiotic that was derived from the bacterium Streptomyces venezuelae and is now produced synthetically. Chloramphenicol is effective against a wide variety of microorganisms, but due to serious side-effects (e.g., damage to the bone marrow, including aplastic anemia) in humans, it is usually reserved for the treatment of serious and life-threatening infections (e.g., typhoid fever). Chloramphenicol is bacteriostatic but may be bactericidal in high concentrations or when used against highly susceptible organisms. Chloramphenicol stops bacterial growth by binding to the bacterial ribosome (blocking peptidyltransferase) and inhibiting protein synthesis.

5.2 Pharmacokinetic properties

Rapidly and completely absorbed from gastrointestinal tract following oral administration (bioavailability 80%).Plasma protein binding is 50-60% in adults and 32% is premature neonates.Hepatic, with 90% conjugated to inactive glucuronide.Half-life in adults with normal hepatic and renal function is 1.5 - 3.5 hours. In patients with impaired renal function half-life is 3 - 4 hours. In patients with severely impaired hepatic function half-life is 4.6 - 11.6 hours. Half-life in children 1 month to 16 years old is 3 - 6.5 hours, while half-life in infants 1 to 2 days old is 24 hours or longer and is highly variable, especially in low birth-weight infants.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections.

6. PHARMACEUTICALPARTICULARS

6.1 List of excipients

Lactose Monohydrate 200 Mesh
Corn Starch Dried
Aerosil 200
Magnesium Stearate
Sodium Lauryl Sulphate

6.2 Incompatibilities

None have been reported or are known

6.3 Shelf life

48 Months

6.4 Special precautions for storage

Store below 30^{o}C in tight container protected from light and moisture.

6.5 Nature and contents of container and special equipment for use, administration or implantation

Chloramphenicol Capsule is presented in a blister of 10 X 10's packed in hardboard carton with leaflet enclosed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. APPLICANT/MANUFACTURER

Drugfield Pharmaceuticals Limited
Lynson Chemical Avenue Km38,
Lagos-Abeokuta Expressway
Sango-Otta, Ogun State, Nigeria
Tel: +2348033513989
Email:Info@drugfieldpharma.com