

CEPHAPIRIN Veterinary—Intramammary-Local

Some commonly used *brand names* for veterinary-labeled products are:
Cefa-Dri; Cefa-Lak; ToDay; and ToMorrow.

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

Category: Antibacterial (intramammary-local).

Indications

General considerations

Cephapirin is a first-generation cephalosporin that has a wide spectrum of activity against gram-positive and gram-negative organisms. **{R-5}**
Cephapirin is more resistant to beta-lactamases than are the penicillins **{R-6}** and so is effective against staphylococci, with the exception of methicillin-resistant staphylococci. **{R-5}**

Accepted

Mastitis (treatment)—*Cattle:* Cephapirin is indicated in the treatment of mastitis caused by susceptible bacteria, such as *Staphylococcus aureus* **{R-1-4; 7}** and *Streptococcus agalactiae*. **{R-1-4}**
Cephalosporins are the primary treatment of choice for acute staphylococcal mastitis **{R-9}**; however, cows with acute or peracute mastitis are often given other medications, such as systemic antibiotics and/or supportive therapy, concurrently with intramammary therapy. **{R-10}**

Regulatory Considerations

U.S. and Canada—

Withdrawal times have been established for cephapirin benzathine and cephapirin sodium intramammary infusion (see the *Dosage Forms* section). **{R-1-4; 17; 18}**

Chemistry

Source: Cephalosporins are semi-synthetic derivatives of metabolic products of the fungus *Cephalosporium acremonium*. **{R-6; 11}**

Chemical group: Beta-lactam antibiotics. **{R-5}**

Chemical name:

Cephapirin benzathine—5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[(acetyloxy)methyl]-8-oxo-7-[[[4-(pyridinylthio)acetyl]amino]-,(6*R-trans*)-, compd. with *N,N*-bis(phenylmethyl)-1,2-ethanediamine (2:1) **{R-12}**.

Cephapirin sodium—5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[(acetyloxy)methyl]-8-oxo-7-[[[4-(pyridinylthio)acetyl]amino]-, monosodium salt, [6*R-trans*]-. **{R-12}**

Molecular formula:

Cephapirin benzathine— $(C_{17}H_{17}N_3O_6S_2)_2 \cdot C_{16}H_{20}N_2$ **{R-12}**.

Cephapirin sodium— $C_{17}H_{16}N_3NaO_6S_2$. **{R-12}**

Molecular weight:

Cephapirin benzathine—1087.27 **{R-12}**.

Cephapirin sodium—445.45. **{R-12}**

Description:

Cephapirin Benzathine USP—White, crystalline powder **{R-21}**.

Cephapirin Sodium USP—White to off-white crystalline powder, odorless or having a slight odor **{R-21}**.

pKa: Cephapirin sodium—2.15 and 7.3. **{R-13}**

Solubility:

Cephapirin Benzathine USP—Practically insoluble in water, in ether, and in toluene; freely soluble in alcohol; soluble in 0.1 *N* hydrochloric acid **{R-21}**.

Cephapirin Sodium USP—Very soluble in water; insoluble in most organic solvents **{R-21}**.

Pharmacology/Pharmacokinetics

Mechanism of action/Effect: Cephapirin produces its bactericidal effect by inhibiting cell wall synthesis. Its action is only effective in actively growing cells.

Distribution: Medications infused into a teat are considered to be fairly evenly distributed in the treated quarter of the healthy mammary gland; however, in an udder affected by moderate to severe mastitis, the presence of edema, blockage of milk ducts, and reduced blood circulation can cause uneven distribution of medication. **{R-14}**

Precautions to Consider

Patient monitoring

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

Bacterial pathogens in milk

(milk samples should be tested 3 weeks after treatment is discontinued; mastitis is not considered bacteriologically cured until samples show an absence of the mastitis-causing organisms)

Clinical signs

(although resolution of clinical signs of mastitis is not an indication that a bacteriologic cure has been achieved **{R-15}**, monitoring of the clinical condition of the mammary gland, teat, and milk produced can aid in diagnosis of a recurrence of mastitis or initial diagnosis of mastitis in another cow in the herd)

Somatic cell count

(somatic cell counts performed on milk to monitor the dairy herd are used primarily to maintain milk quality but are also used to assess the approximate overall effectiveness of mastitis control programs, which may include antibiotic treatment of cows) **{R-10}**

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

Incidence unknown

Cows

Allergic reactions {R-1; 2}—local or systemic; **drug fever {R-19}**

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

Treatment of mastitis in dairy cattle is best achieved by a comprehensive mastitis control program in which herd management is the primary focus. The program should include routine milk testing, good maintenance of milking equipment, and constant evaluation of milking procedures and teat health as well as strategic treatment of clinical cases of mastitis. **{R-16}**

Veterinary Dosing Information

Antibiotic therapy in the dry cow is more effective than treatment during lactation for mastitis caused by *Staphylococcus aureus*. **{R-15; 16;20}**

Choice of antibiotic for treatment of mastitis should be based on knowledge of identity and sensitivity of pathogens causing mastitis in the cow and the dairy herd.

Before intramammary administration of cephapirin, the following actions should be taken: **{R-1-4}**

- The udder should be milked out completely and the teats washed with warm water and a disinfectant. Care should be taken to avoid washing excess dirt down from the udder onto the teat ends. The area should be dried thoroughly. An effective germicidal teat dip should be applied for one minute and then each teat wiped with a separate cotton ball soaked with an antiseptic such as 70% alcohol.
- Persons performing the treatment should wash and dry their hands before each treatment.
- The tip of the syringe should be inserted into the teat end as little as possible and the contents of the syringe should be injected into each streak canal while the teat is held firmly. The medication should then be gently massaged up the teat canal into the udder.

Following treatment, an effective teat dip is recommended on all teats.

Intramammary Dosage Forms

CEPHAPIRIN BENZATHINE INTRAMAMMARY INFUSION USP

Usual dose: Mastitis—*Cows*, nonlactating: Intramammary, 300 mg administered into each quarter of the udder at the time of drying-off. {R-1; 2}

Strength(s) usually available:

U.S.— {R-1; 2; 22}

Veterinary-labeled product(s):

300 mg per 10 mL (OTC) [*Cefa-Dri; ToMorrow*].

Canada— {R-17; 22}

Veterinary-labeled product(s):

300 mg per 10 mL (Rx) [*Cefa-Dri*].

Withdrawal times:

U.S.— {R-1; 2; 22}

Species	Withdrawal time	
	Meat (days)	Milk (hours)
<i>Cows</i> , nonlactating	42	72

Note: Cephapirin benzathine intramammary infusion should not be used any later than thirty days prior to calving.

Canada— {R-17; 22}

Species	Withdrawal time	
	Meat (days)	Milk (hours)
<i>Cows</i> , nonlactating	42	84

Note: Cephapirin benzathine intramammary infusion should not be used any later than thirty days prior to calving.

Packaging and storage: Store between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from freezing.

USP requirements: Preserve in well-closed unit-dose disposable syringes at controlled room temperature. A suspension of Cephapirin Benzathine in a suitable vegetable oil vehicle. Contains a suitable dispersing agent. Label Intramammary Infusion to indicate that it is for veterinary use only. Contains an amount of cephapirin benzathine equivalent to the labeled amount of cephapirin, within –10% to +20%. Meets the requirements for Identification and Water (not more than 1.0%) {R-21}.

CEPHAPIRIN SODIUM INTRAMAMMARY INFUSION USP

Usual dose: Mastitis—*Cows*, lactating: Intramammary, 200 mg into each affected quarter of the udder every twelve hours for two treatments. {R-3; 4}

Strength(s) usually available:

U.S.— {R-3; 4; 22}

Veterinary-labeled product(s):
 200 mg per 10 mL (OTC) [*Cefa-Lak; ToDay*].
 Canada — {**R-18; 22**}
 Veterinary-labeled product(s):
 200 mg per 10 mL (Rx) [*Cefa-Lak*].

Withdrawal times:

U.S. and Canada — {**R-3; 4; 18; 22**}

Species	Withdrawal time	
	Meat (days)	Milk (hours)
Cows, lactating	4	96

Packaging and storage: Store between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from freezing.

USP requirements: Preserve in well-closed unit-dose disposable syringes at controlled room temperature. A suspension of Cephapirin Sodium in a suitable vegetable oil vehicle. Contains a suitable dispersing agent. Label Intramammary Infusion to indicate that it is for veterinary use only. Contains an amount of cephalosporin sodium equivalent to the labeled amount of cephalosporin, within -10% to +20%. Meets the requirements for Identification and Water (not more than 1.0%) {**R-21**}.

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 02/28/03

References

1. Cefa-Dri package insert (Fort Dodge—US). Downloaded 2/16/03 from www.wyeth.com.
2. ToMorrow package insert (Fort Dodge—US). Downloaded 8/6/03 from www.wyeth.com.
3. Cefa-Lak package insert (Fort Dodge—US), Rev 3/00. Downloaded 8/6/03 from www.wyeth.com.
4. ToDay package insert (Fort Dodge—US). Downloaded 8/6/03 from www.wyeth.com.
5. Donowitz GR, Mandell GL. Beta-lactam antibiotics. *N Engl J Med* 1988; 318: 419-26.
6. Caprile KA. The cephalosporin antimicrobial agents: a comprehensive review. *J Vet Pharmacol Ther* 1988; 11(1): 1-32.
7. Owens WE, et al. Efficacy of a cephalosporin dry cow product for treatment of experimentally induced *Staphylococcus aureus* mastitis in heifers. *J Dairy Sci* 1991; 74(10): 3376-82.
8. Watson ADJ. Penicillin G and the alternatives. *Vet Annu* 1985; 25: 277-83.
9. Barragry TB. *Veterinary drug therapy*. Philadelphia: Lea & Febiger, 1994. p. 665.
10. Heath SE. Bovine mastitis. In: Howard JL. *Current veterinary therapy 3 food animal practice*. Philadelphia: W.B. Saunders, 1993. p. 762-9.
11. Papich MG. Clinical pharmacology of cephalosporin antibiotics. *J Am Vet Med Assoc* 1984; 184(3): 344-7.
12. USP dictionary of USAN and international drug names, 2002 ed. Rockville, MD: The United States Pharmacopeial Convention, Inc., 2002.
13. Gennaro AR, editor. *Remington's pharmaceutical sciences*. 18th ed. Easton, PA: Mack Publishing Company, 1990. p. 1199.
14. Jarp J, Bugge HP, Larsen S. Clinical trial of three therapeutic regimens for bovine mastitis. 1989; 124: 630-4.
15. Craven N. Efficacy and financial value of antibiotic treatment of bovine clinical mastitis during lactation—a review. *Br Vet J* 1987; 143: 410-22.
16. Hady PJ, Lloyd JW, Kaneene JB. Antibacterial use in lactating dairy cattle. *J Am Vet Med Assoc* 1993 Jul; 203(2): 210-20.
17. Cephapirin (Cefa-Dri, Wyeth Ayerst—Canada). In: Bennett K, editor. *Compendium of veterinary products*. 3rd ed. Hensall, ON: North American Compendiums Inc., 1993. p. 163.

18. Cephapirin (Cefa-Lak, Wyeth Ayerst—Canada). In: Bennett K, editor. Compendium of veterinary products. 3rd ed. Hensall, ON: North American Compendiums Inc., 1993. p. 164.
19. Panel comment, Rec 3/24/95.
20. Manufacturer comment, Rec 4/20/95.
21. The United States pharmacopeia. The national formulary. USP 26th revision (January 1, 2003). NF 21st ed (January 1, 2003). Rockville, MD: The United States Pharmacopeial Convention, Inc., 2002. p. 398, 400, 2554.
22. Arrijoja-Dechert A, editor. Compendium of Veterinary Products, CD edition. Port Huron, MI: North American Compendiums, Inc., 2002.