# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Chloramphenicol 250 mg Capsules

Cafcol

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 250 mg of Chloramphenicol BP

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Capsule

White, opaque gelatine capsules

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

To be reserved for the treatment of life-threatening infections, particularly those caused by Haemophilus influenza, and typhoid fever, where other antibiotics will not suffice.

### 4.2 Posology and method of administration

Posology:

*Adults (including the elderly):*

The usual dose is 500 mg every 6 hours (50 mg/kg bodyweight daily in 4 divided doses) and treatment should be continued for 2 or 3 days after the patient's temperature has returned to normal. For severe infections (meningitis, septicaemia) this dose may be doubled initially, but it must be reduced as soon as clinically practical.

*Children:*

Not recommended

Method of administration: Oral

## 4.3 Contraindications

Chloramphenicol is contra-indicated in:

- individuals with a history of hypersensitivity or toxic reaction to chloramphenicol or to any of the excipients listed in section 6.1
- prophylaxis or treatment of minor infections
- active immunisation
- porphyria patients
- blood dyscrasias including aplastic anaemia
- patients taking drugs liable to depress bone marrow function (see section 4.5)
- breast-feeding mothers and during pregnancy or labour, due to a risk of foetal/infant damage (Grey Baby syndrome)

## 4.4 Special warnings and precautions for use

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

Determine routine blood profile before therapy and repeat blood studies at appropriate intervals, especially during prolonged or repeated therapy. The drug should be withdrawn if evidence of a significant detrimental effect is seen or depression of any of the blood elements appears to be attributable to chloramphenicol, always weighing these effects against the seriousness and course of the disease under treatment.

Avoid repeated courses of Chloramphenicol and concurrent therapy with other drugs known to cause bone marrow depression. Chloramphenicol should not be used for the treatment of trivial infections. Chloramphenicol should only be used if other treatments are ineffective and its use should always be carefully monitored.

## 4.5 Interaction with other medicinal products and other forms of interaction

Paracetamol: Concurrent administration in patients receiving Paracetamol should be avoided as the half-life of Chloramphenicol is considerably prolonged.

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

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

Warfarin, Phenytoin, Sulphonylureas, Tolbutamide: Chloramphenicol prolongs the elimination, increasing the plasma concentration of drugs including warfarin, phenytoin, sulphonylureas, tolbutamide

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:

The use of chloramphenicol is contra-indicated as the drug crosses the placenta

Breast-feeding:

The use of chloramphenicol is contra-indicated as the drug is excreted in the milk of the lactating mother, therefore mothers taking this drug should not breast feed their infants.

## 4.7 Effects on ability to drive and use machines

Chloramphenicol has no or negligible influence on the ability to drive and use machines.

## 4.8 Undesirable effects

The most serious undesirable effects that may arise are:

Blood and lymphatic disorders

(i) A reversible dose related bone marrow depression

(ii) An irreversible aplastic anaemia with an estimated frequency between 1/4000 & 1/100000

Other undesirable effects (of unknown frequency) are:

Blood and the lymphatic system disorders

Increase in bleeding time

Immune system disorders

Hypersensitivity reactions including allergic skin reactions

Eye disorders

Optic neuritis leading to blindness

Ear and labyrinth disorders

Ototoxicity

Vascular disorders

Acidotic cardiovascular collapse

Gastrointestinal disorders

Nausea, vomiting, glossitis, stomatitis, diarrhoea, enterocolitis

Pregnancy, puerperium and perinatal conditions

"Grey" syndrome, particularly in the newborn, which appears to be related to excessively high plasma levels. The Grey 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 the 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.

### 4.9 Overdose

If more than 12 capsules are swallowed, the stomach should be emptied by gastric lavage and symptomatic treatment instituted. There is no antidote to Chloramphenicol.

If an allergy develops, oral antihistamines may be used. In severe overdosage e.g. Grey 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

ATC code: J01BA01, Antibacterials for Systemic Use - Amphenicols

Chloramphenicol is a broad spectrum antibiotic which acts by interfering with bacterial protein synthesis. It is bacteriostatic effective against a wide range of gram-negative and gram-positive organisms. Particularly susceptible are S. Typhi, H. Influenzae, Neisseria Meningitides and Bordetella Pertussis. It also has anti-rickettsial activity and is active against Chlamydias.

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 when taken orally. Particle size may affect rate of absorption, but will not affect total absorption. Significant serum levels are observable 30 minutes after ingestion and half-life may be 2 – 5 hours. After a single dose of 1 g blood concentrations of about 10 micrograms per ml may be reached after 2 hours.

Blood concentrations above 4 micrograms per ml are usually maintained by a dose of 500 mg every 6 hours.

The drug is widely distributed in body tissues and fluids and enters the cerebro-spinal fluid. Chloramphenicol travels across the placenta into the cerebro-spinal fluid. Chloramphenicol travels across the placenta into the foetal circulation and into breast milk and into the aqueous and vitreous humours of the eye. About 60% in the circulation is bound to plasma protein.

Chloramphenicol is excreted mainly in the urine when 90% is inactivated in the liver mostly by conjugation with glucuronic acid. About 3% is excreted in the bile.

### 5.3 Preclinical safety data

Not applicable.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Pregelatinised maize starch, sodium starch glycollate, magnesium stearate, gelatin and titanium dioxide.

### 6.2 Incompatibilities

None known.

### 6.3 Shelf life

36 months.

### 6.4 Special precautions for storage

Store below 25°C in a dry place in well closed containers.

### 6.5 Nature and contents of container

High density polystyrene with polythene lids and/or polypropylene containers with polypropylene or polythene lids and polyurethane or polythene inserts.
Pack sizes: 100 and 500.

### 6.6 Special precautions for disposal

Not applicable.

## 7 MARKETING AUTHORISATION HOLDER

Chelonia Healthcare Limited
11 Boumpoulinas Street,
3rd floor, 1060 Nicosia
Cyprus

## 8 MARKETING AUTHORISATION NUMBER(S)

PL 33414/0017

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12.11.1986 / 28.11.2008

## 10 DATE OF REVISION OF THE TEXT

31/08/2016