AMINOPENICILLINS Veterinary—Intramammary-Local†

This monograph includes information on the following: Amoxicillin; Hetacillin.

Some commonly used *brand names* for veterinary-labeled products are: *Amoxi-Mast* and *Hetacin-K Intramammary Infusion*.

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

Aminopenicillins have activity against penicillin-sensitive gram-positive bacteria as well as some gram-negative bacteria. Aminopenicillins are susceptible to destruction by beta-lactamases and therefore are not effective against bacteria that produce these enzymes. **{R-1-3}** Most strains of *Klebsiella, Proteus, Pseudomonas,* and *Staphylococcus* **{R-17}** are resistant. **{R-1; 4}**

Accepted

Mastitis (treatment)[1]—*Cows*, lactating: Amoxicillin and hetacillin are indicated in the treatment of mastitis caused by susceptible organisms such as *Streptococcus agalactiae*. **{R-5; 6}** Intramammary therapy alone is indicated only in the treatment of subacute or subclinical mastitis manifested by mild 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-7}**

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

Regulatory Considerations

U.S.—

Withdrawal times have been established. See the *Dosage Forms* section.

Chemistry

Source:

Amoxicillin—Semisynthetic derivative of ampicillin. **{R-8}**

Hetacillin—Derived from the penicillin nucleus, 6-aminopenicillanic acid and chemically related to ampicillin. **{R-6}**

Chemical group: Beta-lactam antibiotics.

Chemical name:

Amoxicillin—4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[amino(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-, trihydrate [2*S*-[2alpha,5alpha,6beta(*S**)]]-. **{R-9}**

Hetacillin potassium—4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-(2,2-dimethyl-5-oxo-4-phenyl-1-imidazolidinyl)-3,3-dimethyl-7-oxo-, monopotassium salt, [2*S*-[2alpha,5alpha,6beta(*S**)]]-. **{R-9}**

Molecular formula:

Amoxicillin—$C_{16}H_{19}N_3O_5S \cdot 3H_2O$. **{R-9}**

Hetacillin potassium—$C_{19}H_{22}KN_3O_4S$. **{R-9}**

Molecular weight:

Amoxicillin—419.45. **{R-9}**

Hetacillin potassium—427.56. **{R-9}**

Description:

Amoxicillin USP—White, practically odorless, crystalline powder. **{R-10}**

Hetacillin potassium—White to light buff, crystalline powder.

Solubility:

Amoxicillin USP—Slightly soluble in water and in methanol; insoluble in carbon tetrachloride and in chloroform. **{R-10}**

Hetacillin potassium—Freely soluble in water; soluble in alcohol.

Pharmacology/Pharmacokinetics

Mechanism of action/Effect: Like other penicillins, the aminopenicillins produce their bactericidal effect by inhibiting bacterial cell wall synthesis. **{R-11}** These antibiotics 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 ampicillin or amoxicillin within the cell wall leads to interference with production of cell wall peptidoglycans and subsequent lysis of the cell in an isoosmotic environment. **{R-11-13}**

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}**

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 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 of mastitis

(although a 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 they are also used to assess the approximate overall effectiveness of mastitis control programs, which may include antibiotic treatment of cows) **{R-7}**

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-6}**—local or systemic

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.

Veterinary Dosing Information

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

The available intramammary aminopenicillin products are formulated for use in the lactating cow only. **{R-15; 16}**

Before administration of intramammary amoxicillin or hetacillin, the following steps should be performed: **{R-5; 6}**

- The udder should be milked out completely and the teats and udder 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 and each teat wiped with a separate cotton ball soaked with an antiseptic such as 70% isopropyl 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.

A teat dip is recommended on all teats following treatment.

AMOXICILLIN

Intramammary Dosage Forms

AMOXICILLIN INTRAMAMMARY INFUSION USP

Usual dose: Mastitis[1]—*Cows,* lactating: Intramammary, 62.5 mg into each affected quarter of the udder every twelve hours for a maximum of three doses. **{R-5}**

Strength(s) usually available:

U.S.— **{R-5}**

Veterinary-labeled product(s):

62.5 mg per 10 mL (Rx) [*Amoxi-Mast*].

Canada—

Veterinary-labeled product(s):

Not commercially available.

Withdrawal times:

U.S.— **{R-5}**

	Withdrawal time	
Species	Meat (days)	Milk (hours)
Cows, lactating	12	60

Packaging and storage: Store below 24 °C (75 °F) **{R-5}**, unless otherwise specified by manufacturer.

USP requirements: Preserve in well-closed disposable syringes. A suspension of Amoxicillin in a suitable vegetable oil vehicle. Label it to indicate that it is intended for veterinary use only. Contains the labeled amount, within –10% to +20%. Contains a suitable dispersing agent and preservative. Meets the requirements for Identification and Water (not more than 1.0%). **{R-10}**

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

HETACILLIN

Summary of Differences

Pharmacology/pharmacokinetics: Hetacillin must undergo a rapid and spontaneous local hydrolysis to ampicillin to be therapeutically active. Hydrolysis is believed to occur in aqueous solution with high efficiency; however, hydrolysis is slower in strongly acidic

environments. **{R-17-19}**

Intramammary Dosage Forms

HETACILLIN POTASSIUM INTRAMAMMARY INFUSION

Note: The dosing and strength of the dosage form available are expressed in terms of ampicillin activity. **{R-6}**

Usual dose: Mastitis[1]—*Cows,* lactating: Intramammary, 62.5 mg (ampicillin activity) into each affected quarter of the udder every twenty-four hours for a maximum of three doses. **{R-6}**

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):

62.5 mg (ampicillin activity) per 10 mL (Rx) [*Hetacin-K Intramammary Infusion*].

Canada—

Veterinary-labeled product(s):

Not commercially available.

Withdrawal times:

U.S.—

	Withdrawal time	
Species	Meat (days)	Milk (hours)
Cows, lactating	10	72

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

USP requirements: Not in USP.**{R-10}**

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

Developed: 06/05/95
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References

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