Package leaflet: Information for the patient

Chloramphenicol 1 g Powder for Solution for Injection
Chloramphenicol Sodium Succinate

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Chloramphenicol 1 g Powder for Solution for Injection is and what it is used for

This medicine contains chloramphenicol, which is an antibiotic used to treat severe infections such as typhoid and meningitis, and should only be used when other antibiotics do not help or are unsuitable. It is also used when oral chloramphenicol cannot be used or when higher amounts of the medicine is needed in the blood.

Chloramphenicol prevents bacteria making an essential nutrient required for growth and multiplication. In time, the number of bacteria are reduced and the infection is controlled, so that treatment can be continued using a more gentle antibiotic.

You must talk to a doctor if you do not feel better or if you feel worse.

2. What you need to know before you use Chloramphenicol 1 g Powder for Solution for Injection

Do not use Chloramphenicol:
- If you have had an allergic reaction (e.g. rash, wheezing) to chloramphenicol before.
- If you are pregnant, or are breast-feeding.

Warnings and precautions:
Talk to your doctor or pharmacist:
- If you have a history of kidney or liver disease.
- If you are already taking any other medicines which may also cause bone marrow depression.
- If you have a cold, viral influenza, throat infection and before using this medicine to prevent bacterial infections.
- If you have recently been or are about to be vaccinated.

This medicine is associated with various forms of anaemia (a decrease in red blood cells), leucopenia (decrease in white blood cells) and thrombocytopenia (decrease in platelets), which in turn leads to a loss of immunity and can progress into leukaemia. It should only be prescribed if less toxic antibiotics are not suitable.

New born babies should be treated with care to avoid Grey Syndrome, which is a serious condition arising from excessive toxic chloramphenicol metabolites. Treatment should be terminated as soon as symptoms are identified.

There is a risk of over-growth of non-susceptible organisms, which can lead to severe diarrhoea up to a few months after this medicine is given to the patient.

Other medicines and Chloramphenicol:
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines .

The following medicines interact with Chloramphenicol 1 g Powder for Solution for Injection, which affects the way that one or the other medicine works:

- Anticoagulants of the coumarin-type (to thin your blood or stop it clotting), antidiabetic agents (e.g. tolbutamide), anti-epileptic agents (e.g. phenytoin and phenobarbital) or rifampicin (an antibiotic).

Pregnancy and breast-feeding
Do not use Chloramphenicol if you are pregnant, or are breast- feeding.

Driving and using machines
Some of the adverse effects that can occur when taking chloramphenicol can affect the ability to drive or use machinery. Do not drive or use machinery if you are affected.

Chloramphenicol 1 g Powder for Solution for Injection contains sodium
This medicine contains 71.2 mg sodium per dose (main component of cooking/table salt) in each vial. This is equivalent to 3.6% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Chloramphenicol 1 g Powder for Solution for Injection

Chloramphenicol 1 g Powder for Solution for Injection will be made into a solution and be given to you by injection in to a vein, or into a muscle under the direction of a medical practitioner. Your doctor will prescribe the required amount (the dose). The dose is decided by taking into account the severity of your condition.

Adults
The recommended dose for adults is 1 g of chloramphenicol every 6-8 hours.

Use in children and adolescents:
The recommended dose for children is 50 mg/kg of chloramphenicol daily in divided doses every 6 hours (no more than this should be given); and 25 mg/kg daily in divided equal doses every 6 hours in new-born and premature infants.

The doctor may give you more in certain cases e.g. if you have septicaemia or meningitis (100 mg/kg/day), but should then be decreased as soon as appropriate. Your doctor will decide how long you need to be treated for.

During treatment your doctor will carry out blood tests to check that:
- Your blood is functioning properly as Chloramphenicol can damage your blood cells.
- Your liver and kidneys are functioning properly as Chloramphenicol may affect these organs.

If you use more Chloramphenicol than you should

In the case of serious overdosage, charcoal haemoperfusion may be effective in removing chloramphenicol from your blood.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor **immediately** if any of the following side effects occur:
- Severe allergic reaction e.g. red raised areas on your skin which may look like spots or be several inches across, which cause itchiness.
- Grey Syndrome – usually in new-born or premature infants, where the skin appears grey, and the infant is listless and weak.
- White blood cells counts (which fight infection) can also drop, increasing the chance of infections and fever.
- Anaemia (a low red blood cell count) that leave you feeling tired and lethargic.

Other side effects may occur, but, the frequency cannot be estimated from the available data:
- Thrombocytopenia (decrease in platelets)
- Dry mouth
- Nausea (feeling sick), vomiting (being sick) and diarrhoea
- Headache
- Depression
- Inflammation or damage to the nerves causing numbness, tingling, pain or muscle weakness
- Blurring, inflammation or temporary loss of vision
- Chloramphenicol may slow down development of immunity, and you may develop infections more frequently, which are difficult to fight off

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any side effects not listed in this leaflet.
You can also report side effects directly 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. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Chloramphenicol 1 g Powder for Solution for Injection

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the vial label and on the carton after EXP. The expiry date refers to the last day of that month.

Keep the vial in the outer carton in order to protect from light.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment

6. Contents of the pack and other information

What Chloramphenicol 1 g Powder for Solution for Injection contains:
- The active substance is Chloramphenicol Sodium Succinate.

There are no other ingredients found in Chloramphenicol 1 g Powder for Solution for Injection. (See end of Section 2 for further information on sodium).

What Chloramphenicol 1 g Powder for Solution for Injection looks like and contents of the pack
Chloramphenicol 1 g Powder for Solution for Injection is available as single glass vials. Each vial contains a freeze-dried powder containing the equivalent of 1g Chloramphenicol.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Eramol (UK) Ltd
Unit 9 North Downs Business Park
Limepit Lane
Sevenoaks
TN13 2TL
United Kingdom

Manufacturer
VUAB Pharma a.s.
Vltavská 53
25263 Roztoky
Czech Republic

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Detailed information on this medicinal product is available on the website of www.mhra.gov.uk.

The following information is intended for healthcare professionals only:

Chloramphenicol 1 g Powder for Solution for Injection
Chloramphenicol sodium succinate
Equivalent to 1 g
chloramphenicol Powder for
solution for injection

After parenteral administration chloramphenicol is rapidly released from chloramphenicol sodium succinate. Chloramphenicol 1 g Powder for Solution for Injection is a broad spectrum antibiotic and is active against many gram-positive organisms and gram-negative organisms, spirillae and rickettsia. It acts by interfering with bacterial protein synthesis. Chloramphenicol is widely distributed in body tissues and fluids and enters the cerebrospinal fluid. Chloramphenicol sodium succinate, free chloramphenicol and metabolites are excreted in the urine.

After intravenous administration of chloramphenicol succinate every 6 hours elimination half lives were 4.03 hours for chloramphenicol and 2.65 hours for chloramphenicol succinate. After intravenous chloramphenicol sodium succinate, steady state peak concentrations were reached on average 18.0 minutes after cessation of the infusion. In infants and children aged 3 days to 16 years the apparent half-life was extremely variable ranging from 1.7 to 12.0 hours.

Chloramphenicol 1 g Powder for Solution for Injection should not be used for trivial infections due to the possibility of severe blood dyscrasias which may prove fatal. Chloramphenicol 1 g Powder for Solution for Injection is indicated for typhoid, meningitis caused by *H. influenzae* and other serious infections caused by bacteria susceptible to chloramphenicol. Chloramphenicol should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the initial treatment of the infections listed above, or when these alternative antibacterial agents have failed to demonstrate efficacy.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

Dosage and administration
Posology
The dose administered and the concentration used is dependent on the severity of the infection. The recommended dose is as follows:

***Adults*:** The equivalent of 1 g of chloramphenicol every 6-8 hours.

Elderly: The recommended adult dose should be given subject to normal hepatic and renal function.

Children: The equivalent of 50 mg/kg chloramphenicol, according to body weight, daily in divided doses every 6 hours (this dose should not be exceeded). The patient should be carefully observed for signs of toxicity.

Premature Infants and Neonates: 25 mg/kg in divided doses.

In exceptional cases, such as patients with septicaemia or meningitis, dosage schedule up to 100 mg/kg/day may be prescribed. However, these high doses should be decreased as soon as clinically indicated. To prevent relapses, treatment should be continued after the temperature has returned to normal for 4 days in rickettsial diseases and for 8-10 days in typhoid fever. The 10 % solution should be given by intravenous injection over a period of about a minute, or in a large volume of fluid, by slow intravenous infusion. The concurrent administration of intravenous Chloramphenicol 1 g Powder for Solution for Injection with topical treatment has been found to be very effective in the treatment of osteomyelitic foci, abscesses, empyema and

skin and urinary infections.

Method of administration
To be given by intravenous or intramuscular injection.

In order to ensure rapid attainment of high blood levels, Chloramphenicol 1 g Powder for Solution for Injection is best administered by intravenous injection. Where this is not possible, however, intramuscular administration may be used, although it should be borne in mind that absorption may be slow and unpredictable.

The injection should be reconstituted with water for injections or sodium chloride injection.

The following dilution table may be useful for the administration of a proportion of the contents of a vial:

Concentration	**Solution strength**	**Volume of diluent to be added**	**Total volume after dilution**
40%	400 mg/ml	1.7 ml	2.5 ml
25%	250 mg/ml	3.2 ml	4.0 ml
20%	200 mg/ml	4.2 ml	5.0 ml

Contraindications and warnings
Chloramphenicol 1 g Powder for Solution for Injection is contraindicated in patients with a previous history of sensitivity and/or toxic reactions to chloramphenicol. It is also contraindicated in pregnancy and whilst breast feeding.

Chloramphenicol 1 g Powder for Solution is to be administered only under the direction of a medical practitioner. It should be reserved for serious infections caused by organisms susceptible to its antimicrobial effects when less toxic antibiotics are ineffective or contraindicated. However, chloramphenicol may be chosen to initiate antibiotic therapy based on the clinical impression. *In vitro* sensitivity tests should be performed concurrently so that the drug may be discontinued as soon as possible if a less toxic antibiotic is indicated by the results of such tests. The decision to continue use of chloramphenicol, rather than another antibiotic when both are suggested by *in vitro* studies to be effective against a specific pathogen, should be based upon severity of the infection, susceptibility of the pathogen to the various antimicrobial drugs, and the efficacy of the various drugs in the infection.

Bone marrow depression and blood disorders
Serious and fatal blood dyscrasias (aplastic anaemia, hypoplastic anaemia, thrombocytopenia, granulocytopenia, and bone marrow depression) are known to occur after the administration of chloramphenicol. In addition, there have been reports of aplastic anaemia attributed to chloramphenicol, which later resulted in leukaemia. Blood dyscrasias have occurred after both short-term and prolonged therapy with this drug. Chloramphenicol must not be used in the treatment of any infection for which a less toxic antibiotic is available.

Patient monitoring

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.

It is essential that adequate haematologic functions be closely monitored during treatment with chloramphenicol. While haematologic determinations may detect early peripheral haematologic changes, such as leucopoenia, reticulocytopenia, or granulocytopenia, before they become irreversible, such determinations cannot be relied on to detect bone marrow depression prior to the development of aplastic anaemia.

It is desirable that patients be hospitalized during therapy, so that appropriate laboratory

determinations and clinical observations can be made.
Baseline haematologic determinations should be made and determinations repeated approximately every two days during therapy. The drug should be discontinued upon appearance of reticulocytopenia, leucopoenia, thrombocytopenia, anaemia, or any other haematologic findings attributable to chloramphenicol. However, such determinations do not exclude the possible later appearance of the irreversible type of bone marrow depression. Repeated courses of the drug should be avoided if at all possible. Treatment should not be continued longer than required to produce a cure with little or no risk of relapse of the disease. Concurrent therapy with other drugs that may cause bone marrow depression should be avoided.

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. 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, therefore, be necessary. Plasma concentration of chloramphenicol may be reduced with concomitant usage of phenobarbital and rifampicin. Chloramphenicol may impede the development of immunity and should therefore not be given during active immunisation.

Hepatic or Renal Impairment
Excessive chloramphenicol serum levels may result from administration of the recommended dose to patients with impaired liver or kidney function, including that due to immature metabolic processes in the infant. Dosage should be adjusted accordingly or, preferably, the serum concentration should be determined at appropriate intervals.

Grey syndrome in infants and neonates
Precaution should be used in therapy of premature and full-term neonates to avoid "Grey Syndrome" toxicity. Serum drug levels should be carefully monitored during therapy of the neonate (newborn infant).
Toxic reactions, including fatalities, have occurred in premature infants and neonates. The signs and symptoms associated with these reactions have been referred to as the "Grey Syndrome".
Although "Grey Syndrome" has been reported in neonates born to mothers after having received chloramphenicol during labour, in most cases therapy with chloramphenicol has been instituted within the first 48 hours of life. The following summarizes the clinical and laboratory determinations that have been made on these patients.

Symptoms first appeared after 3 to 4 days of continued treatment with high doses of chloramphenicol. The symptoms appeared in the following order: abdominal distension with or without emesis, progressive pallid cyanosis, vasomotor collapse, frequently accompanied by irregular respiration, death within a few hours of onset of these symptoms.
The progression of symptoms from onset to death was accelerated with higher dose schedules. Serum drug levels revealed unusually high concentrations of chloramphenicol (over 90 mcg/mL after repeated doses).
Termination of therapy upon early evidence of the associated symptomatology frequently reversed the process with complete recovery following.

General
Chloramphenicol must not be used in the treatment of trivial infections or where it is not indicated, as in colds, viral influenza, infections of the throat or as a prophylactic agent to prevent bacterial infections.

Superinfections
The use of chloramphenicol, as with other antibiotics, may result in an overgrowth of nonsusceptible organisms, including fungi. If infections caused by nonsusceptible organisms

appear during therapy, appropriate measures should be taken.
Clostridium difficile associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including chloramphenicol, and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile.*
C. difficile produces toxins A and B which contribute to the development of CDAD.
Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

Pharmaceutical precautions
Keep the vial in the outer carton in order to protect from light.

Package quantities
Individual vials containing chloramphenicol sodium succinate equivalent to 1 g chloramphenicol.
PL 49160/0001
Keep this medicine out of the sight and reach of children.