

AMINOPENICILLINS (Veterinary—Systemic)

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

Some commonly used *brand names* are:
For veterinary-labeled products—

<i>Amoxi-Drop</i> [Amoxicillin]	<i>Moxilean-50 Suspension</i> [Amoxicillin]
<i>Amoxil Tablets</i> [Amoxicillin]	<i>Polyflex</i> [Ampicillin]
<i>Amoxi-Tabs</i> [Amoxicillin]	

For human-labeled products—

<i>Apo-Ampi</i> [Ampicillin]	<i>Nu-Ampi</i> [Ampicillin]
<i>Novo-Ampicillin</i> [Ampicillin]	

Category: Antibacterial (systemic).

Indications

Note: The text between ^{ELUS} and ^{EL} describes uses that are not included in U.S. product labeling. Text between ^{ELCAN} and ^{EL} describes uses that are not included in Canadian product labeling.

The ^{ELUS} or ^{ELCAN} 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

The aminopenicillins have activity against penicillin-sensitive gram-positive bacteria as well as some gram-negative bacteria. Ampicillin is effective against alpha- and beta-hemolytic streptococci, including *Streptococcus equi*,^(R-1) non-penicillinase-producing *Staphylococcus* species, some *Bacillus anthracis*, and most strains of *Clostridia*.^(R-3) Ampicillin is also effective against gram-negative bacteria, including many strains of *Escherichia coli* (*E. coli*), *Salmonella*, and *Pasteurella multocida*.^(R-3) Amoxicillin has the same spectrum of activity as ampicillin, but has slightly better activity against some gram-negative bacteria, including *E. coli*, and *Salmonella* species.^(R-4) Most anaerobic bacteria, except beta-lactamase-producing strains of *Bacteroides*, are sensitive to amoxicillin.^(R-78) The aminopenicillins are subject to destruction by beta-lactamases and therefore are not effective against some bacteria that produce these enzymes.^(R-1; 3) Most strains of *Klebsiella*, *Proteus*, and *Pseudomonas* are resistant.^(R-1; 23)

Accepted

^{ELCAN} Dermatitis, bacterial (treatment)^{EL}—*Dogs*: Amoxicillin for oral suspension and amoxicillin tablets are indicated in the treatment of bacterial dermatitis caused by susceptible organisms; however, amoxicillin is not the treatment of choice because bacteria that cause dermatitis are often resistant to this medication.^(R-6; 14; 68-70)

Gastroenteritis, bacterial (treatment)—*Cats and dogs*: Amoxicillin for oral suspension, amoxicillin tablets, and ^{ELCAN} ampicillin for injectable suspension^{EL} are indicated and ^{ELUS,CAN} ampicillin for injection^{EL} is used in the treatment of bacterial gastrointestinal tract infections caused by susceptible organisms.^(R-3; 5; 6; 14; 29)

Pneumonia, bacterial (treatment)—

^{ELCAN} *Calves*, nonruminating^{EL}: Ampicillin for injectable suspension is indicated for the treatment of respiratory tract infections caused by susceptible organisms, including some bacterial pneumonias associated with shipping fever complex.^(R-3)

Cats and dogs: ^{ELCAN} Ampicillin for injectable suspension^{EL} is indicated and ^{ELUS,CAN} amoxicillin for oral suspension, amoxicillin tablets, and ampicillin for injection^{EL} are used in the treatment of pneumonia caused by susceptible

organisms.^(R-3; 12)

Cattle: Ampicillin for injectable suspension is indicated for the treatment of respiratory tract infections caused by susceptible organisms, including some bacterial pneumonias associated with shipping fever complex.^(R-3; 5)

^{ELUS,CAN} *Horses*^{EL}: Ampicillin for injection is used for the treatment of pneumonia caused by susceptible organisms.^(R-1)

Skin and soft tissue infections (treatment)—

Cats and dogs: Amoxicillin for oral suspension, amoxicillin tablets, and ampicillin for injectable suspension are indicated and ^{ELUS,CAN} ampicillin for injection^{EL} is used in the treatment of soft tissue infections and wounds caused by susceptible organisms.^(R-3; 5; 6; 14; 29)

^{ELUS,CAN} *Horses*^{EL}: Ampicillin for injection is used in the treatment of skin and soft tissue infections, including abscesses and wounds, caused by susceptible organisms.^(R-1)

^{ELUS,CAN} Strangles (treatment)^{EL}—*Horses*: Ampicillin for injection may be used in the treatment of strangles caused by susceptible *Streptococcus equi*.^(R-1)

Tonsillitis, bacterial (treatment); or

^{ELCAN} Tracheobronchitis, bacterial (treatment)^{EL}; or

Upper respiratory tract infections (treatment)—*Cats and dogs*:

Amoxicillin for oral suspension, amoxicillin tablets, and ampicillin for injectable suspension are indicated and ^{ELUS,CAN} ampicillin for injection^{EL} is used in the treatment of tonsillitis and upper respiratory tract infections caused by susceptible organisms.^(R-3; 5; 6; 14; 29) ^{ELCAN} Amoxicillin for oral suspension and amoxicillin tablets are indicated in the treatment of tracheobronchitis in dogs, caused by susceptible organisms.^{EL(R-6; 14)}

Urinary tract infections, bacterial (treatment)—*Cats and dogs*:

Amoxicillin for oral suspension, amoxicillin tablets, and ampicillin for injectable suspension are indicated while ^{ELUS,CAN} ampicillin for injection and ampicillin capsules^{EL} are used in the treatment of urinary tract infections, including cystitis and urethritis, caused by susceptible organisms.^(R-3; 5; 6; 14; 15; 24; 29)

Potentially effective

^{ELUS,CAN} Bacterial infections (treatment)^{EL}—*Calves*, nonruminating: At one time, amoxicillin tablets were labeled in the United States for use in the treatment of infections in calves caused by susceptible *E. coli*.^(R-8) Although the labeled product is no longer available, oral amoxicillin may be used in the treatment of susceptible infections in calves.

^{ELUS,CAN} Leptospirosis (treatment)^{EL}—*Dogs*: Although the efficacy has not been established, amoxicillin is used in therapy of leptospirosis in dogs. Penicillin and penicillin derivatives (including amoxicillin) are considered to be effective for eliminating leptospiremia, but it is not known if they are effective in terminating the carrier state.^(R-13; 30; 31)

Regulatory Considerations

U.S. and Canada—

Withdrawal times have been established for ampicillin for injectable suspension. See the *Dosage Forms* section.^(R-3; 5; 8)

Chemistry

Source:

Amoxicillin—Semisynthetic derivative of ampicillin.^(R-14)

Ampicillin—Semisynthetic penicillin.^(R-1)

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*-[2 alpha,5 alpha,6 beta(*S**)]]-^(R-16)

Ampicillin—4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic

acid, 6-[(aminophenylacetyl)amino]-3,3-dimethyl-7-oxo-, [2S-[2 alpha,5 alpha,6 beta(S*)]]-.^(R-16)
Ampicillin sodium—4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[(aminophenylacetyl)amino]-3,3-dimethyl-7-oxo-, mono-sodium salt, [2S-[2 alpha,5 alpha,6 beta(S*)]]-.^(R-16)

Molecular formula:

Amoxicillin—C₁₆H₁₉N₃O₅S·3H₂O.^(R-16)
Ampicillin—C₁₆H₁₉N₃O₄S.^(R-16)
Ampicillin sodium—C₁₆H₁₈N₃NaO₄S.^(R-16)

Molecular weight:

Amoxicillin—419.45.^(R-16)
Ampicillin—349.40.^(R-16)
Ampicillin sodium—371.39.^(R-16)

Description:

Amoxicillin USP—White, practically odorless, crystalline powder.^(R-17)
Ampicillin USP—White, practically odorless, crystalline powder.^(R-17)
Ampicillin Sodium USP—White to off-white, odorless or practically odorless, crystalline powder. Is hygroscopic.^(R-17)

pKa:^(R-22)

Amoxicillin—2.8 and 7.2.
Ampicillin—2.7 and 7.3.

Solubility:

Amoxicillin USP—Slightly soluble in water and in methanol; insoluble in carbon tetrachloride and in chloroform.^(R-17)
Ampicillin USP—Slightly soluble in water and in methanol; insoluble in carbon tetrachloride and in chloroform.^(R-17)
Ampicillin Sodium USP—Very soluble in water and in isotonic sodium chloride and dextrose solutions.^(R-17)

Pharmacology/Pharmacokinetics

Note: Unless otherwise noted, pharmacokinetic data in this section are based on intravenous administration of ampicillin or amoxicillin.

There is evidence that administering ampicillin concurrently with either gentamicin or kanamycin does not alter the pharmacokinetics of either of the medications in horses.^(R-34; 84)

Mechanism of action/Effect: Like other penicillins, the aminopenicillins produce their bactericidal effect by inhibiting bacterial cell wall synthesis.^(R-18) These antibiotics must penetrate the cell wall to attach to specific proteins within 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 iso-osmotic environment.^(R-18-20) The aminopenicillins penetrate gram-negative bacterial cell walls more rapidly than do the natural penicillins such as penicillin G and therefore are more efficient in destroying those organisms. Amoxicillin enters the gram-negative cell more easily than does ampicillin; this is considered to be the basis for the greater activity of amoxicillin against some gram-negative bacteria.^(R-19)

Absorption: The aminopenicillins are stable in gastric fluid.^(R-8) One of the primary differences between ampicillin and amoxicillin is the difference in absorption after oral administration. A higher percentage of amoxicillin than of ampicillin is absorbed after oral administration to cats, dogs, pigs, and preruminant calves.^(R-25-28; 46) In people, the more complete oral absorption of amoxicillin leaves less drug remaining in the intestinal tract than does ampicillin; therefore amoxicillin is associated with a lower incidence of diarrhea as a side effect; however, amoxicillin is also less effective than ampicillin in the treatment of some intestinal bacterial infections in people.^(R-20)

In horses, ampicillin sodium is well absorbed following intramuscular or subcutaneous administration; however, oral dosage forms are poorly absorbed by adult horses.^(R-84) Oral absorption of amoxicillin has been reported to be between 5.3 and 10.4%.^{(R-42;}

⁸⁶⁾ Ampicillin trihydrate administered intramuscularly produces lower ampicillin blood concentrations that extend over a longer period of time than does ampicillin sodium.^(R-27; 49)

Note: There is evidence that giving amoxicillin and clavulanate concurrently has little effect on the pharmacokinetics of either medication;^(R-82) therefore, the following information based on dosing with amoxicillin and clavulanate combination may be useful in predicting the absorption of amoxicillin alone.

Calves—^(R-82)

Preruminant calves (2 weeks old): Absorption of amoxicillin when administered orally in combination with clavulanate at doses of 10 to 20 mg per kg of body weight (mg/kg) is 34 to 36%.

Early ruminant calves (6 weeks old): Absorption of amoxicillin and clavulanate combination is much poorer than in preruminant calves given the same oral dose; therapeutic serum amoxicillin concentrations are not achieved in early ruminant calves.

Distribution: The aminopenicillins are rapidly and widely distributed into most body fluids^(R-6; 8; 23; 39) with the exception of fluids of the eye and the prostate gland;^(R-69) also, distribution into cerebrospinal fluid is low unless the meninges are inflamed.^(R-8) Penetration into synovial fluid is high.^(R-21; 34; 75)

Volume of distribution—

Amoxicillin: *Horses*—

Adults:

Area—0.33 liter per kg of body weight (L/kg).^(R-42)
Steady state—0.19 L/kg.^(R-86)

Foals (6 to 7 days of age):

Area—0.37 L/kg.^(R-41)
Steady state—0.27 L/kg.^(R-41)

Ampicillin:

Cats—Area: 0.12 L/kg.^(R-40)

Horses—Steady state: 0.18 L/kg;^(R-23; 86) 0.26 L/kg.^(R-85)

Protein binding:

Amoxicillin—*Horses*: Moderate (37 to 38%).^(R-45)

Ampicillin—

Cattle: Low (18%).^(R-43; 44)

Horses: Very low (6.8 to 8%).^(R-48)

Rabbits: Low (17.5%).^(R-44)

Sheep: Low (13.8%).^(R-43; 44)

Half-life:

Distribution—Ampicillin:

Cats—0.2 hour.^(R-40)

Pigs—0.08 to 0.12 hour.^(R-39)

Elimination—

Amoxicillin:

Goats—1.1 hours.^(R-47)

Horses—

Adults: 0.7 hour;^(R-42) 1.4 hours.^(R-45; 86)

Foals (6 to 7 days of age): 0.7 hour.^(R-41)

Sheep—0.8 hour.^(R-47)

Ampicillin:

Cats—1.2 hours.^(R-40)

Dogs—0.3 hour.^(R-44)

Horses—0.6 hour;^(R-23) 0.7 hour;^(R-85) 1.6 hours;^(R-48) 1.7 hours.^(R-86)

Pigs—0.5 to 0.6 hour.^(R-39)

Rabbits—0.4 hour.^(R-44)

Peak serum concentration: Ampicillin—*Horses*:

6.2 to 9.7 mcg/mL at 16 minutes after an intramuscular ampicillin sodium dose of 10 mg of per kg of body weight (mg/kg).^(R-84)

21.6 mcg/mL in nonpregnant mares after an intramuscular ampicillin sodium dose of 22 mg/kg.^(R-75)

8.9 mcg/mL in pregnant mares after an intramuscular ampicillin sodium dose of 22 mg/kg.^(R-75)

Elimination: Amoxicillin^(R-6) and ampicillin^(R-23) are primarily excreted unchanged in the urine. Ten to twenty-five percent of the administered dose of amoxicillin is excreted in the form of penicilloic acid.

Total clearance—

Amoxicillin:

Goats—11.4 mL per minute per kg of body weight (mL/min/kg).^(R-47)

Foals (6 to 7 days of age) and *horses*—5.7 mL/min/kg.^(R-41; 42)

Sheep—10.1 mL/min/kg.^(R-47)

Ampicillin: *Horses*—3.5 mL/min/kg.^(R-34)

Precautions to Consider

Cross-sensitivity and/or related problems

Animals allergic to one penicillin may be allergic to other penicillins also.^(R-49)

Species sensitivity

Calves—In neonatal calves, ampicillin administered orally at 12 mg per kg of body weight (mg/kg) every eight hours has been shown to cause diarrhea and malabsorption. Aminopenicillins are not recommended for treatment of enteritis in calves unless secondary complications, such as septicemia or bacterial arthritis, are present.^(R-9; 10)

Guinea pigs, hamsters, and rabbits—Oral ampicillin often disturbs the normal microflora; the severity of this side effect makes the use of aminopenicillins in these species contraindicated.^(R-58; 73)

Horses—Large oral doses of the aminopenicillins can disturb the normal cecal microflora and are generally contraindicated.^(R-49; 58)

Ruminants—Oral ampicillin administration disrupts the rumen flora.

Pregnancy/Reproduction

The safety of amoxicillin and ampicillin in the treatment of infections during pregnancy has not been established.^(R-33) Penicillins have been shown to cross the placenta; however, laboratory animal reproduction studies have shown no evidence of adverse effects in the fetus.^(R-28; 33; 36)

Lactation

In humans, penicillins are distributed into milk.^(R-33; 37) Ampicillin has been shown to be distributed into the milk of cows and ewes.^(R-50)

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

Antibacterials, bacteriostatic, such as:

Tetracycline^(R-46)

(because the aminopenicillins act only on cells that are actively reproducing, bacteriostatic antibiotics may decrease the efficacy of amoxicillin and ampicillin by depressing the activity of target cells;^(R-53) however, the clinical significance of this interference is not well documented)

Probenecid

(probenecid is a competitive inhibitor of renal tubular secretion and slows the body clearance of aminopenicillins in horses, calves, pigs, and possibly other species, resulting in increased serum concentrations and longer elimination half-life)^(R-51; 52; 55)

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

Note: Laboratory value alterations relating specifically to use of aminopenicillins in animals appear to be rarely described.

Human laboratory value alterations have been reported and are included in this section.

Human laboratory value alterations^(R-2)

The following laboratory value alterations have been reported in humans, and are included in the human monograph *Penicillins (Systemic)* in *USP DI Volume 1*; these laboratory value alterations are intended for informational purposes only and may or may not be applicable to the use of amoxicillin or ampicillin in the treatment of animals:

With diagnostic test results

Glucose, urine

(high urinary concentrations of a penicillin may produce false positive or falsely elevated test results with copper sulfate tests [Benedict's, *Clinitest*, or Fehling's]; glucose enzymatic tests [*Clinistix* or *Testape*] are not affected)

Direct antiglobulin (Coombs') tests

(false-positive result may occur during therapy with any penicillin)

With physiology/laboratory test values

Alanine aminotransferase (ALT [SGPT]) and

Alkaline phosphatase and

Aspartate aminotransferase (AST [SGOT]) and

Lactate dehydrogenase (LDH)

(serum values may be increased)

Estradiol or

Estriol, total conjugated, or

Estriol-glucuronide or

Estrone, conjugated

(concentrations may be transiently decreased in pregnant women following administration of ampicillin)

White blood cell count

(leukopenia or neutropenia is associated with the use of all penicillins; the effect is more likely to occur with prolonged therapy and severe hepatic function impairment)

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).

Risk-benefit should be considered when the following medical problems exist:

Congestive heart failure or

Renal function impairment or

Electrolyte imbalance due to other causes

(the sodium content of ampicillin sodium administered at high doses may contribute to electrolyte imbalances associated with congestive heart failure, renal function impairment, or other causes; also, because the aminopenicillins are excreted primarily by the kidneys, the dosage regimen should be adjusted to avoid unnecessary accumulation of medication in the plasma and tissues of animals with renal function impairment)^(R-54)

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):

Culture and pathogen susceptibility, *in vitro*, and

Minimum inhibitory concentration (MIC)

(*in vitro* cultures and MIC tests should be done on samples collected prior to aminopenicillin administration to determine pathogen susceptibility)

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 more frequent

Calves

Diarrhea and malabsorption^(R-9)

Note: In healthy neonatal calves, oral administration of 12 mg of ampicillin per kg of body weight (mg/kg) every eight hours has been shown to cause *diarrhea* and *malabsorption*.

Incidence unknown

All species^(R-1; 6; 8; 49)

Hypersensitivity reactions, specifically acute anaphylaxis; hypersensitivity (urticaria, fever)

Horses

Diarrhea—primarily with oral dosage forms^(R-49)

Those indicating need for medical attention only if they continue or are bothersome

Incidence more frequent

Horses

Injection site reaction (mild to moderate heat, pain, or swelling)—with ampicillin trihydrate^(R-1; 57)

Incidence less frequent^(R-63)

Cats and dogs^(R-28)

Anorexia; diarrhea; vomiting

Human side/adverse effects^(R-2)

In addition to the above side/adverse effects reported in animals, the following side/adverse effects have been reported in humans, and are included in the human monograph *Penicillins (Systemic)* in *USP DI Volume 1*; these side/adverse effects are intended for informational purposes only and may or may not be applicable to the use of amox-icillin or ampicillin in the treatment of animals:

Incidence more frequent

Gastrointestinal reactions; oral candidiasis; vaginal candidiasis

Incidence less frequent

Allergic reactions, specifically anaphylaxis; exfoliative dermatitis; serum sickness-like reactions; skin rash, hives, or itching

Incidence rare

***Clostridium difficile* colitis; interstitial nephritis; leukopenia or neutropenia; pain at site of injection; thrombocytopenia; seizures**

Note: *Clostridium difficile colitis* may occur up to several weeks after discontinuation of these medications.

Interstitial nephritis is seen primarily with methicillin, and to a lesser degree with nafcillin and oxacillin, but may occur with any penicillin.

Seizures are more likely to occur in patients receiving high doses of a penicillin and/or patients with severe renal function impairment.

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.**

General Dosing Information

All species: Beta-lactam antibiotics are believed to produce time-dependent bacterial killing; that is, efficacy is related to the time the serum concentrations are maintained above the minimum inhibitory concentration (MIC) of the pathogen. As such, in critical cases frequent dosings (short dosage intervals) may be preferred.

For oral dosage forms only

Calves—Both amoxicillin and ampicillin are more bioavailable in calves when administered in a glucose-glycine-electrolyte solution than when administered with water or milk. Unlike ampicillin, the bioavailability of amoxicillin is not significantly altered by administration with milk as compared with water.^(R-60)

Dogs—There is some decrease in systemic availability when oral amox-icillin or ampicillin is administered after a standard meal instead of on an empty stomach.^(R-25) However, because amoxicillin has twice the oral bioavailability of ampicillin in dogs, the therapeutic efficacy of amoxicillin may be less affected than that of ampicillin by administration with food.^(R-25)

Horses—Oral ampicillin is not recommended in adult horses because of poor oral bioavailability (5%) and the risk of disturbing gastrointestinal bacterial balance, thus causing diarrhea.^(R-49) Amoxicillin trihydrate is also poorly absorbed following oral administration, with a fractional absorption of 10%; oral amoxicillin trihydrate should be used to treat only highly susceptible pathogens.^(R-42)

Sheep—In adult sheep, oral administration of ampicillin does not provide therapeutically significant ampicillin plasma concentrations.^(R-61)

For treatment of adverse effects

Treatment includes the following:

For anaphylaxis:

- Administration of parenteral epinephrine.^(R-6)
- Oxygen administration and respiratory support.
- Parenteral fluid administration as needed.

AMOXICILLIN

Summary of Differences

Pharmacology/pharmacokinetics: Absorption—*Cats, dogs, pigs, and pre-ruminant calves:* A higher percentage of amoxicillin than of ampicillin is absorbed after oral administration.^(R-25-28; 46) In dogs, orally administered amoxicillin is about 70% absorbed.^(R-46)

Oral Dosage Forms

Note: The text between ^{ELUS} and ^{EL} describes uses not included in U.S. product labeling. Text between ^{ELCAN} and ^{EL} describes uses that are not included in Canadian product labeling.

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

AMOXICILLIN FOR ORAL SUSPENSION USP

Usual dose: Antibacterial—*Cats and dogs:* Oral, 10 to 22 mg per kg of body weight every eight, twelve, or twenty-four hours.^(R-14; 26; 69)

Note: ^{ELUS,CAN}Leptospirosis—Although the efficacy has not been established, amoxicillin is used in the treatment of leptospirosis in dogs at an intravenous or oral dose of 22 mg per kg of body weight every six to eight hours.^(R-13; 64) It is not known if this therapy will eliminate the carrier state.^{EL}

Note: As beta-lactams appear to have time-dependent bacterial killing properties, shorter dosing intervals, whenever possible, are recommended to improve efficacy. Once daily dosing should be used only when organisms with very low MICs are suspected.^{(R-}

Strength(s) usually available: When reconstituted according to manufacturer's instructions—
U.S.:^(R-6; 38)

Veterinary-labeled product(s)—
50 mg per mL (Rx) [*Amoxi-Drop*].

Canada:^(R-38)

Veterinary-labeled product(s)—
50 mg per mL (Rx) [*Moxilean-50 Suspension*].

Note: At time of this writing, Canadian veterinary amoxicillin for oral suspension had been unavailable for some time, but not officially discontinued by the manufacturer.

Packaging and storage: Product labeling recommends storing unconstituted product at 25 °C (77 °F), or less.^(R-6) Store in a tight container.

Preparation of dosage form: To reconstitute, add the amount of water recommended by the manufacturer and shake vigorously. Before each use, shake well to resuspend.^(R-6)

Stability: After reconstitution, the suspension retains potency for 14 days. Some products require refrigeration.^(R-6)

USP requirements: Preserve in tight containers, at controlled room temperature. Contains the labeled amount, within –10% to +20%. Contains one or more suitable buffers, colors, flavors, preservatives, stabilizers, sweeteners, and suspending agents. Meets the requirements for Identification, Uniformity of dosage units (single-unit containers), Deliverable volume (multiple-unit containers), pH (5.0–7.5 in the suspension constituted as directed in the labeling), and Water (not more than 3.0%).^(R-17)

AMOXICILLIN TABLETS USP

Usual dose: Antibacterial—*Cats* and *dogs*: See *Amoxicillin For Oral Suspension USP*.

Note: ^{EL,US,CAN} *Calves*, nonruminating—An oral dose of 10 to 22 mg per kg of body weight every eight, twelve, or twenty-four hours has been used in the treatment of susceptible bacterial infections.^{EL, (R-69)}

As beta-lactams appear to have time-dependent bacterial killing properties, shorter dosing intervals, whenever possible, are recommended to improve efficacy. Once daily dosing should be used only when organisms with very low MICs are suspected.^(R-80)

Extra-label withdrawal—There are no established withdrawal times for food-producing animals in the United States or Canada because products labeled for this use are not available. Based on previously available U.S. product labeling, if oral amoxicillin is administered to nonruminating calves at a dose of 8.8 mg per kg of body weight every twelve hours for five days or less, a meat withdrawal time of 20 days should be sufficient to avoid residues.^(R-8)

Strength(s) usually available:

U.S.—^(R-8; 14; 38)

Veterinary-labeled product(s):
50 mg (Rx) [*Amoxi-Tabs*].
100 mg (Rx) [*Amoxi-Tabs*].
150 mg (Rx) [*Amoxi-Tabs*].
200 mg (Rx) [*Amoxi-Tabs*].
400 mg (Rx) [*Amoxi-Tabs*].

Canada—^(R-29; 38)

Veterinary-labeled product(s):
50 mg (Rx) [*Amoxil Tablets*].
100 mg (Rx) [*Amoxil Tablets*; GENERIC].

200 mg (Rx) [*Amoxil Tablets*].

400 mg (Rx) [*Amoxil Tablets*].

Packaging and storage: Product labeling recommends storing this product at 25 °C (77 °F), or less.^(R-14) Store in a tight container.

USP requirements: Preserve in tight containers, at controlled room temperature. Label chewable Tablets to indicate that they are to be chewed before swallowing. Tablets intended solely for veterinary use are so labeled. Contain the labeled amount, within –10% to +20%. Meet the requirements for Thin-layer chromatographic identification test and Dissolution (5% in 30 minutes in water in Apparatus 2 at 75 rpm; and 70% in 20 minutes in water in Apparatus 2 at 75 rpm for products labeled as Chewable Tablets and in Apparatus 2 at 100 rpm for Veterinary products).^(R-17)

AMPICILLIN

Summary of Differences

Pharmacology/pharmacokinetics: Absorption—*Calves*, nonruminating, *cats*, *dogs*, and *pigs*: With oral administration, ampicillin is more poorly absorbed than is amoxicillin; the dosage is adjusted to compensate.^(R-25; 26) In *dogs*, orally administered ampicillin trihydrate is only about 35% absorbed;^(R-46) in *cats*, oral anhydrous ampicillin is about 20 to 40% absorbed.^(R-40)

Additional Dosing Information

See also *General Dosing Information*.

Pharmacology/pharmacokinetics: *Horses*—There is evidence that administering ampicillin concurrently with either gentamicin or kanamycin does not alter the pharmacokinetics of either of the medications.^(R-34; 84)

Parenteral dosage forms—Ampicillin sodium produces higher plasma concentrations than does ampicillin trihydrate; ampicillin trihydrate produces relatively low plasma concentrations but maintains measurable concentrations for a longer period of time.^(R-49)

Oral Dosage Forms

Note: The text between ^{EL,US} and ^{EL} describes uses not included in U.S. product labeling. Text between ^{EL,CAN} and ^{EL} describes uses that are not included in Canadian product labeling.

The ^{EL,US} or ^{EL,CAN} designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

AMPICILLIN CAPSULES USP

Usual dose: ^{EL,US,CAN} Antibacterial^{EL}—

Cats: Oral, 10 to 20 mg per kg of body weight every eight to twenty-four hours.^(R-40; 69)

Dogs: Oral, 20 to 40 mg per kg of body weight every eight to twelve hours.^(R-32; 69)

Note: As beta-lactams appear to have time-dependent bacterial killing properties, shorter dosing intervals, whenever possible, are recommended to improve efficacy. Once daily dosing should be used only when organisms with very low MICs are suspected.^(R-80)

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):
Not commercially available.
Human-labeled product(s):
250 mg (Rx) [GENERIC].
500 mg (Rx) [GENERIC].

Canada—^{R-36; 37}

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

Human-labeled product(s):
250 mg (Rx) [*Apo-Ampi; Novo-Ampicillin; Nu-Ampi*].
500 mg (Rx) [*Apo-Ampi; Novo-Ampicillin; Nu-Ampi*].

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

USP requirements: Preserve in tight containers. Label Capsules to indicate whether the ampicillin therein is in the anhydrous form or is the trihydrate. Contain an amount of ampicillin (anhydrous or as the trihydrate) equivalent to the labeled amount of ampicillin, within -10% to +20%. Meet the requirements for Identification, Dissolution (75% in 45 minutes in water in Apparatus 1 at 100 rpm), Uniformity of dosage units, and Water (not more than 4.0% for the anhydrous and 10.0–15.0% for the trihydrate).^{R-17}

Parenteral Dosage Forms

Note: The dosing and strengths of the dosage forms available are expressed in terms of ampicillin free acid (not the sodium salt).

The text between ^{EL,US} and ^{EL} describes uses not included in U.S. product labeling. Text between ^{EL,CAN} and ^{EL} describes uses that are not included in Canadian product labeling.

The ^{EL,US} or ^{EL,CAN} designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

AMPICILLIN FOR INJECTABLE SUSPENSION USP

Usual dose: Antibacterial—

Cats: Intramuscular or subcutaneous, 10 to 20 mg per kg of body weight every twelve to twenty-four hours.^{R-40}

Dogs: Intramuscular or subcutaneous, 10 to 50 mg per kg of body weight every twelve hours.^{R-32}

Cattle and ^{EL,CAN} *calves*, including *nonruminating calves*^{EL}:

Intramuscular, 4.4 to 11 mg per kg of body weight every twenty-four hours.^{R-3}

Withdrawal times—US: Meat—6 days, Milk—48 hours.^{R-3}

US product labeling listing the above withdrawal times states that treatment should not exceed seven days for withdrawal times to apply.^{R-3} Canada: *Cattle*—Meat: 6 days, Milk: 48 hours.^{R-5} *Pigs*—Meat: 4 days. Canadian product labeling listing the above withdrawal times states that they are based on a dose of 6 mg per kg of body weight every twenty-four hours and a course of therapy not exceeding seven days.^{R-5}

Note: As beta-lactams appear to have time-dependent bacterial killing properties, shorter dosing intervals, whenever possible, are recommended to improve efficacy. Once daily dosing should be used only when organisms with very low MICs are suspected.^{R-80}

Size(s) usually available:

U.S.—^{R-3}

Veterinary-labeled product(s):
10 grams (Rx) [*Polyflex*].
25 grams (Rx) [*Polyflex*].

Canada—^{R-5; 7; 38}

Veterinary-labeled product(s):
25 grams (Rx) [*Polyflex*].

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

Preparation of dosage form:

The sizes may be reconstituted according to manufacturer's directions to one of the following strengths: 100, 200, 250, 300, or 400 mg per mL.

Before each use, shake well to resuspend.^{R-5}

Stability: After reconstitution, the solution retains potency for three months when refrigerated.^{R-3} Canadian product labeling states that this product is stable for one month if storage temperature does not exceed 25 °C.^{R-5}

USP requirements: Preserve in Containers for Sterile Solids. A dry mixture of ampicillin trihydrate and one or more suitable buffers, preservatives, stabilizers, and suspending agents. Contains the equivalent of the labeled amount of ampicillin, within -10% to +20%. Meets the requirements for Identification, Bacterial endotoxins, Sterility, pH (5.0–7.0, in the suspension constituted as directed in the labeling), and Water (11.4–14.0%), and for Uniformity of dosage units, and Labeling under Injections.^{R-17}

AMPICILLIN FOR INJECTION USP

Usual dose: ^{EL,US,CAN} Antibacterial^{EL}—

Cats and dogs: Intramuscular or intravenous, 10 to 20 mg (free acid) per kg of body weight every six to eight hours.^{R-32; 40}

Horses: Intramuscular or intravenous, 10 to 20 mg (free acid) per kg of body weight every six to eight hours.^{R-78; 79}

Note: The dose of 10 to 20 mg per kg of body weight every six to eight hours is sufficient for most sensitive bacteria; however, for infections due to moderately resistant organisms or infections associated with natural tissue barriers, such as those of the central nervous system, doses of up to 25 to 40 mg per kg of body weight every six to eight hours have been used.^{R-83} A possible increased risk of gastrointestinal side effects with increasing dose should be considered.

Size(s) usually available:

U.S.—^{R-1; 38; 76}

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

Human-labeled product(s):
125 mg (free acid) (Rx) [GENERIC].
250 mg (free acid) (Rx) [GENERIC].
500 mg (free acid) (Rx) [GENERIC].
1 gram (free acid) (Rx) [GENERIC].
2 grams (free acid) (Rx) [GENERIC].
10 grams (free acid) (Rx) [GENERIC].

Canada—^{R-77}

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

Human-labeled product(s):
250 mg (free acid) (Rx) [GENERIC].
500 mg (free acid) (Rx) [GENERIC].
1 gram (free acid) (Rx) [GENERIC].
2 grams (free acid) (Rx) [GENERIC].

Packaging and storage: Prior to reconstitution, store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect the reconstituted solution from freezing.

Preparation of dosage form: Dosage form should be reconstituted according to manufacturer's directions.^{R-1}

Stability: See manufacturer's product labeling for stability of unreconstituted and reconstituted product.

Incompatibilities: Extemporaneous admixtures of beta-lactam antibacterials (penicillins and cephalosporins) and aminoglycosides may result in substantial mutual inactivation.

These types of antibacterial agents should not be mixed in the same intravenous bag, bottle, or tubing.

Additional information: This product contains approximately 3 milliequivalents (mEq; millimoles [mmol]) of sodium per gram of ampicillin and could result in electrolyte overload in some animals.^(R-54)

USP requirements: Preserve in Containers for Sterile Solids. Protect the constituted solution from freezing. Contains an amount of Ampicillin Sodium equivalent to the labeled amount of ampicillin within -10% to +15%. Meets the requirements for Constituted solution, Bacterial endotoxins, Particulate matter, Uniformity of dosage units, and for Identification tests, Crystallinity, pH, and Water under Ampicillin Sodium, and for Sterility tests, and Labeling under Injections.^(R-17)

Developed: 07/25/95

Revised: 06/30/02

Interim revision: 07/18/96; 06/02/97; 05/27/98; 10/12/99;
04/04/03; 11/06/06

References

1. Ampicillin package insert (Amp-equine, SmithKline Beecham—US), Rev 5/91, Rec 10/18/94 [discontinued product].
2. Klasco RK, editor. USP DI Drug information for the healthcare professional. Volume I. Greenwood Village, CO: MICROMEDEX; 2006.
3. Ampicillin package insert (Polyflex, Fort Dodge Laboratories, Inc.—US), Rev 2/04. Available at www.wyeth.com. Accessed on September 9, 2006.
4. Nathwani D, Wood MJ. Penicillins. A current review of their clinical pharmacology and therapeutic use. *Drugs* 1993; 45(6): 866-94.
5. Ampicillin product information (Polyflex, Wyeth—Canada). In: Arrijo-Dechert A, editor. Compendium of veterinary products, CD edition. Port Huron, MI: North American Compendiums, Inc., 2006.
6. Amoxicillin package insert (Amoxi-Drop, Pfizer—US), Rev 9/02. Available at www.pfizerah.com. Accessed on September 9, 2006.
7. Telecommunication with Wyeth Animal Health Canada Order Desk. September 9, 2006.
8. Amoxicillin package insert (Amoxi-Bol, SmithKline Beecham—US), Rev 4/92, Rec 10/18/94 [discontinued product].
9. Rollins RE, et al. Diarrhea and malabsorption in calves associated with therapeutic doses of antibiotics: Absorptive and clinical changes. *Am J Vet Res* 1986 May; 47(5): 987-91.
10. Hunt EH. Diarrheal diseases of neonatal ruminants. In: Howard JL. Current veterinary therapy 3. Food animal practice. Philadelphia: W.B. Saunders Company; 1993. p. 103-9.
11. Amoxicillin product information (Amoxicillin 100, Vetoquinol—Canada). Available at www.vetoquinol.ca. Accessed on May 9, 2006.
12. Roudebush P. Infectious pneumonia. In: Kirk RW, Bonagura JD, editors. Current veterinary therapy XI. Small animal practice. Philadelphia: W.B. Saunders Company; 1992. p. 228-36.
13. Adin CA, Cowgill LD. Treatment and outcome of dogs with leptospirosis: 36 cases (1990-1998). *J Am Vet Med Assoc* 2000 Feb 1; 216(3): 371-5.
14. Amoxicillin package insert (Amoxi-Tabs, Pfizer—US), Rev 9/03. Available at www.pfizerah.com. Accessed on September 9, 2006.
15. Ling GV, Gilmore CJ. Penicillin G or ampicillin for oral treatment of canine urinary tract infections. *J Am Vet Med Assoc* 1977 Aug; 171(4): 358-61.
16. USP dictionary of USAN and international drug names, 2006 ed. Rockville, MD: The United States Pharmacopeial Convention, Inc.; 2006.
17. The United States pharmacopeia. The national formulary. USP 29th revision (January 1, 2006). NF 24th ed (January 1, 2006).

18. Rockville, MD: The United States Pharmacopeial Convention, Inc., 2005. Available at www.uspnf.com. Accessed on May 8, 2006.
19. Donowitz GR, Mandell GL. Beta-lactam antibiotics. *N Engl J Med* 1988; 318: 419-26.
20. Papich MG. The beta-lactam antibiotics: clinical pharmacology and recent developments. *Compend Contin Educ Pract Vet* 1987; 9(1): 68-74.
21. Wright AJ, Wilkowski CJ. The penicillins. *Mayo Clin Proc* 1983; 58: 21-32.
22. Beech J, Leitch M, Kohn CW, et al. Serum and synovial fluid levels of sodium ampicillin and ampicillin trihydrate in horses. *J Equine Med Surg* 1979; 3: 350-4.
23. Riviere JE, Craigmill AL, Sundlof SF. Handbook of comparative pharmacokinetics and residues of veterinary antimicrobials. Boca Raton, FL: CRC Press, Inc.; 1991. p. 52.
24. Sarasola P, McKellar QA. Pharmacokinetics and applications of ampicillin sodium as an intravenous infusion in the horse. *J Vet Pharmacol Ther* 1993; 16: 63-9.
25. Watson ADJ, Emslie DR, Martin IC, et al. Effect of ingesta on systemic availability of penicillins administered orally in dogs. *J Vet Pharmacol Ther* 1986; 9: 140-9.
26. Spurluck SL, Wilcke JR. Penicillins and cephalosporins. In: Proceedings of the thirty-second annual convention of the American Association of Equine Practitioners. 1987. p. 175-82.
27. Plumb DC. Veterinary drug handbook. White Bear Lake, MN: PharmaVet Publishing, 1991: 467-9, 480-6.
28. Amoxicillin product labeling. (Amoxil tablets, Pfizer—Canada). Available at www.pfizer.ca. Accessed on September 9, 2006.
29. Greene CE, editor. Infectious diseases of the dog and cat, 2nd ed. Philadelphia: WB Saunders; 1998. p. 279-80.
30. Ross LA. Leptospirosis. In: Bonagura J, Kersey R, editors. Kirk's current veterinary therapy XIII: small animal practice. Philadelphia: WB Saunders. 1999. p. 308-10.
31. Kirk RW, Bonagura JD, editors. Current veterinary therapy XI. Small animal practice. Philadelphia: W.B. Saunders Company; 1992. p. 1234.
32. Ampicillin package insert (Principen, Apotex—US), Rev 4/90, Rec 7/93.
33. Bowman KF, Dix LP, Riond JL, et al. Prediction of pharmacokinetic profiles of ampicillin sodium, gentamicin sulfate, and combination ampicillin sodium-gentamicin sulfate in serum and synovia of healthy horses. *Am J Vet Res* 1986; 47(7): 1590-6.
34. Traver DS, Riviere JE. Ampicillin in mares: a comparison of intramuscular sodium ampicillin or sodium ampicillin-ampicillin trihydrate injection. *Am J Vet Res* 1982 Mar; 43(3): 402-4.
35. Ampicillin package insert (Nu-Ampi, Nu-Pharm—Canada), Rev 1/94, Rec 4/94.
36. Ampicillin (Apo-Ampi, Apotex). In: Krogh CME, editor. CPS Compendium of pharmaceuticals and specialties. 29th ed. Ottawa: Canadian Pharmaceutical Association; 1994. p. 83, 893, 995.
37. Arrijo-Dechert A, editor. Compendium of veterinary products, CD edition. Port Huron, MI: North American Compendiums, Inc., 2006.
38. Galtier P, Charpentreau JL. Pharmacokinetics of ampicillin in pigs. *J Vet Pharmacol Ther* 1979; 2: 173-80.
39. Mercer HD, et al. Bioavailability and pharmacokinetics of several dosage forms of ampicillin in the cat. *Am J Vet Res* 1977 Sep; 38(9): 1353-9.
40. Baggot JD, et al. Bioavailability and disposition kinetics of amoxicillin in neonatal foals. *Equine Vet J* 1988; 20(2): 125-7.
41. Wilson WD, et al. Pharmacokinetics and estimated bioavailability of amoxicillin in mares after intravenous, intramuscular, and oral administration. *Am J Vet Res* 1988 Oct; 49(10): 1688-94.

43. Ziv G, Sulman FG. Binding of antibiotics to bovine and ovine serum. *Antimicrob Agents Chemother* 1972 Sep; 2(3): 206-13.
44. Powers TE, Garg RC. Pharmacotherapeutics of newer penicillins and cephalosporins. *J Am Vet Med Assoc* 1980 May; 10(2): 1054-60.
45. Montesissa C, et al. Pharmacokinetics of sodium amoxicillin in horses. *Res Vet Sci* 1988; 44: 233-6.
46. Yeoman GH. Microbiology and bioavailability of amoxicillin. *Vet Med Small Anim Clin* 1977; 4(suppl): 720-38.
47. Craigmill AL, Pass MA, Wetzlich S. Comparative pharmacokinetics of amoxicillin administered intravenously to sheep and goats. *J Vet Pharmacol Ther* 1992; 15: 72-7.
48. Durr A. Comparison of the pharmacokinetics of penicillin G and ampicillin in the horse. *Res Vet Sci* 1976; 20: 24-9.
49. Sarasola P, McKellar QA. Ampicillin and its congener prodrugs in the horse. *Br Vet J* 1994; 150(2): 173-87.
50. Ziv G, Shani J, Sulman FG. Pharmacokinetic evaluation of penicillin and cephalosporin derivatives in serum and milk of lactating cows and ewes. *Am J Vet Res* 1973 Dec; 34(12): 1561-5.
51. Ziv G, Horsey J. Elevation and prolongation of serum ampicillin and amoxycillin concentrations in calves by the concomitant administration of probenecid. *J Vet Pharmacol Ther* 1979; 2: 187-94.
52. Sarasola P, McKellar QA. Effect of probenecid on disposition kinetics of ampicillin in horses. *Vet Rec* 1992; 131: 173-5.
53. Huber WG. Penicillins. In: Booth NH, McDonald LE. *Veterinary pharmacology and therapeutics*, 5th ed. Ames, IA: Iowa State University Press; 1988. p. 796-812.
54. Riviere JE, Coppoc GL. Dosage of antimicrobial drugs in patients with renal insufficiency. *J Am Vet Med Assoc* 1981 Jan; 178(1): 70-2.
55. Galtier P, Alvinerie M. Enhancement of ampicillin bioavailability in pigs. *J Vet Pharmacol Ther* 1979; 2: 181-6.
56. Mason MJ, Mason KV. A pemphigus foliaceus-like eruption associated with the use of ampicillin in a cat. *Aust Vet J* 1987 Jul; 64(7): 223-4.
57. Traver DS, Riviere JE. Penicillin and ampicillin therapy in horses. *J Am Vet Med Assoc* 1981 Jun; 178(11): 1186-9.
58. Prescott JF, Baggot JD. *Antimicrobial therapy in veterinary medicine*, 2nd ed. Ames, IA: Iowa State University Press; 1993. p. 90-5.
59. Leib MS. Acute vomiting: a diagnostic approach and symptomatic management. In: Kirk RW, Bonagura JD, editors. *Current veterinary therapy XI. Small animal practice*. Philadelphia: W.B. Saunders Company; 1992. p. 583-7.
60. Palmer GH, Bywater RJ, Stanton A. Absorption in calves of amoxicillin, ampicillin, and oxytetracycline given in milk replacer, water or an oral rehydration formulation. *Am J Vet Res* 1983 Jan; 44(1): 68-71.
61. Oukessou M, Toutain PL. Effect of water deprivation on absorption (oral, intramuscular) and disposition of ampicillin in sheep. *J Vet Pharmacol Ther* 1992; 15: 421-32.
62. Braun RK, et al. Efficacy of amoxicillin trihydrate for the treatment of experimentally induced foot rot in cattle. *Am J Vet Res* 1987 Dec; 48(12): 1751-4.
63. Francis ME, Marshall AB, Turner WT. Amoxycillin: clinical trials in dogs and cats. *Vet Rec* 1978 Apr; 102: 377-80.
64. Committee comment, 1/22/02.
65. Hjerpe CA. The bovine respiratory disease complex. In: Howard JL. *Current veterinary therapy 3. Food animal practice*. Philadelphia: W.B. Saunders Company; 1993. p. 653-64.
66. Robinson NE, editor. *Current therapy in equine medicine 3*. Philadelphia: W.B. Saunders Company; 1992. p. 815.
67. Brown MP, et al. Ampicillin trihydrate in foals: serum concentrations and clearance after a single oral dose. *Equine Vet J* 1984; 16(4): 371-3.
68. Panel comment, Rec 2/23/95.
69. Panel comment, Rec 3/9/95.
70. Panel comment, Rec 2/22/95.
71. Panel comment, Rec 3/6/95.
72. Panel comment, Rec 3/29/95.
73. Panel comment, Rec 2/17/95.
74. Panel comment, Rec 2/27/95.
75. Panel comment, Rec 11/28/95.
76. PDR Physicians' desk reference. 48th ed. 1994. Montvale, NJ: Medical Economics Data Production Company; 1994. p. 2571.
77. Krogh, CME, editor. *CPS Compendium of pharmaceuticals and specialties*. 29th ed. Ottawa: Canadian Pharmaceutical Association; 1994. p. 63-4, 995.
78. Panel comment, Rec 6/22/95.
79. Panel comment, Rec 6/29/95.
80. Committee comment, Rec 1/15/02.
81. Bywater RJ, Palmer GH, Buswell JF, Stanton A. Clavulanate and amoxycillin: activity in vitro and bioavailability in the dog. *Vet Rec* 1985; 116: 33-6.
82. Soback S, Bor A, Kurtz B, et al. Clavulanate-potentiated amoxycillin: in vitro antibacterial activity and oral bioavailability in calves. *J Vet Pharmacol Ther* 1987; 10: 105-13.
83. Panel comment, Rec 11/30/95.
84. Firth EC, Klein WR, Nouws JFM, et al. Effect of induced synovial inflammation on pharmacokinetics and synovial concentration of sodium ampicillin and kanamycin sulfate after systemic administration in ponies. *J Vet Pharmacol Ther* 1988; 11: 56-62.
85. Sarasola P, McKellar QA. Pharmacokinetics of bacampicillin in equids. *Am J Vet Res* 1995 Nov; 56(11): 1486-92.
86. Ensink JM, Klein WR, Mevius DJ, et al. Bioavailability of oral penicillins in the horse: a comparison of pivampicillin and amoxicillin. *J Vet Pharmacol Ther* 1992; 15: 221-30.