## FLORFENICOL (Veterinary—Systemic)

- Some commonly used *brand names* for veterinary-labeled products are: *Aquaflor* and *Nuflor*.
- 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 <sup>ELUS</sup> and <sup>EL</sup> describes uses that are not included in U.S. product labeling. Text between <sup>ELCAN</sup> and <sup>EL</sup> describes uses that are not included in Canadian product labeling. The <sup>ELUS</sup> or <sup>ELCAN</sup> designation can signify a lack of product availability in the country indicated. See the *Dosage Forms* section of this monograph to confirm availability.

#### **General considerations**

Florfenicol is a broad-spectrum, primarily bacteriostatic, antibiotic with a range of activity similar to that of chloramphenicol, including many gram-negative and gram-positive organisms; [R-1] however, florfenicol does not carry the risk of inducing human aplastic anemia that is associated with chloramphenicol. [R-13 Florfenicol has been demonstrated to be active in vitro and in vivo against Mannheimia (Pasteurella) haemolytica, Pasteurella multocida, and Haemophilus somnus. [R-1; 2] In vitro studies have demonstrated florfenicol activity against Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, Salmonella typhi, and Shigella dysenteriae<sup>(R-2; 15; 16)</sup> but with at least a 2- to 10-fold higher minimum inhibitory concentration than that for the Mannheimia, Pasteurella and Haemophilus species listed above.<sup>[R-15; 16]</sup> It also has activity against some chloramphenicol-resistant strains of bacteria,<sup>[R-17]</sup> possibly because it is less affected by the major enzyme produced in plasmid-mediated bacterial resistance against chloramphenicol and thiamphenicol.<sup>[R-2; 26]</sup> Although the activity of florfenicol against obligate anaerobes is not addressed in the literature, it is likely to be quite effective.<sup>[R-28]</sup>

### Accepted

- ELCAN Enteric septicemia (treatment)<sup>EL</sup>—*Catfish:* Florfenicol Type A medicated article is indicated in the control of mortality due to enteric septicemia caused by susceptible strains of *Edwardsiella ictaluri*.<sup>(R-36)</sup>
- ELUS Furunculosis (treatment)<sup>EL</sup>—Salmon: Florfenicol Type A medicated article is indicated in the treatment of furunculosis caused by susceptible strains of Aeromonas salmonicida.<sup>(R-11)</sup>
- ELUSKeratoconjunctivitis, infectious (treatment)<sup>EL</sup>—*Cattle:* Florfenicol injection is indicated in Canadian product labeling in the treatment of infectious bovine keratoconjunctivitis caused by *Moraxella bovis*. <sup>[R-3; 33; 34]</sup>

Pneumonia, bacterial (treatment)-

- *Cattle:* Florfenicol injection is indicated in the treatment of bacterial pneumonia and associated respiratory infections (bovine respiratory disease complex) in cattle caused by susceptible *H. somnus, M. haemolytica,* and *P. multocida.*<sup>[R-1; 3]</sup> ELCAN Florfenicol injection is also indicated in the control of bacterial pneumonia and associated respiratory disease in cattle at high risk of developing infection associated with susceptible *H. somnus, M. haemolytica,* and *P. multocida.*<sup>EL[R-1; 3; 32]</sup>
- *Pigs*: <sup>ELCAN</sup>Florfenicol oral solution<sup>EL</sup> and <sup>ELUS</sup>florfenicol injection<sup>EL</sup> are indicated in the treatment of bacterial pneumonia and associated respiratory infections caused by susceptible *Actinobacillus pleuropneumoniae*, *P. multocida*, <sup>ELCAN</sup>Salmonella choleraesuis, and Streptococcus suis Type 2<sup>EL\_(R-3; 37)</sup>

Pododermatitis, infectious (treatment)-Cattle: Florfenicol injection is

indicated in the treatment of infectious pododermatitis (interdigital phlegmon) associated with susceptible *Bacteroides melaninogenicus* and *Fusobacterium necrophorum*.<sup>[R-1; 3; 30]</sup>

### **Regulatory Considerations**

U.S.—

Withdrawal times have been established for florfenicol in catfish and cattle; however, it is not labeled for use in lactating dairy cattle or in veal calves (see the *Dosage Forms* section).<sup>(R-1; 36)</sup>

Canada—

Withdrawal times have been established for florfenicol in cattle and salmon; however, it is not labeled for use in lactating dairy cattle or in veal calves (see the *Dosage Forms* section).<sup>[R-3; 11]</sup>

### Chemistry

Source: A fluorinated derivative of thiamphenicol. [R-12]

**Chemical name:** Acetamide, 2,2-dichloro-*N*-[1-(flouromethyl)-2hydrawy 2 [4 (mathylaylfanyl)phanyllathyl] [*P* (*P*\* 5\*)] <sup>[**R**-4</sup>]

hydroxy-2-[4-(methylsulfonyl)phenyl]ethyl]-[R-(R\*,S\*)]-(R-4) Molecular formula: C<sub>12</sub>H<sub>14</sub>C<sub>12</sub>FNO<sub>4</sub>S.

Molecular weight: 358.21.<sup>{R-4}</sup>

Description: Melting point 153 to 154 °C.<sup>{R-12</sup>}

**Solubility:** Soluble in water. <sup>{R-12; 13</sup>}</sup> Lipid soluble. <sup>{R-13</sup>}</sup>

### Pharmacology/Pharmacokinetics

- **Mechanism of action/Effect:** Florfenicol is a bacteriostatic antibiotic that inhibits protein synthesis by binding to ribosomal subunits of susceptible bacteria, leading to the inhibition of peptidyl transferase<sup>(R-1, 13; 26)</sup> and thereby preventing the transfer of amino acids to growing peptide chains and subsequent protein formation. The bacterial receptor that is the site of action for florfenicol is considered to be the same as that for chloramphenicol and thiamphenicol. <sup>(R-13; 26)</sup> In the treatment of bovine respiratory disease, florfenicol may be considered bactericidal against some *Mannheimia (Pasteurella) hemolytica* and *Pasteurella multocida* when it is administered to achieve minimum inhibitory concentrations (MICs);<sup>(R-14)</sup> the minimum bactericidal concentrations (MBCs) are very close to the MICs.
- Florfenicol has a fluorine atom instead of the hydroxyl group located at C-3 in the structure of chloramphenicol and thiamphenicol.<sup>(R-13)</sup> This may allow florfenicol to be less susceptible to deactivation by bacteria with plasmid-transmissible resistance that involves acetylation of the C-3 hydroxyl group in chloramphenicol and thiamphenicol, and prevents their interaction with bacterial ribosomes.<sup>(R-13; 26)</sup>
- Other actions/effects: Florfenicol, like thiamphenicol, lacks the nitro group located on the chloramphenicol aromatic ring that has been associated with chloramphenicol-induced, non-dose-related, irreversible aplastic anemia in people.<sup>[R-13; 24; 25]</sup> However, chloramphenicol and thiamphenicol also cause a dose-dependent, reversible bone marrow suppression in some animals and people<sup>[R-13]</sup> due to mitochondrial injury.<sup>[R-24]</sup> It is theoretically possible that florfenicol could cause some dose-dependent, reversible bone marrow suppression, but it has not been clinically reported.<sup>[R-13]</sup>

#### Absorption: Bioavailability-

Intramuscular administration: *Calves*, 3 to 6 months of age—78.5% (range 59.3 to 106%), with a dose of 20 mg per kg of body weight (mg/kg).<sup>(R-1;</sup>

Cattle, lactating—38 ± 14%, with a dose of 20 mg/kg.<sup>[R-9]</sup> Horses—81%, with a dose of 22 mg/kg.<sup>[R-19]</sup> Oral administration: Calves, 2 to 5 weeks of age-89%, at a dose of either 11 or 22 mg/kg; however, the absorption was widely variable.  ${}^{\{R-6; 7\}}$  Oral absorption may decrease when florfenicol is administered with milk replacers;  $^{\{R-6;\,7\}}$  one study reported bioavailability that ranged from 44 to 86% among calves when florfenicol was administered 5 minutes after feeding.<sup>{R-7}</sup>

Horses-83.3%, with a dose of 22 mg/kg.<sup>{R-19}</sup>

*Pigs*—24 to 97% with a single dose of 15 mg/kg.<sup>{R-37}</sup> Salmon, Atlantic-96.5%, with a dose of 10 mg/kg when water temperature is  $10.8 \pm 1.5$  °C.<sup>{R-22}</sup>

Note: After intramammary administration of a 20-mg/kg dose to lactating dairy cows, the systemic bioavailability was found to be  $54 \pm 18\%$ .<sup>{**R**-9</sup>}

#### **Distribution:**

Calves, 2 to 5 weeks of age-After multiple oral dosing (11 mg/kg every twelve hours for seven doses), florfenicol was well distributed into many tissues, reaching concentrations of 4 to 8 micrograms per gram (mcg/gram) in lungs, heart, pancreas, skeletal muscle, spleen, and synovia.  $^{[\rm R-6]}$  These concentrations were at least as high as serum concentrations.<sup>(R-6)</sup> Relatively high concentrations were found in bile, kidney, small intestine, and urine.<sup>(R-6)</sup> Concentrations in the brain (1 to 2 mcg/gram), cerebrospinal fluid (2 to 3 micrograms per milliliter [mcg/mL]), and aqueous humor (2 to 3 mcg/mL) have been found to be one quarter to one half the serum concentration in healthy calves.  ${}^{\{R-6\}}$ 

Salmon, Atlantic-Florfenicol is distributed to all organs and tissues with a dose of 10 mg/kg when the water temperature is 8.5 to 11.5 °C.<sup>{R-23}</sup> Concentrations in muscle and blood are similar to serum concentrations, while fat and the central nervous system (CNS) have lower concentrations. Only 25% of serum drug and metabolite concentrations are found in the brain.  $^{\left( R-23\right) }$ 

Volume of distribution (Vd) -- Intravenous administration:

Calves, 2 weeks to 6 months of age— Vd<sub>area</sub>: 0.88 liter per kg (L/kg);<sup>[R-2]</sup> 0.91 L/kg.<sup>[R-6]</sup> Vd<sub>ss</sub>: 0.77 L/kg;<sup>[R-1; 2; 8]</sup> 0.87 L/kg.<sup>[R-6]</sup>

Cattle-

Lactating: Vd<sub>ss</sub>-0.35 L/kg.<sup>{R-9}</sup>

Nonlactating: Vd<sub>area</sub>-0.67 L/kg (range, 0.62 to 0.76 L/kg).<sup>{R-5}</sup> Vd<sub>ss</sub>—0.62 L/kg (range, 0.57 to 0.68 L/kg).<sup>{R-5}</sup> Note: Although the data above imply that lactation causes a decrease in the volume of distribution of florfenicol, other data from these studies, including half-life of elimination and clearance, correlate well between the

two trials, one conducted in lactating and one in nonlacting cattle. The apparent difference here between lactating and nonlactating cattle may be due to calculation methods or dosing.<sup>[R-27]</sup>

Goats, lactating—Vd<sub>ss</sub>:  $0.98 \pm 0.09 \text{ L/kg}$ . {R-18}

 $\textit{Horses}{-\!\!-\!\!Vd_{ss}: 0.72 \pm 0.17 \text{ L/kg.}}^{\text{{\scriptsize $R$-19}$}}$ 

*Pigs*—Vd<sub>ss</sub>: 0.95  $\pm$  0.06 L/kg.<sup>{R-37</sup>}</sup>

Salmon, Atlantic-Vdss: 1.12 L/kg at a water temperature of 10.8  $\pm 1.5 \ ^{\circ}C.^{\{R-22\}}$ 

### **Protein binding:**

Calves, 3 to 6 months of age-

12.7%, with serum concentration of 0.5 mcg/mL.<sup>{R-2</sup>}

13.2%, with serum concentration of 3 mcg/mL.<sup>{R-1; 2</sup>}

18.3%, with serum concentration of 16 mcg/mL.<sup>{R-1; 2</sup>}

Cattle-Considered independent of drug concentration: 17.5%, with serum concentration of 5 mcg/mL.<sup>{R-5}</sup> 18.6%, with serum concentration of 50 mcg/mL.<sup>{R-5}</sup>

#### **Biotransformation:**

Cattle-Approximately 64% of a 20 mg/kg dose of intramuscular

florfenicol administered two times, 48 hours apart, is excreted as parent drug in the urine.<sup>[R-13]</sup> Urinary metabolites include florfenicol amine, florfenicol alcohol, florfenicol oxamic acid, and monochloroflorfenicol. [R-13] Florfenicol and its metabolites, such as monochloroflorfenicol and florfenicol oxamic acid, also are eliminated in the feces. [R-13] Florfenicol amine is the longest-lived major metabolite in the liver, and, therefore, it was used as the marker residue for withdrawal calculations. [R-13]

Salmon, Atlantic-Florfenicol is rapidly metabolized at water temperatures of 8.5 to 11.5 °C and the major metabolite is florfenicol amine.  $^{(R-23)}$ 

#### Half-life:

Distribution-Intravenous administration: Calves, less than 8 weeks of age—0.13 hour (range, 0.075 to 0.27 hour);<sup>[R-6]</sup> 0.098 hour (range, 0.081 to 0.17 hour).<sup>[R-7]</sup>

Elimination-Intravenous administration:

Calves, less than 8 weeks of age—2.86 hours (range, 2.3 to 3.39 hours);<sup>(R-7)</sup> 3.71 hours (range, 3.5 to 4.11 hours). {R-6}

Calves, 3 to 6 months of age—2.6 hours (range, 2.4 to 3 hours).<sup>[R-2; 8]</sup>

Cows

Lactating: 2.9 hours. [R-9]

Nonlactating: 3.2 hours.<sup>{R-5}</sup> Goats, lactating—2.3  $\pm$  0.2 hours.<sup>{R-18}</sup>

*Horses*— $1.8 \pm 0.9$  hours.<sup>{**R**-19}</sup>

*Pigs*—2.2  $\pm$  0.3 hours.<sup>{**R**-37}</sup>

Salmon, Atlantic-12.2 hours at a water temperature of  $10.8 \pm 1.5 \ ^{\circ}C.^{\{R-22\}}$ 

Intramuscular administration (terminal half-life): Calves, 3 to 6 months of age—18.3 hours (range, 8.3 to 44 hours).<sup>{R-1;</sup>

#### **Concentrations:**

Peak serum concentration-

Intramuscular administration:

- Calves, 3 to 6 months of age-3 mcg per mL (range, 1.43 to 5.6 mcg/mL) at 3.33 hours (range, 0.75 to 8 hours), with a dose of 20 mg/kg.  $^{(R-1;\,2;\,8)}$
- Cows, lactating—2.3 mcg/mL at 3 hours, with a dose of 20 mg/kg.<sup>[R-9]</sup>
- Horses  $4 \pm 1.2$  mcg/mL at  $1.3 \pm 0.5$  hours, with a dose of 22 mg/kg. <sup>(R-19)</sup>

Oral administration:

Calves, less than 8 weeks of age— $11.32 \pm 4.04 \text{ mcg/mL}$  at  $2.5 \pm 0.72$  hours, with a dose of 22 mg/kg.<sup>{R-7}</sup>

*Horses*—13.8  $\pm$  4.8 mcg/mL at 1.1  $\pm$  0.5 hours, with a dose of 22 mg/kg. <sup>(**R**-19)</sup>

Salmon, Atlantic-4 mcg/mL at 10.3 hours, with a dose of 10 mg/kg when water temperature is 10.8  $\pm$  1.5 °C.  $^{\text{\{R-22\}}}$ 

Note: After intramammary administration of 20 mg/kg to lactating dairy cows, the peak serum concentration was 6.9 mcg/mL at 6 hours.  $^{[{\bf R} \cdot {\bf 9}]}$ 

Other serum concentration-Oral administration in drinking water: Pigs-Florfenicol serum concentration was maintained at greater than 1 mcg/mL during most of the 5-day administration of drinking water containing florfenicol at a concentration of 400 mg per gallon. {R-37}

- Peak milk concentration-
  - Intramuscular administration: Cows, lactating-1.6 mcg/mL at 10 hours, with a 20 mg/kg dose.<sup>[R-9]</sup>

Intravenous administration:

- Cows, lactating-5.4 mcg/mL at 3 hours, with a 20 mg/kg dose. [R-9]
- Goats, lactating—13.2  $\pm$  1.9 mcg/mL at 1 hour, with a 25 mg/kg dose. {R-18}

#### **Duration of action:**

- *Calves*, 3 to 6 months of age—The serum concentration of florfenicol was maintained above 1 mcg per mL for  $22.3 \pm 5.9$  hours after intramuscular administration and  $11.5 \pm 1.1$  hours after intravenous administration of 20 mg/kg.<sup>(R-2)</sup>
- Salmon, Atlantic—Plasma concentrations were maintained above the minimum inhibitory concentration of 0.8 mcg/mL reported for Aeromonas salmonicida, Vibrio anguillarum, and V. salmonicida for 36 to 40 hours after a single oral florfenicol dose of 10 mg/kg in water temperatures of  $10.8 \pm 1.5$  °C.<sup>[R-22]</sup>

#### **Elimination:**

- *Calves*, less than 8 weeks of age—Approximately 50% of a 22 mg/ kg intravenous dose is eliminated unchanged in the urine within 30 hours.<sup>(B-7)</sup>
- Cattle—Approximately 64% of a 20 mg/kg intramuscular dose administered two times, 48 hours apart, is excreted as parent drug in the urine.<sup>(R-13)</sup>
- *Horses*—Approximately 13% of a 22 mg/kg intravenous dose, 7% of the same dose given intramuscularly, and 6% when given orally, is excreted unchanged in the urine in the first 30 hours.<sup>(R-19)</sup>
- Rats—Approximately 60 to 70% of a 20 mg/kg oral dose administered once a day for 7 days is eliminated in the urine. (R-13)
  Approximately 20 to 30% is eliminated in the feces in the first 24 hours after a 20 mg/kg oral dose. (R-13)

Total clearance-Intravenous administration:

#### Calves—

- Less than 8 weeks of age: 2.9 mL per minute per kg (range, 2.44 to 4 mL/min/kg).<sup>[R-6; 7]</sup>
- 3 to 6 months of age: 3.75 mL/min/kg (range, 3.17 to 4.31 mL/ min/kg).<sup>[R-1; 2; 8]</sup>

Cows—

- Lactating: 2.7 ± 0.6 mL/min/kg.<sup>[R-9]</sup> Nonlactating: 2.45 mL/min/kg (range, 2.25 to 2.67 mL/min/kg).<sup>[R-5]</sup>
- Goats, lactating—8.1  $\pm$  2.6 mL/min/kg.<sup>{R-18}</sup>
- Horses-6.7 ± 1.7 mL/min/kg.<sup>{R-19}</sup>
- $Pigs = 5.6 \pm 0.6 \text{ mL/min/kg}.^{\{\mathbf{R}-37\}}$
- Salmon, Atlantic—1.4 mL/min/kg when water temperature is 10.8  $\pm$  1.5 °C.<sup>(R-22)</sup>

### **Precautions to Consider**

### **Pregnancy/Reproduction**

The effects of florfenicol on reproductive performance and pregnancy have not been determined. <sup>[R-1]</sup> According to product labeling, administration to breeding cattle or pigs is not recommended. <sup>[R-3;</sup> <sub>37]</sub>

#### Lactation

The effect of florfenicol on lactation has not been determined.<sup>[R-1]</sup> Goats: Florfenicol concentration in milk equals serum concentration when serum concentrations are nearly constant.<sup>[R-18]</sup>

#### Medical considerations/Contraindications

- The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance).
- Except under special circumstances, this medication should not be used when the following medical problem exists:
- » Previous allergic or toxic reaction to florfenicol

### Side/Adverse Effects

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

#### Those indicating need for medical attention

Note: There is no documentation of dose-dependent, reversible bonemarrow suppression caused by florfenicol use in animals; however, the protection against human aplastic anemia, due to the difference in structure of florfenicol from chloramphenicol, does not necessarily protect against suppression of mitochondrial protein synthesis in bone marrow and subsequent reversible anemia.<sup>[R-13]</sup> This phenomenon is not considered a side/adverse effect with normal clinical use, but an awareness of this possibility may be useful if long-term therapy with this medication is considered.

### Incidence unknown

#### Horses, ponies

*Diarrhea, mild*—in one study, occurred in all three horses and three ponies administered a single dose of 22 mg per kg of body weight by either the oral or parenteral route<sup>(R-19)</sup>

### Those indicating need for medical attention only if they

#### continue or are bothersome Incidence more frequent

Incidence Pigs

### Peri-anal inflammation; rectal eversion

Note: Peri-anal inflammation and rectal eversion may occur in 50% or more of pigs administered parenteral florfenicol and may last up to a week.<sup>(R-3)</sup> Transient peri-anal inflammation has also been reported in some pigs with orally administered florfenicol.<sup>(R-37)</sup>

Incidence unknown

### Catfish

Hematopoietic/lymphopoietic tissue decrease

Note: A minimal to mild dose-related decrease in hematopoietic/lymphopoietic tissue was noted in the kidneys and spleens of some catfish administered 10 mg per kg of body weight for twenty days (twice the duration recommended on product labeling).<sup>[R-36]</sup>

#### Cattle

#### Decreased food consumption, transient;<sup>[R-1; 3]</sup> decreased water consumption, transient;<sup>[R-1]</sup> diarrhea, transient;<sup>[R-1; 3]</sup> local tissue reactions—more severe if administered at injection sites other than the neck<sup>[R-10]</sup>

Note: In a controlled study over 43 days, florfenicol administration had no long-term effect on body weight, rate of weight gain, or feed consumption, although a transient decrease in food and water consumption occurred at the start of therapy.<sup>(R-1; 10)</sup>

#### Overdose

For more 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.

#### **Clinical effects of overdose**

- The following effects have been selected on the basis of their potential clinical significance (possible signs in parentheses where appropriate)—not necessarily inclusive:
- Calves, with intramuscular administration of 200 mg per kg of body weight (mg/kg) repeated in forty-eight hours (10 times the labeled dose)<sup>[R-1]</sup>

Anorexia, marked;<sup>{R-1</sup>} decreased body weight;<sup>{R-1</sup>} decreased rumen activity;<sup>{R-10</sup></sup> decreased water consumption;<sup>{R-1;10</sup></sup> ketosis, slight—secondary to anorexia;<sup>{R-10</sup>} serum enzymes, including alanine aminotransferase [SGPT], aminoacyltransferase [GGT], aspartate aminotransferase [SGOT], and lactase dehydrogenase [LDH], mildy increased;<sup>{R-10</sup>} soft feces<sup>(R-10)</sup>

Dogs, 4- to 6-month-old, with oral administration of 10 to 12 mg/kg a

### day for thirteen weeks $^{\{R-10\}}$

### Hepatotoxicity

*Dogs*, 4-month-old, with oral administration of 30 to 100 mg/kg a day for thirteen weeks<sup>(R-10)</sup>

*Central nervous system vacuolization; hematopoietic changes* with the 100-mg/kg dose; *renal tubule dilation*—with the 100mg/kg dose; *testicular atrophy*—with the 100-mg/kg dose

Pigs, with oral administration in the drinking water at a concentration of 1200 to 2000 mg per gallon (3 to 5 times the labeled dose) for 15 to 16 days (3 times the labeled duration) or with 4000 mg/gal (10 times the labeled dose) for 5 to 6 days:<sup>(R-37)</sup>
 Constipation, transient; decreased feed consumption

#### Treatment of overdose

There is no specific treatment for florfenicol overdose. Therapy should be supportive.

### **General Dosing Information**

Minimum inhibitory concentration (MIC) of florfenicol against *Edwardsiella ictaluri* isolated from channel catfish between 1998 and 2001:<sup>(R-36)</sup>

Organism	Number of Isolates	MIC <sub>90</sub> (mcg/mL)	MIC range (mcg/mL)
Edwardsiella ictaluri	95	0.25	0.25

Minimum inhibitory concentrations (MICs) of florfenicol were determined for pathogens involved in natural bovine respiratory complex in the U.S., Canada, and Europe between 1990 and 1993:<sup>[R-1]</sup>

Organism	Number of	MIC <sub>50</sub>	MIC <sub>90</sub>
	Isolates	(mcg/mL)	(mcg/mL)
Bacteroides melaninogen-	20	0.25	0.25
icus			
Fusobacterium necrophorum	33	0.25	0.25
Haemophilus somnus	66	0.25	0.5
Mannheimia haemolytica	398	0.5	1
Pasteurella multocida	350	0.5	0.5

Note: MIC can vary according to pathogen strain; therefore, cattle in different geographic locations may harbor organisms with different MICs.<sup>(R-10)</sup>

Minimum inhibitory concentrations (MICs) of florfenicol against bacterial isolates of swine from diagnostic laboratory and clinical field studies conducted in the United States between 1990 and 2001.<sup>[R-37; 38]</sup>

Organism	Number of Isolates	MIC <sub>90</sub> (mcg/mL)	MIC Range (mcg/mL)
Actinobacillus pleuropneu- moniae	360	0.5	≤0.125- 2.0
Pasteurella multocida	335	0.5	≤0.125- 2.0
Salmonella choleraesuis	46	4.0	2.0-4.0
Streptococcus suis Type 2	203	2.0	0.5-2.0

#### For treatment of adverse effects

Recommended treatment consists of the following: For anaphylaxis

· Parenteral epinephrine and cardiovascular support.

• Oxygen administration and respiratory support.

### **Oral Dosage Forms**

Note: The text between <sup>ELUS</sup> and <sup>EL</sup> describes uses not included in U.S. product labeling. Text between <sup>ELCAN</sup> and <sup>EL</sup> describes uses that are not included in Canadian product labeling. The <sup>ELUS</sup> or <sup>ELCAN</sup> designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

### FLORFENICOL ORAL SOLUTION

Usual dose: <sup>ELCAN</sup>Pneumonia, bacterial<sup>EL</sup>—*Pigs*: Oral, 400 mg per gallon of water (100 parts per million), administered as the only source of water for five days.<sup>[R-37]</sup> <u>Withdrawal time</u>—US: Meat—16 days.<sup>[R-37]</sup>

### Strength(s) usually available:

U.S.— Veterinary-labeled product(s): 23 mg per mL (Rx) [Nuflor 2.3% Concentrate Solution].<sup>(R-37)</sup>

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

- **Packaging and storage:** Store between 2 and 25 °C (36 and 77 °F), unless otherwise specified by the manufacturer.<sup>[R-37]</sup> This product should not be stored in galvanized metal containers.<sup>[R-37]</sup>
- **Incompatibilities:** Product labeling states that the recommendations on proportioner setting should be followed to avoid drug precipitation. Automatic water proportioners should not be used if water hardness is greater than 275 parts per million. Galvanized metal watering systems should not be used and chlorinaters should not be operated while the medication is being adminstered.<sup>(R-37)</sup>
- **Caution:** Product labeling recommends that handlers should not allow this medication to contact their skin, eyes, or clothing.<sup>[R-37]</sup> If eyes are accidently exposed, flush with water for 15 minutes; if skin is accidently exposed, wash with soap and water and remove contaminated clothing. If irritation persists, a doctor should be consulted.<sup>[R-37]</sup>

Keep out of the reach of children. [R-37]

USP requirements: Not in USP. {R-31}

# FLORFENICOL TYPE A MEDICATED ARTICLE Usual dose:

- <sup>LCAN</sup>Enteric septicemia (treatment)<sup>EL</sup>—*Catfish:* Oral, 10 mg per kg of body weight a day for ten days, administered in the only ration, according to manufacturer labeling. <sup>(R-36)</sup> <u>Withdrawal time</u>—US: Meat—12 days. <sup>(R-36)</sup>
- ELUS Furunculosis EL\_Salmon: Oral, 10 mg per kg of body weight a day for ten days, administered in the only ration, according to manufacturer labeling. (R-11)

<u>Withdrawal time</u>—Canada: Meat—12 days.<sup>{R-11</sup>}</sup> This product is not labeled for use in fish maintained at water temperatures less than 5 °C.

#### Strength(s) usually available:<sup>{R-35}</sup>

#### U.S.-

Veterinary-labeled product(s): 500 grams per kg of premix (Veterinary Feed Directive) [Aquaflor].<sup>[R-36]</sup>

Canada—

Veterinary-labeled product(s):

500 grams per kg of premix (Rx) [Aquaflor].<sup>{R-11</sup>}</sup>

- **Packaging and storage:** Store between 2 and 30 °C (36 and 86 °F), unless otherwise specified by the manufacturer.<sup>[R-36]</sup> Keep separate from other feeds.<sup>[R-11]</sup> Store in a dry place.<sup>[R-29]</sup>
- Stability: Premix should be used within 12 months of opening pouch.<sup>(R-11)</sup> Medicated feed should be used within 6 months of the manufacture date.<sup>(R-11)</sup>
- **Caution:** Product labeling recommends that handlers wear protective clothing when handling this medication, avoid inhalation of dust and contact with skin and eyes, and wash with soap and water after handling.<sup>[R-11]</sup> If eyes are accidently exposed, flush thoroughly with water. If irritation persists, a doctor should be consulted.<sup>[R-11]</sup>

Keep out of the reach of children.  $^{\{ R-11\} }$ 

USP requirements: Not in USP.<sup>{R-31}</sup>

#### **Parenteral Dosage Forms**

Note: The text between <sup>ELUS</sup> and <sup>EL</sup> describes uses not included in U.S. product labeling. Text between <sup>ELCAN</sup> and <sup>EL</sup> describes uses that are not included in Canadian product labeling.

The <sup>ELUS</sup> or <sup>ELCAN</sup> designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

#### **FLORFENICOL INJECTION**

#### Usual dose:

- EL<sup>US</sup>Keratoconjunctivitis, infectious<sup>EL</sup>;
- Pneumonia (treatment); or
- Pododermatitis, infectious—Cattle:
  - Intramuscular, 20 mg per kg of body weight, to be repeated in forty-eight hours. <sup>{R-1; 3</sup>}</sup>
  - Subcutaneous, 40 mg per kg of body weight as a single dose.  ${}^{(R-1)}$
- ELCAN Pneumonia (control) <sup>EL</sup>—*Cattle*: Subcutaneous, 40 mg per kg of body weight as a single dose. <sup>[R-1; 32]</sup>

Withdrawal times: US—*Cattle*: Meat—28 days with intramuscular administration, 38 days with subcutaneous administration. This product is not labeled for use in female dairy cattle 20 months of age or older, veal calves, calves under 1 month of age, or calves being fed an all-milk diet<sup>[R-1]</sup> as withdrawal times have not been studied. If florfenicol is injected at sites other than the neck, local reaction may result in trim loss of edible tissue at slaughter.<sup>[R-1]</sup> Canada—*Cattle*: Meat—36 days with intramuscular administration, 55 days with subcutaneous administration.<sup>[R-3]</sup> This product is not labeled for use in lactating dairy cattle.<sup>[R-3]</sup>

- Pneumonia (treatment)—<sup>ELUS</sup>Pigs<sup>EL</sup>: Intramuscular, 15 mg per kg of body weight, to be repeated in forty-eight hours.<sup>[R-3]</sup> <u>Withdrawal times</u>—Canada: *Pigs*—Meat: 15 days.<sup>[R-3]</sup> To reduce the risk of excess trim at the injection site, pigs should not be slaughtered for 21 days after last administration.<sup>[R-3]</sup>
- Note: No more than 10 mL should be injected at each site.<sup>(R-1; 3)</sup> According to the product labeling, if clinical improvement is not noted within twenty-four hours, the diagnosis should be reevaluated.<sup>(R-1)</sup>

### Strength(s) usually available:<sup>{R-35}</sup>

U.S.-

Veterinary-labeled product(s): 300 mg per mL (Rx) [Nuflor].<sup>{R-1}</sup>

Canada—

Veterinary-labeled product(s):

300 mg per mL (Rx) [*Nuflor*].<sup>{**R**-3</sup>

- **Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer. Protect from freezing.
- **Caution:** Florfenicol injection can be irritating to eyes and skin; therefore, avoid direct contact with skin, eyes, and clothes.<sup>[R-1]</sup> In case of accidental eye exposure, flush with water for 15 minutes; for skin exposure, wash with soap and water.<sup>[R-1]</sup> Remove exposed clothing and consult a physician if irritation persists. Accidental injection may cause local irritation and a physician should be consulted immediately.<sup>[R-1]</sup>
- Additional information: The light yellow to straw color of the solution does not affect potency.<sup>{R-1}</sup>

USP requirements: Not in USP. {R-31}

Developed: 07/08/98 Revised: 6/30/02 Interim revision: 10/15/99; 04/04/03; 11/06/06

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