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 Palmilate 125; Karomycin Palmilate 250; and Victon.
- 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 ELUS and EL describes uses that are not included in U.S. product labeling. Text between ELUS,CAN and ELUS describes uses that are not included in Canadian product labeling. The ELUS or ELUS,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. The species treated with chloramphenicol include dogs, cats, and horses.

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.
Chemical name:
- Chloramphenicol—Acetamide, 2,2-dichloro-N-[2-hydroxy-1-(hydroxymethyl)-2-[(4-nitrophenyl)ethyl]-[R-(R*,R*)].
- Chloramphenicol palmitate—Hexadecanoic acid, 2-[(2,2-dichloroacetyl)amino]-3-hydroxy-3-(4-nitrophenyl) propyl ester, [R-(R*,R*)].
- Chloramphenicol sodium succinate—Butanedioic acid, monol[(2,2-dichloroacetyl)amino]-3-hydroxy-3-(4-nitrophenyl)propyl]ester, [R-(R*,R*)].
Molecular formula:
- Chloramphenicol—C_{11}H_{12}Cl_{2}N_{2}O_{5}.<ref>[R-8]</ref>
- Chloramphenicol palmitate—C_{11}H_{12}Cl_{2}N_{2}O_{5}.<ref>[R-9]</ref>
- Chloramphenicol sodium succinate—C_{11}H_{12}Cl_{2}N_{2}NaO_{5}.<ref>[R-8]</ref>
Molecular weight:
- Chloramphenicol—323.13.<ref>[R-9]</ref>
- Chloramphenicol palmitate—561.54.<ref>[R-9]</ref>
- Chloramphenicol sodium succinate—445.18.<ref>[R-9]</ref>
Description:<ref>[R-10]</ref>
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:<ref>[R-10]</ref>
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 peptide 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.<ref>[R-11]</ref>

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
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.\(^{[R-4]}\)

**Note:** Although aplastic anemia has occurred in human patients as a result of chloramphenicol administration, it has not been documented in animals.\(^{[R-4]}\) 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:

### 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.\(^{[R-4]}\) 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:

#### 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, \textit{in vitro}, and

- Minimum inhibitory concentration (MIC)
  \textit{(in vitro} cultures and MIC tests should be done on samples collected prior to chloramphenicol administration to determine pathogen susceptibility)

### Those indicating need for medical attention

**All species**

- Anemia; bone marrow suppression; \(= major clinical significance\)
  (or "gray baby syndrome") almost always occurs in newborn infants treated with inappropriately high doses of chloramphenicol.

- Gray syndrome—\textit{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

  - \textit{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. 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. Chloramphenicol palmitate is not absorbed well after oral administration to fasted cats.

**Oral Dosage Forms**

Note: The dosing and strengths of the dosage forms available are expressed in terms of chloramphenicol base. The text between ELUS and EL describes uses not included in U.S. product labeling. Text between ELUS and CAN describes uses that are not included in Canadian product labeling. The ELUS or 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:** Antibacterial—

- **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.
- **Horses**
  - Oral, 45 to 60 mg per kg of body weight every eight hours.

**Strength(s) usually available:**

- **U.S.—**
  - 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.

**CHLORAMPHENICOL PALMITATE ORAL SUSPENSION USP**

**Usual dose:** Antibacterial—

- **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**
    - 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.

**CHLORAMPHENICOL TABLETS USP**

**Usual dose:** Antibacterial—

- **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.
- **Horses**
  - Oral, 45 to 60 mg per kg of body weight every eight hours.

**Strength(s) usually available:**

- **U.S.—**
  - Veterinary-labeled product(s):
    - 250 mg (base) per mL (Rx) [Viceton].
    - 500 mg (base) per mL (Rx) [Viceton].
    - 1000 mg (base) per mL (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 elus and elc describes uses not included in U.S.
product labeling. Text between elus and elc describes uses that are
not included in Canadian product labeling.
The ELUS or ELUC 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: elus,eluc—
Antibacterial—
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.

Table 1. Pharmacokinetic Parameters

<table>
<thead>
<tr>
<th>Species</th>
<th>Elimination half-life (hours)</th>
<th>First order elimination rate constant (min⁻¹)</th>
<th>VolD (L/kg)</th>
<th>Total body clearance (mL/min/kg)</th>
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</thead>
<tbody>
<tr>
<td>Cats</td>
<td>5.1</td>
<td>0.0023</td>
<td>2.36</td>
<td>5.55</td>
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<tr>
<td>Dogs</td>
<td>1.20 ± 0.10</td>
<td>0.0098 ± 0.001</td>
<td>0.85 ± 0.06</td>
<td>8.57 ± 0.83</td>
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<tr>
<td>Horses</td>
<td>0.63 ± 0.04</td>
<td>0.0188 ± 0.001</td>
<td>1.41 ± 0.08</td>
<td>26.14 ± 1.28</td>
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</tbody>
</table>

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