CHLORAMPHENICOL (Veterinary—Systemic)

Some commonly used *brand names* are:

For veterinary-labeled products—*Chlor 250; Chlor 500; Chlor 1000; Chloromycetin; Chlor Palm 125; Chlor Palm 250; Duricol; Karomycin Palmitate 125; Karomycin Palmitate 250;* and *Viceton*.

For human-labeled products—*Chloromycetin* and *Novochlorocap*.

Note: For a listing of dosage forms and brand names by country availability, see the *Dosage Forms* section(s).

Category:

Antibacterial (systemic).

Indications

Note: The text between [EL-US] and [EL] describes uses that are not included in U.S. product labeling. Text between [EL-CAN] and [EL] describes uses that are not included in Canadian product labeling.

The [EL-US] or [EL-CAN] designation can signify a lack of product availability in the country indicated. See the *Dosage Forms* section of this monograph to confirm availability.

Accepted

Chloramphenicol is a broad-spectrum antibiotic shown to have specific activity against a wide variety of organisms that are the causative agents of several disease conditions in domestic animals. Such organisms include staphylococci and streptococci; some gram-negative organisms, such as *Bordetella bronchiseptica, Escherichia coli,* and *Salmonella* species; anaerobic bacteria; and rickettsiae.{R-11} The species treated with chloramphenicol include dogs, [EL-US] cats [EL], and [EL-US,CAN] horses [EL].

Regulatory Considerations

U.S.—

Food and Drug Administration regulations ban chloramphenicol from use in animals that are used for food production. There are no safe residue levels, and no withdrawal times have been established.

Chloramphenicol Tablets USP are labeled for veterinary use only.

Canada—

Chloramphenicol is prohibited from use in food-producing animals by the Canadian Health Protection Branch.

Chloramphenicol Tablets USP are labeled for veterinary use only.

Chemistry

Source: Originally derived from *Streptomyces venezuelae*.{R-8}

Chemical name:

Chloramphenicol—Acetamide, 2,2-dichloro-*N*-[2-hydroxy-1-(hydroxymethyl)-2-(4-nitrophenyl)ethyl]-, [*R*-(*R**,*R**)]-.{R-9}

Chloramphenicol palmitate—Hexadecanoic acid, 2-[(2,2-dichloroacetyl)amino]-3-hydroxy-3-(4-nitrophenyl) propyl ester, [*R*-(*R**,*R**)]-.{R-9}

Chloramphenicol sodium succinate—Butanedioic acid, mono[2-[(2,2-dichloroacetyl)amino]-3-hydroxy-3-(4-nitrophenyl)propyl]ester, monosodium salt, [*R*-(*R**,*R**)]-.{R-9}

Molecular formula:

Chloramphenicol—$C_{11}H_{12}Cl_2N_2O_5$.{R-9}

Chloramphenicol palmitate—$C_{27}H_{42}Cl_2N_2O_6$.{R-9}

Chloramphenicol sodium succinate—$C_{15}H_{15}Cl_2N_2NaO_8$.{R-9}

Molecular weight:

Chloramphenicol—323.13.{R-9}

Chloramphenicol palmitate—561.54.{R-9}

Chloramphenicol sodium succinate—445.18.{R-9}

Description:{R-10}

Chloramphenicol USP—Fine, white to grayish white or yellowish white, needle-like crystals or elongated plates. Its solutions are practically neutral to litmus. Is reasonably stable in neutral or moderately acid solutions. Its alcohol solution is dextrorotatory and its ethyl acetate solution is levorotatory.

Chloramphenicol Palmitate USP—Fine, white, unctuous, crystalline powder, having a faint odor.

Chloramphenicol Sodium Succinate USP—Light yellow powder.

Solubility:{R-10}

Chloramphenicol USP—Slightly soluble in water; freely soluble in alcohol, in propylene glycol, in acetone, and in ethyl acetate.

Chloramphenicol Palmitate USP—Insoluble in water; freely soluble in acetone and in chloroform; soluble in ether; sparingly soluble in alcohol; very slightly soluble in solvent hexane.

Chloramphenicol Sodium Succinate USP—Freely soluble in water and in alcohol.

Pharmacology/Pharmacokinetics

Note: See also *Table 1. Pharmacokinetic Parameters* at the end of this monograph.

Mechanism of action/Effect:

Chloramphenicol is bacteriostatic. However, it may be bactericidal in high concentrations or when used against highly susceptible organisms.

Chloramphenicol, which is lipid soluble, diffuses through the bacterial cell membrane and reversibly binds to the 50 S subunit of the bacterial ribosomes where transfer of amino acids to growing peptide chains is prevented (perhaps by suppression of peptidyl transferase activity), thus inhibiting peptide bond formation and subsequent protein synthesis.

Absorption:

Chloramphenicol is rapidly absorbed from the gastrointestinal tract after oral administration in many simple-stomach animals.

Cats—Chloramphenicol palmitate is not absorbed well after oral administration to fasted cats.{R-1; 2}

Distribution:

Chloramphenicol diffuses readily into all body tissues, but at different concentrations. Highest concentrations are found in the liver and kidneys of dogs.

The lungs, spleen, heart, and skeletal muscles contain concentrations similar to that in the blood. Chloramphenicol reaches significant concentrations in the aqueous and vitreous humors of the eye. Within 3 to 4 hours after administration, the concentration in the cerebrospinal fluid reaches, on the average, 50% of the concentration in the serum. The percentage increases if there is inflammation of the meninges.

Chloramphenicol diffuses readily into milk and pleural and ascitic fluids and crosses the placenta, attaining concentrations of about 75% of that in maternal blood.

Biotransformation: Chloramphenicol is rather rapidly metabolized, mainly in the liver, by conjugation with glucuronic acid.

Elimination: Approximately 55% of a single daily dose can be recovered from the urine of a treated dog. A small fraction of this is in the form of unchanged chloramphenicol. The unchanged chloramphenicol is excreted by glomerular filtration (5 to 10%), whereas 80% is excreted via tubular secretion as inactive metabolite.

Precautions to Consider

Species sensitivity

Cats—Chloramphenicol should not be used in the cat for more than

14 days because it can cause dose-related blood dyscrasias.[R-2] The reported increased susceptibility of cats to development of blood dyscrasias relative to dogs or horses may be attributable to chloramphenicol's significantly longer elimination half-life in the cat.[R-6]

Pediatrics

All species

In the fetus and neonate, the immature liver cannot conjugate chloramphenicol, and toxic concentrations of active drug accumulate.

Dogs and cats

Sudden death has been reported in puppies and kittens receiving intravenous chloramphenicol.

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

Digitalis glycosides
(chloramphenicol decreases the rate of elimination of digitalis glycosides, which may lead to their accumulation to toxic concentrations)[R-3]

Erythromycin
(erythromycin and chloramphenicol compete for the same ribosome; therefore, the 2 medications may antagonize each other if used concurrently)

Medications metabolized by the mixed function oxidase system, especially:
Phenobarbital or
Primidone
(chloramphenicol irreversibly inhibits the hepatic microsomal enzymes of the cytochrome P450 complex, which may potentiate the effects of other medications that are metabolized by this complex)

Pentobarbital
(pentobarbital-induced anesthesia in dogs can be significantly prolonged by concurrent administration of chloramphenicol)[R-4]

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on the condition; » = major clinical significance):

» Complete blood counts (CBCs)
(CBCs may be required during therapy with chloramphenicol, particularly during prolonged administration, to detect aplastic anemia or bone marrow depression)

Culture and susceptibility, *in vitro*, and
Minimum inhibitory concentration (MIC)
(*in vitro* cultures and MIC tests should be done on samples collected prior to chloramphenicol administration to determine pathogen susceptibility)

Side/Adverse Effects

Note: Although aplastic anemia has occurred in human patients as a result of chloramphenicol administration, it has not been documented in animals.[R-6; 7] A dose-related reversible bone marrow suppression may occur, sometimes manifesting as pancytopenia or agranulocytosis.

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and, for humans, symptoms in parentheses where appropriate)—not necessarily inclusive:

Those indicating need for medical attention

All species

Anorexia; bone marrow suppression;[R-7] ***depression; diarrhea and vomiting***[R-6]

Note: Intermediate metabolites are thought to be responsible for the reversible *bone marrow suppression* seen in domestic animals.
The effect is dose-dependent, often occurring with long-term therapy.

Human side/adverse effects[R-12]

In addition to the above side/adverse effects reported in animals, the following side/adverse effects have been reported in humans, and are included in the human monograph *Chloramphenicol (Systemic)* in *USP DI Volume I;* these side/adverse effects are intended for informational purposes only and may or may not be applicable to the use of chloramphenicol in the treatment of animals:

Note: The hematologic toxicity of chloramphenicol can manifest itself in 1 of 2 ways—either as a reversible bone marrow depression or an idiosyncratic aplastic anemia. Bone marrow depression is dose-related and most commonly seen when serum concentrations of chloramphenicol exceed 25 mcg/mL. Bone marrow changes are usually reversible when chloramphenicol is discontinued. Aplastic anemia is an idiosyncratic reaction that occurs in 1 of every 25,000 to 40,000 courses of treatment. It is not related to dose or duration of therapy. Most cases have been associated with oral chloramphenicol, and the onset of aplasia may not occur until weeks or months after treatment with chloramphenicol has been discontinued.

Incidence less frequent
Blood dyscrasias; gastrointestinal reaction

Incidence rare
Gray syndrome—in neonates only; ***hypersensitivity reactions; neurotoxic reactions; optic neuritis; peripheral neuritis***

Note: *Gray syndrome* (or ''gray baby syndrome'') almost always occurs in newborn infants treated with inappropriately high doses of chloramphenicol. Typically, the infant has been started on chloramphenicol within the first 48 hours of life; symptoms first appear after 3 to 4 days of continued treatment with high doses of chloramphenicol; and serum concentrations are high, often between 40 and 200 mcg/mL. If detected early and chloramphenicol is discontinued, the infant may have a complete recovery. On rare occasion, older patients, including adults with severe liver disease, have also had a gray syndrome–type reaction.

Symptoms of possible fatal, irreversible bone marrow depression
Pale skin; sore throat and fever; unusual bleeding or bruising; unusual tiredness or weakness

Note: *Pale skin, sore throat and fever, unusual bleeding or bruising, unusual tiredness or weakness* may be symptoms of irreversible bone marrow depression leading to aplastic anemia, and the need for immediate medical attention if they occur weeks or months after medication is discontinued.

Overdose

For information in cases of overdose or unintentional ingestion, **contact the American Society for the Prevention of Cruelty to Animals (ASPCA) National Animal Poison Control Center** (888-426-4435 or 900-443-0000; a fee may be required for consultation) **and/or the drug manufacturer.**

Client Consultation

Because of the risk of idiosyncratic aplastic anemia that occurs in

people after exposure to chloramphenicol, extreme care during administration to animals should be exercised. Animals do not appear prone to develop the idiosyncratic aplastic anemia that can occur in people weeks or months after cessation of drug therapy.{R-5} In humans, the reported incidence of idiosyncratic aplastic anemia following chloramphenicol exposure ranges from 1/25,000 to 1/40,000. Aplastic anemia in humans may occur following oral, intramuscular, intravenous, ophthalmic, and/or topical administration. Due to these risks, chloramphenicol is banned in food-producing animals in the United States and people should avoid other types of exposure as well.

When administering chloramphenicol to animals, people should avoid direct contact with the medication (for example, avoid opening the capsules).

General Dosing Information

Most susceptible infectious disease organisms will respond to chloramphenicol therapy in 3 to 5 days when the recommended dosage regimen is followed.

If no response to chloramphenicol therapy is obtained in 3 to 5 days, use should be discontinued and the diagnosis reviewed.

Cats—Chloramphenicol should not be used in the cat for more than 14 days because it can cause dose-related blood dyscrasias.{R-2}

Chloramphenicol palmitate is not absorbed well after oral administration to fasted cats.{R-1; 2}

Oral Dosage Forms

Note: The dosing and strengths of the dosage forms available are expressed in terms of chloramphenicol base.

The text between EL[US] and EL describes uses not included in U.S. product labeling. Text between EL[CAN] and EL describes uses that are not included in Canadian product labeling.

The EL[US] or EL[CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CHLORAMPHENICOL CAPSULES USP

Usual dose: EL[CAN]Antibacterial[EL]—

Dogs: Oral, 45 to 60 mg per kg of body weight every eight hours.

EL[US]*Cats*[EL]: Oral, 13 to 20 mg per kg of body weight every twelve hours.

Note: The oral dose for cats is based on the best information available, which may, however, underestimate the dose needed in some cases. Doses of 25 to 50 mg per kg of body weight every twelve hours have been recommended, and may be necessary for some infections, but could increase the risk of side effects.

EL[US]*Horses*[EL]: Oral, 45 to 60 mg per kg of body weight every eight hours.

Strength(s) usually available:

U.S.—{R-11; 12}

Veterinary-labeled product(s):
50 mg (Rx) [*Duricol*].
100 mg (Rx) [*Duricol*].
250 mg (Rx) [*Duricol*].
500 mg (Rx) [*Duricol*].

Human-labeled product(s):
Not commercially available.

Canada—

Veterinary-labeled product(s):
Not commercially available.

Human-labeled product(s):
Not commercially available.

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container.

USP requirements: Preserve in tight containers. Contain the labeled amount, within –10 to +20%. Meet the requirements for Identification, Dissolution (85% in 30 minutes in 0.01 *N* hydrochloric acid in Apparatus 1 at 100 rpm), and Uniformity of dosage units.{R-10}

CHLORAMPHENICOL PALMITATE ORAL SUSPENSION USP

Usual dose: EL[US]Antibacterial[EL]—

Dogs: Oral, 45 to 60 mg per kg of body weight every eight hours.

Cats: Oral, 13 to 20 mg per kg of body weight every twelve hours.

Note: The oral dose for cats is based on the best information available, which may, however, underestimate the dose needed in some cases. Doses of 25 to 50 mg per kg of body weight every twelve hours have been recommended, and may be necessary for some infections, but could increase the risk of side effects.

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):
Not commercially available.

Canada—{R-11}

Veterinary-labeled product(s):
25 mg (base) per mL (Rx) [*Chlor Palm 125; Karomycin Palmitate 125*].
50 mg (base) per mL (Rx) [*Chlor Palm 250; Karomycin Palmitate 250*].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight, light-resistant container. Protect from freezing.

USP requirements: Preserve in tight, light-resistant containers. Contains an amount of chloramphenicol palmitate equivalent to the labeled amount of chloramphenicol, within –10 to +20%. Contains one or more suitable buffers, colors, flavors, preservatives, and suspending agents. Meets the requirements for Identification, Uniformity of dosage units (suspension packaged in single-unit containers), Deliverable volume (suspension packaged in multiple-unit containers), pH (4.5–7.0), and Limit of polymorph A.{R-10}

CHLORAMPHENICOL TABLETS USP

Usual dose: Antibacterial—

Dogs: Oral, 45 to 60 mg per kg of body weight every eight hours.

EL[US,CAN]*Cats*[EL]: Oral, 13 to 20 mg per kg of body weight every twelve hours.

Note: The oral dose for cats is based on the best information available, which may, however, underestimate the dose needed in some cases. Doses of 25 to 50 mg per kg of body weight every twelve hours have been recommended, and may be necessary for some infections, but could increase the risk of side effects.

EL[US,CAN]*Horses*[EL]: Oral, 45 to 60 mg per kg of body weight every eight hours.

Strength(s) usually available:{R-11}

U.S.—

Veterinary-labeled product(s):
250 mg (Rx) [*Viceton*].
500 mg (Rx) [*Viceton*].
1000 mg (Rx) [*Viceton*].

Canada—

Veterinary-labeled product(s):
250 mg (Rx) [*Chlor 250*].

500 mg (Rx) [*Chlor 500*].
1000 mg (Rx) [*Chlor 1000*].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container.

USP requirements: Preserve in tight containers. Label Tablets to indicate that they are for veterinary use only and are not to be used in animals raised for food production. Contain the labeled amount, within –10 to +20%. Meet the requirements for Identification, Disintegration (60 minutes), and Uniformity of dosage units.

Parenteral Dosage Forms

Note: The dosing and strengths of the dosage forms available are expressed in terms of chloramphenicol base.

The text between [EL(US)] and [EL] describes uses not included in U.S. product labeling. Text between [EL(CAN)] and [EL] describes uses that are not included in Canadian product labeling.

The [EL(US)] or [EL(CAN)] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CHLORAMPHENICOL SODIUM SUCCINATE FOR INJECTION USP

Usual dose: [EL(US,CAN)] Antibacterial [EL]—

Cats: Intramuscular, intravenous, or subcutaneous, 12 to 30 mg (base) per kg of body weight every twelve hours.

Dogs and *horses*: Intramuscular, intravenous, or subcutaneous, 45 to 60 mg (base) per kg of body weight every six to eight hours.

Strength(s) usually available: {R-8; 12}

U.S.—

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):

1 gram (base) per vial (Rx) [GENERIC].

Canada—

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):

1 gram (base) (Rx) [*Chloromycetin*].

Packaging and storage: Prior to reconstitution, store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer.

Preparation of dosage form: To prepare a 10% (100-mg-per-mL) solution, add 10 mL of an aqueous diluent such as sterile water for injection or 5% dextrose injection to each 1-gram vial. {R-8}

USP requirements: Preserve in Containers for Sterile Solids. Contains an amount of chloramphenicol sodium succinate equivalent to the labeled amount of chloramphenicol, within –10 to +15%. Meets the requirements for Bacterial endotoxins, Sterility, Particulate matter, and Limit of free chloramphenicol (not more than 2.0%), and for Identification, Specific rotation, pH, and Water under Chloramphenicol Sodium Succinate. {R-10}

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Table 1. Pharmacokinetic Parameters

Species	Elimination half-life (hours)	First order elimination rate constant (min^{-1})	Vol_D (L/kg)	Total body clearance (mL/min/kg)
Cats	5.1	0.0023	2.36	5.55
Dogs	1.20 ± 0.10	0.0098 ± 0.001	0.85 ± 0.06	8.57 ± 0.83
Horses	0.63 ± 0.04	0.0188 ± 0.001	1.41 ± 0.08	26.14 ± 1.28

References

1. Watson ADJ. Effect of ingesta on systemic availability of chloramphenicol from 2 oral preparations in cats. J Vet Pharm Ther 1979; 2: 117-21.
2. Panel comment, Rec 3/8/94.
3. Davis LE. Emergency drugs. In: Zaslow IM, editor. Veterinary trauma and critical care. Philadelphia: Lea and Febiger 1984. p. 287-338.
4. Teske RH, Carter GG. Effect of chloramphenicol on pentobarbital-induced anesthesia in dogs. J Am Vet Med Assoc 1971 Sep; 159(6): 777-80.
5. Booth NH, McDonald LE. Veterinary pharmacology and therapeutics, 6th ed. Ames: Iowa State University Press 1988. p. 837-8.
6. Plumb DC. Veterinary drug handbook. St. Paul: PharmaVet Publishing 1991. p. 530-4.
7. Weiss DJ. Aplastic anemia. In: Kirk RW, Bonagura JD, editors. Current veterinary therapy XI small animal practice. Philadelphia: W.B. Saunders 1992. p. 479-84.
8. Chloromycetin Sodium Succinate Product Information (King Pharmaceuticals—US), Rev 5/99. Downloaded 2/16/03 from www.kingpharm.com.
9. USP dictionary of USAN and international drug names, 2006 ed. Rockville, MD: The United States Pharmacopeial Convention, Inc., 2006.
10. The United States pharmacopeia. The national formulary. USP 29th revision (January 1, 2006). NF 24th ed (January 1, 2006). Rockville, MD: The United States Pharmacopeial Convention, Inc., 2006. Available at www.uspnf.com. Accessed on September 14, 2006.
11. Arrioja-Dechert A, editor. Compendium of veterinary products, CD ed. Port Huron, MI: North American Compendiums, Inc. 2006.
12. Klasco RK, editor. USP DI Drug information for the healthcare professional. Volume I. Greenwood Village, CO: MICROMEDEX, Inc.; 2006.