Chloramphenicol Sodium Succinate

Brand names	Chloromycetin, generic
Medication error potential	None reported
Contraindications and warnings	**U.S. boxed warning:** Serious and fatal blood dyscrasias (aplastic anemia, hypoplastic anemia, thrombocytopenia, and granulocytopenia). Cases of chloramphenicol-associated aplastic anemia have resulted in leukemia and have occurred with both short- and long-term use. These adverse effects may occur weeks to months after completion of therapy.[1] **Contraindications:** Should not be used in individuals with a history of previous hypersensitivity and/or toxic reaction to chloramphenicol.[1] It must not be used in the treatment of trivial infections or where it is not indicated, as in colds, influenza, infections of the throat; or as a prophylactic agent to prevent bacterial infections.[1] **Other warnings:** Prolonged use may cause superinfection and/or *Clostridium difficile*-associated diarrhea (CDAD), which has been reported and may range in severity from mild diarrhea to fatal colitis.[1] If CDAD is suspected or confirmed, appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile,* and surgical evaluation should be instituted as clinically indicated.[1]
Infusion-related cautions	None reported
Dosage	Inappropriate for mild-to-moderate infections.[1,2] When used, dosing should be optimized by measuring serum chloramphenicol concentrations.[1-3] **Neonates (see Significant Adverse Events in the Comments section)** **Loading dose:** Loading dose of 20 mg/kg followed in 12 hours by maintenance doses[4] **Maintenance dose:** Although the manufacturer recommends 25 mg/kg/day divided q 6 hr,[1] most sources recommend more conservative dosing in neonates.[3-11] **Premature, ≤1200 g:** 22 mg/kg q 24 hr[6] **Premature, ≤2000 g and ≤1 week:** 25 mg/kg q 24 hr[6] **Term, <2 weeks:** 25 mg/kg/day divided q 12 hr[3,5,7-10] **Term, 2–4 weeks:** 25–50 mg/kg/day divided q 12 hr[3,5,7-10] **Infants and children:** 50 mg/kg/day divided q 6 hr.[1,2,5,8-20] Because of the emergence of vancomycin-resistant *Enterococcus*, some have recommended 75–100 mg/kg/day divided q 6 hr for the treatment of meningitis.[1,18-21] Other investigators noted that 100 mg/kg/day may be unnecessary and only increases the incidence of toxicity.[5,14,15] Larger dosage (e.g., 100 mg/kg/day) may be required for severe infections and should only be given to maintain the serum chloramphenicol concentration within a "therapeutic" range.[1]
Dosage adjustment in organ dysfunction	Adjust dosage in patients with hepatic[8-11] or renal[21,22] dysfunction. When possible, dosage should be adjusted based on serum chloramphenicol concentrations. (See Pharmacokinetics in the Comments section.)[1]
Maximum dosage	100 mg/kg/day.[2,8,10,11] In neonates <2 weeks of age, 25 mg/kg/day[1] and 50 mg/kg/day in neonates <4 weeks of age.[1,24] Maximum *adult* dose should not exceed 2–4 g/day.[1] When large doses are used, serum concentration monitoring is imperative.
Additives	Contains 2.25 mEq (52 mg) sodium/g of chloramphenicol sodium succinate.[25]
Suitable diluents	D2.5W, D5W, D10W, NS, ½NS, LR, D5¼NS, D5½NS, D5LR, D5NS[25]

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Maximum concentration	100 mg/mL.[25] Concentrations of 128 mg/mL (osmolality 473 mOsm/kg) were recommended as suitable for peripheral infusion in fluid-restricted individuals.[25]
Preparation and delivery	*Parenteral products should be visually inspected for particulate matter and discoloration before use. Refer to appropriate references for more information on compatibility with other drugs and solutions, compatibility following Y-site delivery, and suggested storage and extended stability.*[25] **Stability:** The reconstituted solution is stable for 30 days at room temperature and activity is retained for 24 hours at pH 3.6–7.5 in D5W.[25] Cloudy solution should not be used.[25]
IV push	100 mg/mL over ≥1 minute[1]
Intermittent infusion	20–25 mg/mL over 15–60 minutes[6,17,25]
Continuous infusion	Although concentration and solution type were not provided, chloramphenicol has been given by this method.[27]
Other routes of administration	Although the product has been administered IM, the drug may be less effective and administration by this route in not recommended.[1] Has been administered intraventricularly in an *adult*.[28]
Comments	**Significant adverse events:** Fatalities associated with gray syndrome (e.g., abdominal distension, progressive pallid cyanosis, circulatory collapse with irregular respirations, acidosis, and myocardial depression) may result from drug accumulation in patients with immature or impaired hepatic or renal function or in those receiving unusually large doses.[29-33] Symptoms generally first appear after 3–4 days and death may occur within hours of the onset of symptoms.[1] Because the syndrome is generally associated with serum concentrations >90 mg/L, individualize dosage based on serum concentrations.[1] **Pharmacokinetics:** About 30% of chloramphenicol sodium succinate is renally eliminated unchanged as an inactive ester. The remainder is biotransformed to active chloramphenicol or chloramphenicol glucuronide. Decreased renal elimination of chloramphenicol sodium succinate cause an accumulation of the succinate ester, which results in increase availability of the prodrug for conversion to chloramphenicol. Patients with significant decrease in renal function continue to metabolize chloramphenicol sodium succinate, but accumulate the major metabolite (e.g., chloramphenicol glucuronide). Premature infants and neonates or those with significant hepatic or renal dysfunction have an inability to conjugate and excrete chloramphenicol sodium succinate, chloramphenicol, or chloramphenicol glucuronide which causes accumulation of these moieties that results in higher concentrations of chloramphenicol and more prolonged clearance. Both of these place the patient at risk for toxicity.[22] **Monitoring:** Hematological studies, which should be obtained at baseline and repeated every 2 days, are essential and may detect early peripheral blood changes.[1] The drug should be discontinued upon appearance of reticulocytopenia, leukopenia, thrombocytopenia, anemia or any other blood dyscrasias attributable to chloramphenicol. However, normal blood tests do not exclude the possibility of later appearance of irreversible type of bone marrow depression.[1] Serum chloramphenicol concentrations should be collected 90 minutes after completion of the IV dose (peak) and immediately prior to the next dose (trough). Dose adjustments should be based on desired serum chloramphenicol concentrations. For serous infections infections the target concentrations are: peak: 10–25 mg/L; trough: 5–10 mg/L.[38] Higher serum concentration may be required in patients with meningitis. **Drug interactions:** Chloramphenicol inhibits the metabolism of several drugs (e.g., phenytoin, phenobarbital, tolbutamide, dicumarol, cyclosporine, and tacrolimus).[35-37] Likewise, many drugs (e.g., rifampin, phenobarbital, and phenytoin) decrease chloramphenicol concentrations. Chloramphenicol should not be given with other medications know to cause bone marrow suppression.[1] Consult appropriate resources for dosing recommendations before combining any drug with chloramphenicol.