Norfenicol®
(florfenicol)
Injectable Solution
300 mg/mL

For intramuscular and subcutaneous use in beef and
non-lactating dairy cattle only.

Not for use in female dairy cattle 20 months of age or
older or in calves to be processed for veal.

CAUTION: Federal law restricts this drug to use by or on
the order of a licensed veterinarian.

DESCRIPTION: Norfenicol® Injectable Solution is a
solution of the synthetic antibiotic florfenicol. Each
milliliter of sterile Norfenicol Injectable Solution contains
300 mg of florfenicol, 250 mg 2-pyrrolidone, and glycerol
formal qs.

INDICATIONS: Norfenicol Injectable Solution is
indicated for treatment of bovine respiratory disease
(BRD) associated with Mannheimia haemolytica,
Pasteurella multocida, and Histophilus somni, and for the
treatment of bovine interdigital phlegmon (foot rot, acute
interdigital necrobacillosis, infectious pododermatitis)
associated with Fusobacterium necrophorum and
Bacteroides melaninogenicus. Also, it is indicated for
the control of respiratory disease in cattle at high risk of
developing BRD associated with Mannheimia
haemolytica, Pasteurella multocida, and Histophilus
somni.

DOSAGE AND ADMINISTRATION: For treatment of
bovine respiratory disease (BRD) and bovine interdigital
phlegmon (foot rot): Norfenicol Injectable Solution
should be administered by intramuscular injection to
cattle at a dose rate of 20 mg/kg body weight (3 mL/100
lbs). A second dose should be administered 48 hours
later. Alternatively, Norfenicol Injectable Solution can
be administered by a single subcutaneous (SC) injection
to cattle at a dose rate of 40 mg/kg body weight (6
mL/100 lbs). Do not administer more than 10 mL at each
site. The injection should be given only in the neck.

For control of respiratory disease in cattle at high-risk
of developing BRD: Norfenicol Injectable Solution
should be administered by a single subcutaneous
injection to cattle at a dose rate of 40 mg/kg body weight
(6 mL/100 lbs). Do not administer more than 10 mL at each
site. The injection should be given only in the neck.

ADVERSE REACTIONS:

Clinical improvement should be evident in most treated
subjects within 24 hours of initiation of treatment. If a
positive response is not noted within 72 hours of
initiation of treatment, the diagnosis should be re-evaluated.

CONTRAINdications: Do not use in animals that have
shown hypersensitivity to florfenicol.

WARNINGS: NOT FOR HUMAN USE. KEEP OUT OF
REACH OF CHILDREN. This product contains materials
that can be irritating to skin and eyes. Avoid direct
contact with skin, eyes, and clothing. In case of
accidental eye exposure, flush with water for 15
minutes. In case of accidental skin exposure, wash with
soap and water. Remove contaminated clothing. Consult
a physician if irritation persists. Accidental injection of
this product may cause local irritation. Consult a
physician immediately. The Material Safety Data Sheet
(MSDS) contains more detailed occupational safety
information.

For customer service, adverse effects reporting, and/or
a copy of the MSDS, call 1-866-591-5777.

PRECAUTIONS: Not for use in animals intended for
breeding purposes. The effects of florfenicol on bovine
reproductive performance, pregnancy, and lactation
have not been determined. Toxicity studies in dogs, rats,
and mice have associated the use of florfenicol with
testicular degeneration and atrophy. Intramuscular
injection may result in local tissue reaction which
persists beyond 28 days. This may result in trim loss of
edible tissue at slaughter. Tissue reaction at injection
sites other than the neck is likely to be more severe.

RESIDUE WARNINGS: Animals intended for human
consumption must not be slaughtered within 28 days of
the last intramuscular treatment. Animals intended
for human consumption must not be slaughtered
within 33 days of subcutaneous treatment. This
product is not approved for use in female dairy cattle
20 months of age or older, including dry dairy cows.
Use in these cattle may cause drug residues in milk
and/or in calves born to these cows. A withdrawal
period has not been established in pre-ruminating
calves. Do not use in calves to be processed for veal.

PRODUCT INFORMATION

 NORFENICOL INJECTABLE SOLUTION DOSAGE GUIDE

<table>
<thead>
<tr>
<th>ANIMAL WEIGHT (lbs)</th>
<th>IM DOSAGE</th>
<th>SC DOSAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>3.0 mL/100 lb Body Weight (mL)</td>
<td>6.0 mL/100 lb Body Weight (mL)</td>
</tr>
<tr>
<td>200</td>
<td>6.0</td>
<td>12.0</td>
</tr>
<tr>
<td>300</td>
<td>9.0</td>
<td>18.0</td>
</tr>
<tr>
<td>400</td>
<td>12.0</td>
<td>24.0</td>
</tr>
<tr>
<td>500</td>
<td>15.0</td>
<td>30.0</td>
</tr>
<tr>
<td>600</td>
<td>18.0</td>
<td>36.0</td>
</tr>
<tr>
<td>700</td>
<td>21.0</td>
<td>42.0</td>
</tr>
<tr>
<td>800</td>
<td>24.0</td>
<td>48.0</td>
</tr>
<tr>
<td>900</td>
<td>27.0</td>
<td>54.0</td>
</tr>
<tr>
<td>1000</td>
<td>30.0</td>
<td>60.0</td>
</tr>
</tbody>
</table>

Recommended Injection Location

Do not inject more than 10 mL per injection site.

Table 1.

Pharmacokinetic Parameter Values for Florfenicol Injectable Solution

<table>
<thead>
<tr>
<th>Pharmacokinetic Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T½ (hr)</td>
<td>18.3**</td>
</tr>
<tr>
<td>AUC (µg·hr/mL)</td>
<td>44.0</td>
</tr>
<tr>
<td>Cmax (µg/mL)</td>
<td>30.0</td>
</tr>
<tr>
<td>Tmax (hr)</td>
<td>8.00</td>
</tr>
</tbody>
</table>

* harmonic mean Cmax, Maximum serum concentration

** The lowest MIC to encompass 50% to 90% of the most susceptible isolates, respectively.

References:


For intramuscular and subcutaneous use in beef and
non-lactating dairy cattle only.

ANADA 200-591, Approved by FDA
ADVERSE REACTIONS: Inappetence, decreased water consumption, or diarrhea may occur transiently following treatment.

CLINICAL PHARMAOCOLOGY: The pharmacokinetic disposition of florfenicol injectable solution was evaluated in feeder calves following single intramuscular (IM) administration at the recommended dose of 20 mg/kg body weight. Florfenicol injectable solution was also administered intravenously (IV) to the same cattle in order to calculate the volume of distribution, clearance, and percent bioavailability (Table 1).

**TABLE 1. Pharmacokinetic Parameter Values for Florfenicol Following IM Administration of 20 mg/kg Body Weight to Feeder Calves (n=10).**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (µg/mL)</td>
<td>3.07*</td>
<td>1.43 - 5.60</td>
</tr>
<tr>
<td>Tmax (hr)</td>
<td>3.33</td>
<td>0.75 - 8.00</td>
</tr>
<tr>
<td>T ½ (hr)</td>
<td>18.3**</td>
<td>8.30 - 44.0</td>
</tr>
<tr>
<td>AUC (µg-min/mL)</td>
<td>442**</td>
<td>3200 - 6250</td>
</tr>
<tr>
<td>Bioavailability (%)</td>
<td>78.5</td>
<td>59.3 - 106</td>
</tr>
<tr>
<td>Vdss (L/kg)**</td>
<td>0.77</td>
<td>0.68 - 0.85</td>
</tr>
<tr>
<td>Clr (mL/min/kg)**</td>
<td>3.75</td>
<td>3.17 - 4.31</td>
</tr>
</tbody>
</table>

* harmonic mean
** mean value
*** following IV administration

Florfenicol was detectible in the serum of most animals through 60 hours after intramuscular administration with a mean concentration of 0.19 µg/mL. The protein binding of florfenicol was 12.7%, 13.2%, and 18.3% at serum concentrations of 0.5, 3.0, and 16.0 µg/mL, respectively.

MICROBIOLOGY: Florfenicol is a synthetic, broad-spectrum antibiotic active against many Gram-negative and Gram-positive bacteria isolated from domestic animals. It acts by binding to the 50S ribosomal subunit and inhibiting bacterial protein synthesis. Florfenicol is generally considered a bacteriostatic drug, but exhibits bactericidal activity against certain bacterial species. In vitro studies demonstrate that florfenicol is active against the bovine respiratory disease (BRD) pathogens Mannheimia haemolytica, Pasteurella multocida, and Histophilus somni, and that florfenicol exhibits bactericidal activity against strains of *M. haemolytica* and *H. somni*. Clinical studies confirm the efficacy of florfenicol against BRD as well as against commonly isolated bacterial pathogens in bovine interdigital phlegmon including *Fusobacterium necrophorum* and *Bacteroides melaninogenicus*.

The minimum inhibitory concentrations (MICs) of florfenicol for BRD organisms were determined using isolates obtained from natural infections from 1990 to 1993. The MICs for interdigital phlegmon organisms were determined using isolates obtained from natural infections from 1973 to 1997 (Table 2).

**TABLE 2. Florfenicol Minimum Inhibitory Concentration (MIC) Values* of Indicated Pathogens Isolated from Natural Infections of Cattle.**

<table>
<thead>
<tr>
<th>Indicated Pathogens</th>
<th>Year of Isolation</th>
<th>Number of isolates</th>
<th>MIC&lt;sub&gt;90&lt;/sub&gt; ** (µg/mL)</th>
<th>MIC&lt;sub&gt;90&lt;/sub&gt; ** (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mannheimia haemolytica</td>
<td>1990 to 1993</td>
<td>398</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>Pasteurella multocida</td>
<td>1990 to 1993</td>
<td>350</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Histophilus somni</td>
<td>1990 to 1993</td>
<td>66</td>
<td>0.25</td>
<td>0.5</td>
</tr>
<tr>
<td>Fusobacterium necrophorum</td>
<td>1973 to 1997</td>
<td>33</td>
<td>0.25</td>
<td>0.25</td>
</tr>
<tr>
<td>Bacteroides melaninogenicus</td>
<td>1973 to 1997</td>
<td>20</td>
<td>0.25</td>
<td>0.25</td>
</tr>
</tbody>
</table>

* The correlation between the in vitro susceptibility data and clinical effectiveness is unknown.
** The lowest MIC to encompass 90% to 99% of the most susceptible isolates, respectively.

ANIMAL SAFETY: A 10X safety study was conducted in feeder calves. Two intramuscular injections of 200 mg/kg were administered at a 48-hour interval. The calves were monitored for 14 days after the second dose. Marked anorexia, decreased water consumption, decreased body weight, and increased serum enzymes were observed following dose administration. These effects resolved by the end of the study.

A 1X, 3X, and 5X (20, 60, and 100 mg/kg) safety study was conducted in feeder calves for 3X the duration of treatment (6 injections at 48-hour intervals). Slight decrease in feed and water consumption was observed in the 1X dose group. Decreased feed and water consumption, body weight, urine pH, and increased serum enzymes, were observed in the 3X and 5X dose groups. Depression, soft stool consistency, and dehydration were also observed in some animals (most frequently at the 3X and 5X dose levels), primarily near the end of dosing.

A 43-day controlled study was conducted in healthy cattle to evaluate effects of florfenicol injectable solution administered at the recommended dose on feed consumption. Although a transient decrease in feed consumption was observed, florfenicol injectable solution administration had no long-term effect on body weight, rate of gain, or feed consumption.

STORAGE INFORMATION: Store at or below 77°F (25°C). Refrigeration is not required. Excursions permitted up to 86°F (30°C). Brief exposure to temperature up to 104°F (40°C) may be tolerated provided the mean kinetic temperature does not exceed 77°F (25°C); however, such exposure should be minimized. The solution is light yellow to straw colored. Color does not affect potency. Use within 28 days of first vial puncture.

HOW SUPPLIED: Norfenicol Injectable Solution is packaged in 100 mL, 250 mL, and 500 mL sterile multiple-dose vials.


Restricted Drug – California. Use Only as Directed.

Made in the UK.
Manufactured by: Norbrook Laboratories Limited, Newry, BT35 6PU, Co. Down, Northern Ireland.

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