

PENICILLIN G Veterinary—Intramammary-Local†

Some commonly used *brand names* for veterinary -labeled products are *Go-dry* and *Masti-Clear*.

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

†Not commercially available in Canada.

Category: Antibacterial (intramammary-local).

Indications

General Considerations

The spectrum of activity of penicillin G includes many aerobic and anaerobic gram-positive organisms. Penicillin G is highly susceptible to beta-lactamases and has little activity against organisms that can produce these enzymes. In addition, penicillin G is ineffective against bacteria that are resistant by certain other mechanisms, such as having a relatively impermeable cell wall. Therefore, penicillin G has little activity against many staphylococci and most gram-negative bacteria.

Accepted

Mastitis (treatment)¹—*Cattle*: Penicillin G is indicated in the treatment of mastitis in cattle {**R-1**; **2**; **7**} caused by susceptible organisms such as *Streptococcus agalactiae* {**R-7**; **20**}. Intramammary therapy alone is indicated only in the treatment of subacute mastitis manifested by mild inflammatory changes in the milk or udder. Acute or peracute mastitis, in which gross inflammatory changes in the milk or udder or systemic signs appear, requires administration of other medications also, which may include systemic antibiotics and/or supportive therapy. {**R-5**}

¹Not included in Canadian product labeling or product not commercially available in Canada.

Regulatory Considerations

U.S.—

Withdrawal times have been established for penicillin G procaine intramammary infusion (see the *Dosage Forms* section {**R-1**}).

Chemistry

Source: Produced by the mold *Penicillium*. {**R-8**}

Chemical group: Beta-lactam antibiotics. {**R-8**; **9**}

Chemical name: Penicillin G procaine—4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 3,3-dimethyl-7-oxo-6-[(phenylacetyl)amino]-, [2*S*-(2 alpha,5 alpha,6 beta)]-, compd. with 2-(diethylamino)ethyl 4-aminobenzoate (1:1) monohydrate. {**R-10**}

Molecular formula: Penicillin G procaine—

$C_{16}H_{18}N_2O_4S \cdot C_{13}H_{20}N_2O_2 \cdot H_2O$. {**R-10**}

Molecular weight: Penicillin G procaine—588.72. {**R-10**}

Description: Penicillin G Procaine USP—White crystals or white, very fine, microcrystalline powder. Is odorless or practically odorless, and is relatively stable in air. Its solutions are dextrorotary. Is rapidly inactivated by acids, by alkali hydroxides, and by oxidizing agents {**R-17**}.

pKa: 2.7. {**R-11**; **12**}

Solubility: Penicillin G Procaine USP—Slightly soluble in water; soluble in alcohol and in chloroform {**R-17**}.

Pharmacology/Pharmacokinetics

Mechanism of action/Effect: The penicillins produce their bactericidal effect by inhibiting cross-linkages during bacterial cell wall synthesis. {**R-9**} Penicillin G must penetrate the cell wall to attach to specific proteins on the inner surface of the bacterial cell membrane.

In actively growing cells, the binding of penicillin within the cell wall leads to interference with production of cell wall peptidoglycans and subsequent lysis of the cell in a hypo- or iso-osmotic environment. {R-9; 13}

Distribution: Medications infused into a teat are considered to be fairly evenly distributed in that 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 causes uneven distribution. {R-14} After penicillin G procaine is infused into a mammary gland, it is also partially distributed into the other quarters of the gland, {R-4; 15} into the local lymph circulation, and to some degree into the plasma and other tissues. {R-16}

Peak serum concentration: In healthy animals, after intramammary administration of 400 mg (404,000 Units) of penicillin G procaine in combination with the same amount of dihydrostreptomycin sulfate, the peak serum concentration of penicillin G is 0.07 mcg/mL at 4 hours. {R-16}

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):

Bacteriologic pathogen identification in milk

(milk samples should be tested 3 weeks after the end of treatment; mastitis is not considered bacteriologically cured until samples show an absence of the mastitis-causing organisms {R-2})

Clinical signs

(although a resolution of clinical signs of mastitis is not an indication that a bacteriologic cure has been achieved {R-18}, 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 also to approximately assess the overall effectiveness of mastitis control programs that may include antibiotic treatment of cows) {R-5}

Side/Adverse Effects

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

Incidence unknown

Cows

Allergic reactions—theoretically possible locally or systemically

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 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-7}

Veterinary Dosing Information

Antibiotic therapy in the dry cow is measurably more effective than treatment during lactation. **{R-7; 18}**

Choice of antibiotic for treatment of mastitis should be based on knowledge of culture and sensitivity of pathogens causing mastitis in the cow and the dairy herd. **{R-19}**

Before administration of intramammary penicillin G procaine, the following steps should be performed: **{R-1}**

- 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. **{R-6}**
- 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 **{R-6}** 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.

An effective teat dip is recommended on all teats following treatment.

For the lactating cow, treated quarters should not be milked for at least six hours after treatment but should be milked at regular intervals thereafter. **{R-2}**

Intramammary Dosage Forms

PENICILLIN G PROCAINE INTRAMAMMARY INFUSION USP

Usual dose: Antibacterial¹—*Cattle:*

Dry cow (nonlactating)—Intramammary, 100,000 Units into each quarter of the udder at the time of drying-off. **{R-1}**

Lactating cow—Intramammary, 100,000 Units into each affected quarter of the udder every twelve hours for a maximum of three doses. **{R-2}**

Strength(s) usually available:

U.S.— **{R-1; 2}**

Veterinary-labeled product(s):

100,000 Units per 10 mL (OTC) [*Go-dry* (dry cow only);

Masti-Clear (lactating cow only)].

Canada— **{R-3}**

Veterinary-labeled product(s):

Not commercially available.

Withdrawal times:

U.S. **{R-1; 2}**—

Species	Withdrawal time	
	Meat (days)	Milk (hours)
<i>Cows</i>		
Nonlactating	14	72
Lactating	3	60

Packaging and storage: Store between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. **{R-1; 2}**

USP requirements: Preserve in well-closed disposable syringes. A suspension of Penicillin G Procaine in a suitable vegetable oil vehicle. Label it to indicate that it is for veterinary use only. Contains an amount of penicillin G procaine equivalent to the labeled amount of penicillin G, within –10% to +15%. Meets the requirements for Identification and Water (not more than 1.4%). **{R-17}**

¹Not included in Canadian product labeling or product not commercially available in Canada.

Developed: 03/08/95

Interim revision: 04/24/96; 05/19/97; 07/08/98; 10/15/99; 06/30/02
02/28/03

References

1. Go-dry (G.C. Hanford Mfg. Co—US), Rev 10/92, Rec 7/22/94.
2. Masti-Clear (G.C. Hanford Mfg. Co—US), Rec 2/19/03.
3. Arrijoja-Dechert A, editor. Compendium of veterinary products, CD edition. Port Huron, MI: North American Compendiums, Inc., 2002.
4. Hawkins GE, Cannon RY, Paar CF. Concentration of penicillin in milk from noninfused quarters following infusion of one quarter. *J Dairy Sci* 1962; 45: 1020-2.
5. Heath SE. Bovine mastitis. In: Howard JL. Current veterinary therapy 3 food animal practice. Philadelphia: W.B. Saunders, 1993. p. 762-9.
6. Panel comment, Rec 12/6/94.
7. Hady PJ, Lloyd JW, Kaneene JB. Antibacterial use in lactating dairy cattle. *J Am Vet Med Assoc* 1993 Jul; 203(2): 210-20.
8. Watson ADJ. Penicillin G and the alternatives. *Vet Annu.* 1985; 25: 277-83.
9. Donowitz GR, Mandell GL. Beta-lactam antibiotics. *N Engl J Med* 1988; 318: 419-26.
10. USP dictionary of USAN and international drug names, 2002 ed. Rockville, MD: The United States Pharmacopeial Convention, Inc.; 2002.
11. Prescott JF, Baggot JD. Antimicrobial therapy in veterinary medicine, 2nd ed. Ames, IA: Iowa State University Press, 1993. p. 81-9.
12. Ziv G, et al. Pharmacokinetic evaluation of penicillin and cephalosporin derivatives in serum and milk of lactating cows and ewes. *Am J Vet Res* 1973; 34(12): 1561-5.
13. Wright AJ, Wilkowski CJ. The penicillins. *Mayo Clin Proc* 1983; 58: 21-32.
14. Jarp J, Bugge HP, Larsen S. Clinical trial of three therapeutic regimens for bovine mastitis. 1989; 124: 630-4.
15. Anifantakis EM. Excretion rates of antibiotics in milk of sheep and their effect on yogurt production. *J Dairy Sci* 1982; 65: 426-9.
16. Franklin A, Rantzen M, Obel N, et al. Concentrations of penicillin, streptomycin, and spiramycin in bovine udder tissue liquids. *Am J Vet Res* 1986 Apr; 47(4): 804-7.
17. 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. 1415, 2573.
18. Craven N. Efficacy and financial value of antibiotic treatment of bovine clinical mastitis during lactation—a review. *Br Vet J* 1987; 143: 410-22.
19. Panel comment , Rec 11/18/94.
20. Panel comment, Rec 11/18/94.