Chloramphenicol Sodium Succinate

(BANM, rINNM)

Chloramfenikolio natrio sukcinatas; Chloramfenikol-sukcinát sodná sůl; Chloramphenicol α-Sodium Succinate; Chloramphénicol, succinate sodique de; Chloramphenicoli natrii succinas; Kloramfenikol Süksinat Sodyum; Klóramfenikol-hidrogénszukcinátnátrium; Kloramfenikolinatriumsuksinaatti; Kloramfenikolnatriumsuccinat; Succinato sódico de cloranfenicol.

Хлорамфеникола Натрия Сукцинат

$C_{15}H_{15}Cl_2N_2NaO_8$ = 445.2.

CAS — 982-57-0.

ATC — D06AX02; D10AF03; G01AA05; J01BA01; S01AA01; S02AA01; S03AA08.

ATC Vet — QD06AX02; QD10AF03; QG01AA05; QJ01BA01; QS01AA01; QS02AA01; QS03AA08.

Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet. Chin*. includes Chloramphenicol Hydrogen Succinate.

Ph. Eur. 6.2 (Chloramphenicol Sodium Succinate). A white or yellowish-white hygroscopic powder. Very soluble in water; freely soluble in alcohol. A 25% solution in water has a pH of 6.4 to 7.0. Store in airtight containers. Protect from light.

USP 31 (Chloramphenicol Sodium Succinate). A light yellow powder. Freely soluble in water and in alcohol. pH of a solution in water containing the equivalent of chloramphenicol 25% is between 6.4 and 7.0. Store in airtight containers.

Incompatibility. Incompatibility or loss of activity has been reported between chloramphenicol and a wide variety of other substances. Other factors, especially drug concentration, may play a part and many incompatibilities are chiefly seen with concentrated solutions.

Adverse Effects and Treatment

Chloramphenicol may cause serious and sometimes fatal adverse effects. Some of its toxicity is thought to be due to effects on mitochondrial protein synthesis. The most serious adverse effect of chloramphenicol is bone-marrow depression, which can take two different forms. The first is a fairly common dose-related reversible depression occurring usually when plasma-chloramphenicol concentrations exceed 25 micrograms/mL and is characterised by morphological changes in the bone marrow, decreased iron utilisation, reticulocytopenia, anaemia, leucopenia, and thrombocytopenia. This effect may be due to inhibition of protein synthesis in the mitochondria of bone marrow cells.

The second and apparently unrelated form of bone-marrow toxicity is severe irreversible aplastic anaemia. This is fairly rare, with a suggested incidence of about 1:20 000 to 1:50 000, although the incidence varies throughout the world, and is not considered to be dose-related. The aplasia usually develops after a latent period of weeks or even months and has been suggested to be the result of a nitrated benzene radical produced *in vivo*. It is considered that there may be some genetic or biochemical predisposition, but there is no way of identifying susceptible patients. Although the majority of cases were after oral use, aplasia has also occurred after intravenous and topical (eye drops) use of chloramphenicol. Survival is most likely in those with early onset aplasia, but they may subsequently develop acute myeloid leukaemia.

A toxic manifestation—the 'grey syndrome'—characterised by abdominal distension, vomiting, ashen colour, hypothermia, progressive pallid cyanosis, irregular respiration, and circulatory collapse followed by death in a few hours or days, has occurred in premature and other newborn infants given large doses of chloramphenicol. The syndrome is associated with high plasma concentrations of chloramphenicol, due to reduced capacity for glucuronidation and decreased glomerular filtration in children of this age, leading to drug accumulation. Recovery is usually complete if the drug is withdrawn early enough after onset, but up to 40% of infants with the full-blown syndrome may die. The syndrome has also been reported in infants born to mothers given chloramphenicol in late pregnancy. A similar syndrome has been reported in adults and older children given very high doses.

Prolonged oral use of chloramphenicol may induce bleeding, either by bone-marrow depression or by reducing the intestinal flora with consequent inhibition of vitamin K synthesis. Haemolytic anaemia has occurred in some patients with the Mediterranean form of glucose 6-phosphate dehydrogenase deficiency, but is rare in patients with milder forms of the deficiency.

Peripheral as well as optic neuritis has been reported, usually in patients treated over prolonged periods. Although ocular symptoms are often reversible if treatment is withdrawn early, permanent visual impairment or blindness has occurred.

Other neurological symptoms have included encephalopathy with confusion and delirium, mental depression, and headache. Ototoxicity has also occurred, especially after the use of ear drops.

Hypersensitivity reactions including rashes, fever, and angioedema may occur especially after topical use; anaphylaxis has occurred but is rare. Jarisch-Herxheimer reactions may also occur. Gastrointestinal symptoms including nausea, vomiting, and diarrhoea can follow oral use. Disturbances of the oral and intestinal flora may cause stomatitis, glossitis, and rectal irritation. Patients may experience an intensely bitter taste after rapid intravenous use of chloramphenicol sodium succinate.

Aplastic anaemia. A review[1] of the toxicity of chloramphenicol and related drugs, including the potential role of the *p*-nitro group in producing aplastic anaemia, indicated that derivatives such as thiamphenicol, which lack this grouping, are not associated with increased incidence of aplastic anaemia.

1. Yunis AA. Chloramphenicol: relation of structure to activity and toxicity. *Ann Rev Pharmacol Toxicol* 1988; **28:** 83–100.

Overdosage. Charcoal haemoperfusion was found to be far superior to exchange transfusion in the removal of chloramphenicol from blood, although it did not prevent death in a 7-week-old infant with the 'grey syndrome' after a dosage error.[1]

1. Freundlich M, *et al*. Management of chloramphenicol intoxication in infancy by charcoal hemoperfusion. *J Pediatr* 1983; **103:** 485–7.

Precautions

Chloramphenicol is contra-indicated in patients with a history of hypersensitivity or toxic reaction to the drug. It should never be given systemically for minor infections or for prophylaxis. Repeated courses and prolonged treatment should be avoided and it should not be used in patients with pre-existing bone-marrow depression or blood dyscrasias. Routine periodic blood examinations are advisable in all patients, but will not warn of aplastic anaemia.

Use of chloramphenicol with other drugs liable to depress bone-marrow function should be avoided.

Reduced doses should be given to patients with hepatic impairment. Excessive blood concentrations may also occur after usual doses in patients with severe renal impairment and in premature and full-term neonates who have immature metabolic processes. Monitoring of plasma-chloramphenicol concentrations may be desirable in patients with risk factors. A suggested range for peak plasma concentrations is 10 to 25 micrograms/mL and for trough concentrations 5 to 15 micrograms/mL.

Neonates should never be given chloramphenicol systemically, unless it may be life-saving and there is no alternative treatment, because of the risk of the 'grey syndrome'. The use of chloramphenicol is probably best avoided during pregnancy.

Chloramphenicol may interfere with the development of immunity and it should not be given during active immunisation.

Breast feeding. Chloramphenicol is distributed into breast milk[1] and the American Academy of Pediatrics[2] considers that its use by mothers during breast feeding may be of concern, since there have been reports of possible idiosyncratic bone-marrow suppression in the infant.

1. Havelka J, *et al.* Excretion of chloramphenicol in human milk. *Chemotherapy* 1968; **13:** 204–11.
2. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid*.; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 25/05/04)

Ocular use. Ocular chloramphenicol is widely used in the UK for the treatment of superficial eye infections. In view of the potential for serious toxicity, such as aplastic anaemia, after systemic absorption some, particularly in the USA, have advised that its ocular use should be restricted to situations where there is no alternative treatment.[1] However, apart from patients with a personal or family history of blood dyscrasias, the use, particularly of short courses, was defended by several specialists in the UK,[2-4] and the arguments have been the subject of several reviews.[5-7] Prospective case-control studies were considered necessary to clarify the risk.[8] One such study,[9] involving 145 patients with aplastic anaemia and 1226 controls, found that only 3 of the patients had been exposed to ocular chloramphenicol, and calculated that the absolute risk was no more than 0.5 cases per million treatment courses. Similarly, data[10] from 2 other studies revealed that none of 426 patients with aplastic anaemia and 7 of 3118 controls had used chloramphenicol eye drops. In a survey[11] of patients who received prescriptions for chloramphenicol eye drops the risk of serious haematological toxicity was 3 per 442 543 patients or 3 per 674 148 prescriptions.

1. Doona M, Walsh JB. Use of chloramphenicol as topical eye medication: time to cry halt? *BMJ* 1995; **310:** 1217–18.
2. Mulla RJ, *et al.* Is it time to stop using chloramphenicol on the eye: fears are based on only six cases. *BMJ* 1995; **311:** 450.
3. Buckley RJK, *et al.* Is it time to stop using chloramphenicol on the eye: safe in patients with no history of blood dyscrasia. *BMJ* 1995; **311:** 450.
4. Hall AV, *et al.* Is it time to stop using chloramphenicol on the eye: risk is low in short courses. *BMJ* 1995; **311:** 450–1.
5. McGhee CNJ, Anastas CN. Widespread ocular use of topical chloramphenicol: is there justifiable concern regarding idiosyncratic aplastic anaemia? *Br J Ophthalmol* 1996; **80:** 182–4.
6. Rayner SA, Buckley RJ. Ocular chloramphenicol and aplastic anaemia: is there a link? *Drug Safety* 1996; **14:** 273–6.
7. Titcomb L. Ophthalmic chloramphenicol and blood dyscrasias: a review. *Pharm J* 1997; **258:** 28–35.
8. Gordon-Smith EC, *et al.* Is it time to stop using chloramphenicol on the eye: prospective study of aplastic anaemia should give definitive answer. *BMJ* 1995; **311:** 451.
9. Laporte J-R, *et al.* Possible association between ocular chloramphenicol and aplastic anaemia—the absolute risk is very low. *Br J Clin Pharmacol* 1998; **46:** 181–4.
10. Wiholm B-E, *et al.* Relation of aplastic anaemia to use of chloramphenicol eye drops in two international case-control studies. *BMJ* 1998; **316:** 666.
11. Lancaster T, *et al.* Risk of serious haematological toxicity with use of chloramphenicol eye drops in a British general practice database. *BMJ* 1998; **316:** 667.

Porphyria. Chloramphenicol has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Sodium content. Each g of chloramphenicol sodium succinate represents about 2.2 mmol of sodium.

Interactions

Chloramphenicol is inactivated in the liver and may, therefore, interact with drugs that are metabolised by hepatic microsomal enzymes. For example, chloramphenicol enhances the effects of coumarin anticoagulants, such as dicoumarol and warfarin, some hypoglycaemics such as chlorpropamide and tolbutamide, and antiepileptics such as phenytoin. Conversely, the metabolism of chloramphenicol may be increased by inducers of hepatic enzymes such as phenobarbital or rifampicin. Some other interactions affecting the activity of chloramphenicol are discussed below.

Chloramphenicol may decrease the effects of iron and vitamin B_{12} in anaemic patients and has occasionally impaired the action of oral contraceptives.

For the effects of chloramphenicol on the activity of other antibacterials, see Antimicrobial Action, below.

Antiepileptics. Serum concentrations of chloramphenicol are usually reduced by the hepatic enzyme induction that occurs with *phenobarbital*,[1,2] and similar reductions have been reported in a case study during *phenytoin* use.[3] Conversely, elevated and potentially toxic serum-chloramphenicol concentrations have resulted during phenytoin use,[2] apparently due to competition for binding sites, although increased metabolism may alternatively lead to decreased serum-chloramphenicol concentrations.

For reference to the effects of chloramphenicol on phenobarbital and phenytoin, see p.493 and p.498, respectively.

1. Bloxham RA, *et al.* Chloramphenicol and phenobarbitone—a drug interaction. *Arch Dis Child* 1979: **54:** 76–7.
2. Krasinski K, *et al.* Pharmacologic interactions among chloramphenicol, phenytoin and phenobarbital. *Pediatr Infect Dis* 1982; **1:** 232–5.
3. Powell DA, *et al.* Interactions among chloramphenicol, phenytoin, and phenobarbital in a pediatric patient. *J Pediatr* 1981; **98:** 1001–3.

Ciclosporin. For the effect of chloramphenicol on ciclosporin, see p.1825.

Cimetidine. Fatal aplastic anaemia of rapid onset has occurred in 2 patients who received intravenous chloramphenicol and cimetidine.[1,2] As there is usually a latent period of 2 weeks to 12 months before aplastic anaemia develops after chloramphenicol therapy it is plausible that an additive or synergistic effect may

have occurred between the 2 drugs to cause bone-marrow toxicity.

1. Farber BF, Brody JP. Rapid development of aplastic anemia after intravenous chloramphenicol and cimetidine therapy. *South Med J* 1981; **74:** 1257–8.
2. West BC, *et al.* Aplastic anemia associated with parenteral chloramphenicol: review of 10 cases, including the second case of possible increased risk with cimetidine. *Rev Infect Dis* 1988; **10:** 1048–51.

Cyclophosphamide. For the effect of chloramphenicol on cyclophosphamide, see p.703.

Oral contraceptives. For the effect of chloramphenicol on oral contraceptives, see Hormonal Contraceptives, p.2068.

Paracetamol. A report of an increase in chloramphenicol half-life from 3.25 to 15 hours when intravenous paracetamol was given to 6 patients in intensive care 2 hours after intravenous chloramphenicol[1] has not been confirmed by subsequent studies in patients receiving oral paracetamol. A study in 5 children found that the half-life of intravenous chloramphenicol was reduced from 3 to 1.2 hours, concomitant with an increase in clearance, when oral paracetamol was given 30 minutes beforehand.[2] Furthermore, a study in 26 children found no evidence of altered disposition when oral paracetamol was given to patients receiving intravenous chloramphenicol,[3] and no significant change in chloramphenicol pharmacokinetics was found in 5 patients given oral chloramphenicol and paracetamol.[4]

1. Buchanan N, Moodley GP. Interaction between chloramphenicol and paracetamol. *BMJ* 1979; **2:** 307–8.
2. Spika JS, *et al.* Interaction between chloramphenicol and acetaminophen. *Arch Dis Child* 1986; **61:** 1121–4.
3. Kearns GL, *et al.* Absence of a pharmacokinetic interaction between chloramphenicol and acetaminophen in children. *J Pediatr* 1985; **107:** 134–9.
4. Stein CM, *et al.* Lack of effect of paracetamol on the pharmacokinetics of chloramphenicol. *Br J Clin Pharmacol* 1989; **27:** 262–4.

Tacrolimus. For the effect of chloramphenicol on tacrolimus, see p.1845.

Antimicrobial Action

Chloramphenicol is a bacteriostatic antibiotic with a broad spectrum of action against both Gram-positive and Gram-negative bacteria, as well as some other organisms.

Mechanism of action. Chloramphenicol is thought to enter sensitive cells by an active transport process. Within the cell it binds to the 50S subunit of the bacterial ribosome at a site adjacent to the site of action of the macrolides and clindamycin, and inhibits bacterial protein synthesis by preventing attachment of aminoacyl transfer RNA to its acceptor site on the ribosome, thus preventing peptide bond formation by peptidyl transferase. The block in protein synthesis results in a primarily bacteriostatic action, although it may be bactericidal to some organisms, including *Haemophilus influenzae*, *Neisseria meningitidis*, and *Streptococcus pneumoniae*, at higher concentrations.

Spectrum of activity. Chloramphenicol has activity against many types of bacteria, although in most cases there are less toxic alternatives available. The following pathogens are usually susceptible (but see also Resistance, below).

Gram-positive cocci including staphylococci such as *Staph. epidermidis* and some strains of *Staph. aureus*, and streptococci such as *Str., pneumoniae*, *Str. pyogenes*, and the viridans streptococci. Meticillin-resistant staphylococci and *Enterococcus faecalis* are commonly found to be resistant.

Other Gram-positive species including *Bacillus anthracis*, *Corynebacterium diphtheriae*, and anaerobes such as *Peptococcus* and *Peptostreptococcus* spp. are usually susceptible.

Gram-negative cocci such as *Neisseria meningitidis* and *N. gonorrhoeae* are usually highly sensitive, as are *Haemophilus influenzae* and a variety of other Gram-negative bacteria including *Bordetella pertussis*, *Brucella abortus*, *Campylobacter* spp., *Legionella pneumophila*, *Pasteurella*, and *Vibrio* spp. The Enterobacteriaceae vary in their susceptibility, and many strains have shown acquired resistance, but *Escherichia coli*, and strains of *Klebsiella* spp., *Proteus mirabilis*, *Salmonella*, *Shigella*, and *Yersinia* spp. have been reported to be susceptible. Many strains of *Enterobacter*, indole-positive *Proteus*, and *Serratia* spp. are resistant, or at best moderately susceptible. *Pseudomonas aeruginosa* is invariably resistant, although *Burkholderia* (formerly *Pseudomonas*) spp. may be susceptible.

Some Gram-negative anaerobes are susceptible, or moderately so, including *Bacteroides fragilis*, *Veillonella*, and *Fusobacterium* spp.

Other susceptible organisms include *Actinomyces* spp., *Leptospira* spp., spirochaetes such as *Treponema pallidum*, Chlamydiaceae, Mycoplasma spp., and Rickettsia spp. *Nocardia* spp. are resistant. Chloramphenicol is ineffective against fungi, protozoa, and viruses.

Activity with other antimicrobials. As with other bacteriostatic antimicrobials, the possibility exists of an antagonistic effect if chloramphenicol is given with a bactericidal drug, and some antagonism has been demonstrated *in vitro* between chloramphenicol and various beta lactams and aminoglycosides, but the clinical significance of most of these interactions is usually held to be doubtful. Chloramphenicol may competitively inhibit the effects of macrolides or lincosamides such as clindamycin because of the adjacency of their binding sites on the ribosome.

Resistance. Acquired resistance has been widely reported, although the prevalence of resistance has tended to decline where use of the drug has become less frequent. The most commonly seen form of resistance has been the production of an acetyltransferase that inactivates the drug. Such resistance is usually plasmid-mediated and may be associated with resistance to other drugs such as the tetracyclines. Other mechanisms that may reduce sensitivity to chloramphenicol include reduced permeability or uptake, and ribosomal mutation.

The actual incidence of resistance varies considerably in different countries and different centres. Epidemics of chloramphenicol-resistant *Salmonella* and *Shigella* spp. have occurred in the past, and although the prevalence of resistance in *Salmonella* spp. has been reported to be negligible except in parts of South or Southeast Asia, resistant salmonellal infections acquired in these regions are increasingly being seen elsewhere. Resistance among *Haemophilus* and *Neisseria* spp. occurs, and the latter may be problematic in developing countries, although it does not yet seem to be widespread. However, resistant strains of enterococci and pneumococci are reported to be relatively common in some areas, and over 50% of staphylococcal strains have been reported to show resistance in some hospitals.

Pharmacokinetics

Chloramphenicol is readily absorbed when given by mouth. Blood concentrations of 10 micrograms/mL or more may be reached about 1 or 2 hours after a single oral dose of 1 g, and blood concentrations of about 18.5 micrograms/mL have been reported after multiple 1-g doses. Chloramphenicol palmitate is hydrolysed to chloramphenicol in the gastrointestinal tract prior to absorption, and the sodium succinate, which is given parenterally, is probably hydrolysed to free drug mainly in the liver, lungs, kidneys, and plasma; such hydrolysis may be incomplete in infants and neonates, contributing to the variable pharmacokinetics in this age group. Chloramphenicol sodium succinate is, even in adults, only partially and variably hydrolysed, so that blood concentrations of chloramphenicol obtained after the sodium succinate parenterally are often lower than those obtained after oral chloramphenicol, with up to 30% of a dose excreted unchanged in the urine before hydrolysis can take place (but see under Administration, below).

Chloramphenicol is widely distributed in body tissues and fluids; it enters the CSF, giving concentrations of about 50% of those existing in the blood even in the absence of inflamed meninges; it diffuses across the placenta into the fetal circulation, into breast milk, and into the aqueous and vitreous humours of the eye. It also enters the aqueous humour after topical application. Up to about 60% in the circulation is bound to plasma protein. The half-life of chloramphenicol has been reported to range from 1.5 to 4 hours; the half-life is prolonged in patients with severe hepatic impairment and is also much longer in neonates. Renal impairment has relatively little effect on the half-life of the active drug, due to its extensive metabolism, but may lead to accumulation of the inactive metabolites.

Chloramphenicol is excreted mainly in the urine but only 5 to 10% of an oral dose appears unchanged; the remainder is inactivated in the liver, mostly by conjugation with glucuronic acid. About 3% is excreted in the bile. However, most is reabsorbed and only about 1%, mainly in the inactive form, is excreted in the faeces.

The absorption, metabolism, and excretion of chloramphenicol are subject to considerable interindividual variation, especially in infants and children, making monitoring of plasma concentrations necessary to determine pharmacokinetics in a given patient.

Uses and Administration

The risk of life-threatening adverse effects, particularly bone-marrow aplasia, has severely limited the clinical usefulness of chloramphenicol, although it is still widely used in some countries. It should never be given systemically for minor infections and regular blood counts are usually advisable during treatment. The third-generation cephalosporins replaced chloramphenicol for many of its former indications. There are consequently few unambiguous indications for the use of chloramphenicol. It has been used in severe typhoid and other salmonellal infections, although it does not eliminate the carrier state. Chloramphenicol is an alternative to a third-generation cephalosporin in the treatment of bacterial meningitis, both empirically and against sensitive organisms such as *Haemophilus influenzae*. It may be used as part of a multi-drug regimen for the treatment of inhalation and gastrointestinal anthrax. It has been used in the treatment of severe anaerobic infections, particularly in brain abscesses, and in infections below the diaphragm where *Bacteroides fragilis* is often implicated; however, other drugs are usually preferred. Although the tetracyclines remain the treatment of choice in rickettsial infections such as typhus and the spotted fevers, chloramphenicol is also used as an alternative where the tetracyclines cannot be given.

Other bacterial infections in which chloramphenicol may be used as an alternative to other drugs include ehrlichiosis, severe gastro-enteritis (including *Salmonella* enteritis, cholera, and *Yersinia* enteritis), gas gangrene, granuloma inguinale, severe *Haemophilus influenzae* infections (for example in epiglottitis), listeriosis, severe melioidosis, plague (especially if meningitis develops), pneumonia, psittacosis, Q fever, tularaemia (especially when meningitis is suspected), and Whipple's disease. For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

Chloramphenicol is extensively used in the topical treatment of ear and, in particular, eye infections, despite the fact that many of these are mild and self-limiting. It is also used topically in the treatment of skin infections.

When given orally, chloramphenicol is usually used as capsules or as a suspension of chloramphenicol palmitate. When oral use is not feasible, water-soluble chloramphenicol sodium succinate may be given intravenously, but oral therapy should be substituted as soon as possible; an intravenous dose should be injected over at least 1 minute. Intramuscular injection is controversial because of doubts whether absorption is adequate. In some countries chloramphenicol has been given rectally.

Doses are expressed in terms of chloramphenicol base and are similar whether given orally or intravenously. Chloramphenicol palmitate 1.7 g and chloramphenicol sodium succinate 1.4 g are each equivalent to about 1 g of chloramphenicol base.

For adults and children the usual dose is 50 mg/kg daily in divided doses every 6 hours; up to 100 mg/kg daily may be given in meningitis or severe infections due to moderately resistant organisms, although these higher doses should be reduced as soon as possible. It has been recommended that treatment should be continued after the patient's temperature has returned to normal for a further 4 days in rickettsial diseases, and for 8 to 10 days in typhoid fever, to minimise the risk of relapse.

Where there is no alternative to the use of chloramphenicol, premature and full-term neonates may be given daily doses of 25 mg/kg, in 4 divided doses, and full-term infants over the age of 2 weeks may be given up to 50 mg/kg daily, in 4 divided doses. Monitoring of plasma concentrations is essential to avoid toxicity.

In patients with hepatic impairment or severe renal impairment, the dose of chloramphenicol may need to be reduced because of decreased metabolism or excretion.

In the treatment of eye infections, chloramphenicol is usually applied as a 0.5% solution or as a 1% ointment.

For bacterial infections in otitis externa, chloramphenicol has been given as ear drops in a strength of 5 or 10%.

Chloramphenicol has also been used in the form of other derivatives including the arginine succinate, the cinnamate, the glycinate, the glycinate sulfate, the palmitoylglycolate, the pantothenate, the steaglate, the stearate, and the hydrogen succinate.

Administration. When parenteral use of chloramphenicol is necessary the intravenous route is generally preferred, although the intramuscular route has been advocated. Adequate serum concentrations after intramuscular injection have been reported,[1,2] although this is contrary to the widely held belief that chloramphenicol sodium succinate is poorly absorbed by this route. Pain on injection was also claimed to be minimal.[1] After a study in children with bacterial meningitis,[3] treatment with intramuscular chloramphenicol for 2 or 3 days followed by oral therapy has been suggested, although a later study[2] found that the intramuscular route produced therapeutic concentrations when the oral route did not. However, it has been said[4] that children describe intramuscular chloramphenicol as amongst the worst treatments they ever receive, and certainly much worse than the insertion of intravenous cannulae.

1. Shann F, *et al.* Absorption of chloramphenicol sodium succinate after intramuscular administration in children. *N Engl J Med* 1985; **313:** 410–14.
2. Weber MW, *et al.* Chloramphenicol pharmacokinetics in infants less than three months of age in the Philippines and The Gambia. *Pediatr Infect Dis J* 1999; **18:** 896–901.
3. Shann F, *et al.* Chloramphenicol alone versus chloramphenicol plus penicillin for bacterial meningitis in children. *Lancet* 1985; **ii** 681–3.
4. Coulthard MG, Lamb WH. Antibiotics: intramuscular or intravenous? *Lancet* 1985; **ii:** 1015.

Enterococcal infections. Chloramphenicol has been reported to be effective against vancomycin-resistant *Enterococcus faecium*.[1-3] Although no significant effect of chloramphenicol on mortality was found in one small study,[4] a retrospective analysis[5] of the outcomes of 6 patients with bacteraemia due to vancomycin-resistant *Enterococcus faecium* concluded that chloramphenicol was effective and should be considered as a treatment option.

1. Norris AH, *et al.* Chloramphenicol for the treatment of vancomycin-resistant enterococcal infections. *Clin Infect Dis* 1995; **20:** 1137–44.
2. Papanicolaou GA, *et al.* Nosocomial infections with vancomycin-resistant Enterococcus faecium in liver transplant recipients: risk factors for acquisition and mortality. *Clin Infect Dis* 1996; **23:** 760–6.
3. Mato SP, *et al.* Vancomycin-resistant Enterococcus faecium meningitis successfully treated with chloramphenicol. *Pediatr Infect Dis J* 1999; **18:** 483–4.
4. Lautenbach E, *et al.* The role of chloramphenicol in the treatment of bloodstream infection due to vancomycin-resistant Enterococcus. *Clin Infect Dis* 1998; **27:** 1259–65.
5. Ricaurte JC, *et al.* Chloramphenicol treatment for vancomycin-resistant Enterococcus faecium bacteremia. *Clin Microbiol Infect* 2001; **7:** 17–21.

Preparations

BP 2008: Chloramphenicol Capsules; Chloramphenicol Ear Drops; Chloramphenicol Eye Drops; Chloramphenicol Eye Ointment; Chloramphenicol Sodium Succinate Injection;
USP 31: Chloramphenicol and Hydrocortisone Acetate for Ophthalmic Suspension; Chloramphenicol and Polymyxin B Sulfate Ophthalmic Ointment; Chloramphenicol and Prednisolone Ophthalmic Ointment; Chloramphenicol Capsules; Chloramphenicol Cream; Chloramphenicol for Ophthalmic Solution; Chloramphenicol Ophthalmic Ointment; Chloramphenicol Ophthalmic Solution; Chloramphenicol Otic Solution; Chloramphenicol Palmitate Oral Suspension; Chloramphenicol Sodium Succinate for Injection; Chloramphenicol, Polymyxin B Sulfate, and Hydrocortisone Acetate Ophthalmic Ointment.

Proprietary Preparations (details are given in Part 3)
Arg.: A-Solmicina-C†; Anuar; Bio-Gelin†; Bioticaps; Chloromycetin; Farmicetina; Isopto Fenicol; Klonalfenicol; Pluscloran; Poenfenicol; Quemicetina; Quotal NF†; ***Austral.:*** Chloromycetin; Chlorsig; ***Austria:*** Halomycetin; Kemicetin; Oleomycetin; ***Belg.:*** Isopto Fenicol; Kemicetina†; ***Braz.:*** Amplobiotic†; Arifenicol; Auridonal†; Clorafenil; Cloranfenil†; Farmicetina†; Feniclor†; Fenicloran†; Neo Fenicol; Profenicol; Quemicetina; Sintomicetina; Uni Fenicol; Visalmin; Vixmicina; ***Canad.:*** Chloromycetin; Diochloram†; Pentamycetin; ***Chile:*** Chloromycetin; Clorampast; Gemitin; Quemicetina†; ***Fin.:*** Chloromycetin; Oftan Akvakol; Oftan Chlora; ***Fr.:*** Cebenicol†; ***Ger.:*** Aquamycetin-N†; Chloramsaar N†; Oleomycetin†; Paraxin; Posifenicol C; Thilocanfol C; ***Gr.:*** Chloranic; Ursa-Fenol; ***Hong Kong:*** Aristophen; Chloment†; Chloroph; Chlorsig; Europhenicol; Kemicetine; Spersanicol†; Vista-Phenicol†; Xepanicol; ***Hung.:*** Chlorocid†; ***India:*** Biophenicol; Chloraxin; Chloromycetin; Kemicetine Otological†; Kemicetine†; Paraxin; Reclor; Vanmycetin; Vitamycetin; ***Indon.:*** Chloramex; Chlorbiotic; Cloramidina; Colain; Colme; Combicetin; Empeecetin; Enkacetyn; Fenicol; Ikamicetin; Isotic Salmicol; Kalmicetine; Kemicetine; Lanacetine; Licoklor; Microtina; Neophenicol; Palmicol; RECO; Ribocine; Spersanicol; Suprachlor; Xepanicol; ***Irl.:*** Chloromycetin; ***Israel:*** Chloroptic; Chlorphenicol; Phenicol; Synthomycine; ***Ital.:*** Chemicetina; Cloramfen†; Mycetin; Sificetina; Vitamfenicolo; ***Malaysia:*** Beaphenicol; Nicol; Spersanicol†; Xepanicol†; ***Mex.:*** Abefen; Alcan†; Bariclor; Brocil; Chloromycetin; Clomicin; Clorafen; Cloramed; Cloramfeni; Clorampler; Cloran; Cloranmicron; Clorazin; Clordil; Clorfenil; Clorofunon; Clorotan; Diarman; Dilclor; Estreptopal; Exacol; Fenicol; Fenisol; Fenizzard; Lebrocetin; Leclor A; Naxo; Oftadil; Omycet; Palcol; Palmiclor; Palmifer; Palmisol; Proclonil; Pronicol; Quemicetina; Uniclor; Vixin†; ***Neth.:*** Globenicol†; ***NZ:*** Chloromycetin; Chlorsig; Isopto Fenicol†; ***Philipp.:*** Anphechlor; Aphrenil; Biomycetin; Chloro-S; Chloromycetin; Chlorsig; Clovicol; Esnicol; Fen-Alcon; Forastrol; Genphenil; Gerafen; Kemicetine; Klorfen; Medimycetin; Metrophenicol; Oliphenicol; Optomycin; Pediachlor; Penachlor; ***Pol.:*** Detreomycyna; ***Port.:*** Clorocil; Dermimade Cloranfenicol; Fenoptic†; Micetinoftalmina; ***Rus.:*** Synthomycin (Синтомицин); ***S.Afr.:*** Chloramex; Chlorcol; Chloromycetin; Chloroptic†; Chlorphen; Lennacol; Spersanicol; ***Singapore:*** Beaphenicol†; Isopto Fenicol; Kemicetine; Spersanicol†; Vanafen-S†; ***Spain:*** Chemicetina; Chloromycetin†; Cloranfenic†; Normofenicol†; ***Swed.:*** Chloromycetin; ***Switz.:*** Septicol; Spersanicol†; ***Thai.:*** Antibi-Otic; Archifen; Chloracil; Chloramno; Chloroph; Chlorosin; Cogenate; Cogetine; Fenicol†; Generin; Kemicetine†; Koro†; Levomycetin; Mycochlorin; Nicolmycetin†; Opsaram†; Pharmacetin; Silmycetin; Synchlolim; Unison Ointment; Vanafen; ***Turk.:*** Armisetin; Kemicetine; Klorasuksinat; ***UK:*** Brochlor; Chloromycetin; Golden Eye; Kemicetine; Optrex Infected Eyes; ***USA:*** Ak-Chlor†; Chloromycetin; Chloroptic†; ***Venez.:*** Chloromycetin†; Cloftal; Cloramfesa†; Quemicetina†.

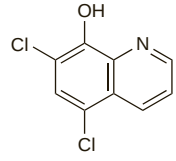
Multi-ingredient: ***Arg.:*** Acnoxin; Antiflogol; Bioftal; Clorfibrase; Colirio Antibiotico CNH; Esodar; Eubetal Biotic†; Fluoropoen; Iruxol; Klonovan; Neocortizul; Oftal; Oftalmoflogol†; Poenbioptal; Quemicetina con Hidrocortisona; Quemicetina Nasal Compuesta; Vistacloran†; ***Austria:*** Cortison Kemicetin; Oleomycetin-Prednison; ***Belg.:*** De Icol; ***Braz.:*** Dermofibrin C†; Dexaclor†; Dexafenicol; Epitezan; Fenidex; Fibrase; Fibrinase c/Cloranfenicol; Gino-Fibrase; Gyno Iruxol; Iruxol; Kollagenase com cloranfenicol; Naxogin Composto; Oto-Biotic†; Otofenicol-D†; Otomicina; Otopen†; Ouvidonal; Procutan†; Regencel; Regenom; Sulnil; ***Canad.:*** Pentamycetin-HC; ***Chile:*** Cortifenol H†; Gemitin con Prednisolona; Naxogin Compositum; Otandrol; Sintoftona; Spersadex Comp†; ***Cz.:*** Betabioptal†; Spersadex Compositum; ***Denm.:*** Spersadex Comp; ***Fin.:*** Iruxol; Oftan C-C; Oftan Dexa-Chlora; ***Fr.:*** Cebedexacol; ***Ger.:*** Aquapred; Berlicetin; Ichthoseptal; Oleomycetin-Prednison†; Spersadex Comp†; Spersadexolin†; ***Gr.:*** Chlorapred; Cortiphenol H; Dexachlor; Dispersadron-C; Geypirina; Nezefib; Spersadexoline†; Sulfachloramphenicol; Sulfanicole; ***Hong Kong:*** Chlomy-P†; Chloram-D; Cortiphenol H; Eurodron; Ginetris†; Neo-Dex (Improved); Sonexa-C; Spersadex Comp; Spersadexoline†; ***Hung.:*** Chlorocid-H†; Spersadex Comp†; ***India:*** Belmycetin-C; Candibiotic; Chlormixin; Chloromycetin Ear Drops; Cortison Kemicetine†; Dexosyn-C; Kemicetine Antiozena; Kemicetine Otological†; Ocupol; Ocupol-D; Otek-AC+; Otek-AC†; Paraxin Ear†; Perfocyn; Pyrimon; ***Indon.:*** Chloramphecort; Chloramphecort-H; Colsancetine; Gynoxa; Indoson; Kemiderm; Kloramixin; Kloramixin D; Klorfeson; Naxogin Complex; Otolin; Particol; Ramicort; Spersadex Comp; ***Israel:*** Phenimixin; Tarocidin; Tarocidin D; Threolone; ***Ital.:*** Antibioptal; Betabioptal; Cloradex; Colbiocin; Cortison Chemicetina; Cosmiciclina; Dexoline; Eubetal Antibiotico; Idracemi; Iruxol; Vasofen; Vitecaf; Xantervit Antibiotico; ***Malaysia:*** De Icol; Spersadex Comp†; Spersadexoline; ***Mex.:*** Cloran Otico; Cloxona-O; Fibrase; Levodexan; Levofenil; Nispil; Ofodex; Otalgan; Otifar; Otolone†; Poral; Pre Clor; Soldrin; Solfranicol; Sulfa Cloran; Trecloran; Ulcoderma; ***Norw.:*** Spersadex med kloramfenikol; ***Philipp.:*** Dexanicol; Spersadex Compound; ***Port.:*** Cloranpectina†; Clorcorticil†; Medrivas Antibiotico; Predniftalmina; ***Rus.:*** Candibiotic (Кандибиотик); Colbiocin (Колбиоцин); Cortomycetin (Кортомицетин); Iruxol (Ируксол); Levomecol (Левомеколь); Levosin (Левосин); ***S.Afr.:*** Covomycin; Covomycin-D; Covotop; Spersacet C†; Spersadex Comp; Spersadexoline; ***Singapore:*** Spersadex Comp†; Spersadexoline†; ***Spain:*** Blefarida; Cloram Zinc; Cloran Hemidex; Cortison Chemicet Topica; Dermisone Epitelizante; Dexam Constric†; Fluo Fenic; Icol; Medrivas Antib; Otosedol Biotico; Predni Azuleno; ***Switz.:*** Spersacet C†; Spersadex Comp; Spersadexoline†; ***Thai.:*** Archifen; Chlorotracin; Dermasol; Levoptin; Spersadexoline; Vagicin; ***UK:*** Actinac; ***Venez.:*** Clorasona; Deicol†; Otandrol†.

Chloroxine *(USAN)*

Cloroxinum; 5,7-Dichlorochinolin-8-ol; 5,7-Dichloroquinolin-8-ol; Kloroxin.

Хлороксин

$C_9H_5Cl_2NO$ = 214.0.
CAS — 773-76-2.



Profile
Chloroxine is a halogenated hydroxyquinoline with antibacterial and antifungal properties similar to those of clioquinol (p.254). It is used topically in the treatment of dandruff and seborrhoeic dermatitis of the scalp. It has also been given orally in preparations for gastrointestinal disorders.

Choroxine is a component of halquinol (p.286).

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Endiaron; ***USA:*** Capitrol.

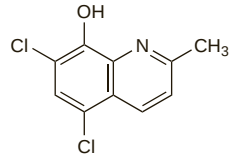
Multi-ingredient: ***Cz.:*** Endiform†; Triaderm; Triamcinolon Compositum†; Triamcinolon E; Triamcinolon-Galena†; ***Ital.:*** Beben Clorossina.

Chlorquinaldol *(BAN, rINN)*

Chlorochinaldol; Chlorquinaldolum; Clorquinaldol; Kloorikinaldoli; Klorkinaldol. 5,7-Dichloro-2-methylquinolin-8-ol.

Хлорхинальдол

$C_{10}H_7Cl_2NO$ = 228.1.
CAS — 72-80-0.
ATC — D08AH02; G01AC03; P01AA04; R02AA11.
ATC Vet — QD08AH02; QG01AC03; QR02AA11.



Pharmacopoeias. In *Pol*.

Profile
Chlorquinaldol is a halogenated hydroxyquinoline with properties similar to those of clioquinol (p.254). It is mainly applied topically in infected skin conditions and in vaginal infections.

Preparations

Proprietary Preparations (details are given in Part 3)
Hung.: Chlorosan†; ***Venez.:*** Agel†.

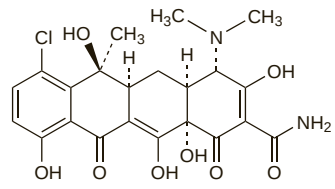
Multi-ingredient: ***Arg.:*** Nerisona C; ***Braz.:*** Bi-Nerisona; ***Chile:*** Bi-Nerisona; ***Cz.:*** Colposeptine†; Proctospre†; ***Denm.:*** Locoidol; ***Fin.:*** Locoidol†; ***Fr.:*** Nerisone C; ***Ger.:*** Nerisona C†; Proctospre†; ***Hong Kong:*** Colposeptine; Nerisone C; ***Indon.:*** Nerisona Combi; ***Irl.:*** Locoid C; ***Israel:*** Multiderm; ***Ital.:*** Impetex; Nerisona C; ***Mex.:*** Bi-Nerisona; ***Norw.:*** Locoidol; ***NZ:*** Locoid C; Nerisone C; ***Philipp.:*** Nerisona Combi; ***Pol.:*** Chlorchinaldin H; Gynalgin; Laticort-CH; ***Port.:*** Locoid C†; Nerisona C; Trophoseptine; ***Rus.:*** Gynalgin (Гиналгин); ***Singapore:*** Nerisone C†; ***Spain:*** Amplidermis; Claral Plus; Quinortar†; ***Switz.:*** Anginazol; ***Turk.:*** Colposeptine; Impetex; Nerisona C; ***UK:*** Locoid C; ***Venez.:*** Binerisona.

Chlortetracycline *(BAN, rINN)*

Chlortétracycline; Chlortetracyclinum; Clortetraciclina; Kloritetrasykliini; Klortetracyclin. (4*S*,4a*S*,5a*S*,6*S*,12a*S*)-7-Chloro-4-dimethylamino-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxonaphthacene-2-carboxamide; 7-Chlorotetracycline.

Хлортетрациклин

$C_{22}H_{23}ClN_2O_8$ = 478.9.
CAS — 57-62-5.
ATC — A01AB21; D06AA02; J01AA03; S01AA02.
ATC Vet — QA01AB21; QD06AA02; QJ01AA03; QJ51AA03; QS01AA02.



Chlortetracycline Bisulfate *(rINNM)*

Bisulfato de clortetraciclina; Chlortétracycline, Bisulfate de; Chlortetracycline Bisulphate *(BANM)*; Chlortetracyclini Bisulfas.

Хлортетрациклина Бисульфат

Pharmacopoeias. In *US* for veterinary use only.
USP 31 (Chlortetracycline Bisulfate). Store in airtight containers. Protect from light.