Chloramphenicol Capsules 250mg
SUMMARY OF PRODUCT CHARACTERISTICS

This summary of product characteristics focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities (term to be revised).
The medicine may be authorized for additional or different uses by national medicines regulatory authorities.

1. Name of the medicinal product
Chloramphenicol Capsules BP 250 mg

2. Qualitative and quantitative composition
Each hard capsule contains 250 mg of chloramphenicol

For the full list of excipients, see section 6.1.

3. Pharmaceutical form
Hard capsules

Off-white, hard gelatin capsules

4. Clinical particulars
4.1 Therapeutic indications
Typhoid fever and life-threatening infections, particularly those caused by Haemophilus influenzae where other antibiotics will not suffice.

4.2 Posology and method of administration
Posology

Adults and elderly

The normal dose is 50 mg/kg body weight daily in 4 divided doses. For severe infections (meningitis, septicaemia) this dose may be doubled initially, but it must be reduced as soon as clinically practical.

Paediatric population

The safety and efficacy of Chloramphenicol Capsules BP 250 mg have not yet been established in children.

Method of administration

For oral administration.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Chloramphenicol is contra-indicated in prophylaxis or treatment of minor infections; during active immunisation; and in porphyria patients.

Chloramphenicol is contra-indicated in patients taking drugs liable to depress bone marrow function (see section 4.5).

Chloramphenicol must not be used in breast-feeding mothers and during pregnancy or labour, due to a risk of foetal/ infant damage (Gray Baby syndrome).

4.4 Special warnings and precautions for use
Chloramphenicol should only be used if other treatments are ineffective and its use should always be carefully monitored.

Dose reduction and plasma level monitoring may be required in patients with hepatic or renal impairment; in the elderly; and in patients concurrently treated with interacting drugs (see section 4.5).

Periodic blood testing should be conducted during prolonged or repeated treatment. Chloramphenicol should be discontinued if a significant detrimental effect is seen.

This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction
Warfarin, phenytoin, sulphonylureas and tolbutamide

Chloramphenicol prolongs the elimination, increasing the blood levels, of drugs including warfarin, phenytoin, sulphonylureas, tolbutamide.

Anticonvulsants and anticoagulants

Doses of anticonvulsants and anticoagulants may need to be adjusted if given concurrently.

Penicillins and rifampicin

Complex effects (including reduced / increased plasma levels) requiring monitoring of chloramphenicol plasma levels have been reported with co-administration of penicillins and rifampicin.

Paracetamol

Concurrent administration of paracetamol should be avoided as this prolongs chloramphenicol half-life.

Calcineurin Inhibitors (CNIs) Ciclosporin and Tacrolimus

Treatment with chloramphenicol possibly increases the plasma levels of the CNIs ciclosporin and tacrolimus.

Barbiturates

The metabolism of chloramphenicol is accelerated by barbiturates, such as phenobarbitone, leading to reduced plasma concentrations. There is a possible decrease in the metabolism of phenobarbitone with concomitant chloramphenicol administration.

Oestrogens

There is a small risk that chloramphenicol may reduce the contraceptive effect of oestrogens.

Hydroxocobalamin

Chloramphenicol reduces the response to hydroxocobalamin.

Drugs causing agranulocytosis

Chloramphenicol is contra-indicated in patients taking drugs liable to suppress bone marrow function (see section 4.3). These include:

- Carbamazapine
- Sulphonamides
- Phenylbutazone
- Penicillamine
- Cytotoxic agents
- Some antipsychotics, including clozapine and particularly depot antipsychotics
- Procainamide
- Nucleoside reverse transcriptase inhibitors
- Propylthiouracil

4.6 Fertility, pregnancy and lactation

Pregnancy

Chloramphenicol crosses the placenta. Therefore chloramphenicol is contraindicated during pregnancy (see section 4.3).

Breast-feeding

Chloramphenicol is excreted in breast milk. Therefore chloramphenicol is contraindicated during breast-feeding (see section 4.3).

Fertility

No human data on the effects of chloramphenicol on fertility is available.

4.7 Effects on ability to drive and use machines

Chloramphenicol Capsules BP 250 mg have no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as follows: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/100,000), not known (cannot be estimated from the available data).

Blood and lymphatic disorders

Rare:	(i) A reversible dose related bone marrow depression. (ii) An irreversible aplastic anaemia
Not known:	Increase in bleeding time.

Immune system disorders

Not known:	Hypersensitivity reactions including allergic skin reactions.

Eye disorders

Not known: Optic neuritis leading to blindness.

Ear and labyrinth disorders

Not known: Ototoxicity.

Vascular disorders

Not known: Acidotic cardiovascular collapse.

Gastrointestinal disorders

Not known: Nausea, vomiting, glossitis, stomatitis, diarrhoea, enterocolitis.

Pregnancy, puerperium and perinatal conditions

Not known: "Gray" syndrome, particularly in the newborn, which appears to be related to excessively high plasma levels. The Gray baby syndrome consists of abdominal distension, pallid cyanosis, vomiting, progressing to vasomotor collapse, irregular respiration and death within a few hours of onset of symptoms. (These symptoms are thought to be dose related and rapid clearance of chloramphenicol has been associated with recovery).

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 via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Where adverse effects show signs of developing administration must be stopped immediately and treatment is mainly supportive. If an allergy develops, oral antihistamines may be used. In severe overdosage e.g. Gray Baby Syndrome, there is a need for a rapid reduction in plasma levels and it has been reported that resin haemoperfusion (XAD-4) substantially increases Chloramphenicol clearance.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antibacterials for systemic use, amphenicols, ATC Code: J 01 BA 01.

Chloramphenicol is a broad-spectrum antibiotic acting by interfering with bacterial protein synthesis

The most important action on the body tissue is the adverse one of bone marrow depression. There is significant plasma protein binding and the drug is largely inactivated in the liver.

5.2 Pharmacokinetic properties

Chloramphenicol is readily and rapidly absorbed from the G.I. tract. Particle size may affect rate of absorption, but will not affect total absorption. Significant serum levels observable 30 minutes after ingestion and half life may be 2 – 5 hours.

Chloramphenicol is widely distributed in body tissues and fluids. It is found in Cerebro-spinal fluid. It crosses the placental barrier and diffuses into breast milk.

There is significant plasma protein binding (up to 60%).

Excretion is mainly in the urine and largely inactivated in the liver.

5.3 Preclinical safety data

None.

6. Pharmaceutical particulars

6.1 List of excipients

Sodium lauryl sulphate

Potato starch

Magnesium stearate

Talc

Gelatin

Titanium dioxide (E171).

6.2 Incompatibilities

There are no significant incompatibilities with the product.

6.3 Shelf life

3 years.

6.4 Special precautions for storage
Store in a cool dry place in the original package.

6.5 Nature and contents of container
Container with a High Density Polypropylene (HDPP) body and a Low Density Polyethylene (LDPE) cap.

Pack sizes: 30, 50, 60, 100 and 1000 capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
No special requirements for disposal.

7. SUPPLIER

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