soluble in water or other aqueous solutions. After reconstitution, ampicillin sodium has a pH of 8–10 at a concentration of 10 mg/mL. Commercially available ampicillin sodium for injection has approximately 3 mEq of sodium per gram of ampicillin.

Potency of the ampicillin salts is expressed in terms of ampicillin anhydrous.

Ampicillin may also be known as: aminobenzylpenicillin, ampicillinum, ampicillinum anhydricum, anhydrous ampicillin, AY-6108, BRL-1341, NSC-528986, or P-50; many trade names are available.

Storage/Stability/Compatibility

Ampicillin anhydrous or trihydrate capsules and powder for oral suspension should be stored at room temperature (15–30°C). After reconstitution, the oral suspension is stable for 14 days if refrigerated (2–8°C); 7 days when kept at room temperature.

Ampicillin trihydrate for injection (*Polyflex*®) is stable for 12 months if refrigerated (2–8°C); 3 months when kept at room temperature.

Ampicillin sodium for injection is relatively unstable after reconstitution and should generally be used within 1 hour of reconstitution. As the concentration of the drug in solution increases, the stability of the drug decreases. Dextrose may also speed the destruction of the drug by acting as a catalyst in the hydrolysis of ampicillin.

While most sources recommend using solutions of ampicillin sodium immediately, studies have demonstrated that at concentrations of 30 mg/mL, ampicillin sodium solutions are stable up to 48 hours at 4°C in sterile water for injection or 0.9% sodium chloride (72 hours if concentrations are 20 mg/mL or less). Solutions with a concentration of 30 mg/mL or less have been shown to be stable up to 24 hours in solutions of lactated Ringer's solution if kept at 4°C. Solutions of 20 mg/mL or less are reportedly stable up to 4 hours in D_5W if refrigerated.

Ampicillin sodium is reportedly **compatible** with the following additives (see the above paragraph for more information): heparin sodium, chloramphenicol sodium succinate, procaine HCl and verapamil HCl.

Ampicillin sodium is reportedly **incompatible** with the following additives: amikacin sulfate, chlorpromazine HCl, dopamine HCl, erythromycin lactobionate, gentamicin HCl, hydralazine HCl, hydrocortisone sodium succinate, kanamycin sulfate, lincomycin HCl, oxytetracycline HCl, polymyxin B sulfate, prochlorperazine edisylate, sodium bicarbonate and tetracycline HCl. Compatibility is dependent upon factors such as pH, concentration, temperature and diluent used; consult specialized references or a hospital pharmacist for more specific information.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Ampicillin Trihydrate Injection Powder for Suspension: 10 g and 25 g (of ampicillin) vials; *Polyflex*® (Fort Dodge); (Rx). Approved for use in dogs, cats, and cattle. Withdrawal times at labeled doses (cattle; do not treat for more than 7 days): Milk = 48 hours; Slaughter = 6 days (144 hours).

HUMAN-LABELED PRODUCTS:

Ampicillin Sodium Powder for Injection: 250 mg, 500 mg, 1 g, & 2 g in vials; generic; (Rx)

Ampicillin Capsules (as trihydrate): 250 mg, & 500 mg; *Principen*® (Geneva); generic; (Rx)

Ampicillin (as the trihydrate) Powder for Oral Suspension: 125 mg/5 mL & 250 mg/5 mL when reconstituted in 100 mL and 200 mL; *Principen*® (Geneva); (Rx)

AMPICILLIN SODIUM + SULBACTAM SODIUM

(am-pi-***sill***-in; sul-***bak***-tam) Unasyn®

INJECTABLE POTENTIATED AMINOPENICILLIN

Prescriber Highlights

- Parenteral potentiated aminopenicillin that may be used for infections where amoxicillin/clavulanate would be appropriate but when an injectable antibiotic is required
- Hypersensitivity reactions possible; contraindicated in patients with documented severe hypersensitivity to penicillins
- Usually dosed IM or IV q6–8h

Uses/Indications

Ampicillin sodium/sulbactam sodium in a 2:1 ratio is effective when used parenterally for several types of infections caused by many beta-lactamase-producing bacterial strains of otherwise resistant *E. coli*, *Pasturella* spp., *Staphylococcus* spp., *Klebsiella*, and *Proteus*. Other aerobic bacteria commonly susceptible to this combination include *Streptococcus*, *Listeria monocytogenes*, *Bacillus anthracis*, *Salmonella*, *Pasturella*, and *Acinetobacter*. Anaerobic bacterial infections caused by *Clostridium*, *Bacteroides*, *Fusobacterium*, *Peptostreptococcus* or *Propionibacterium* may be effectively treated with ampicillin/sulbactam.

Type I beta-lactamases that may be associated with *Citrobacter*, *Enterobacter*, *Serratia* and *Pseudomonas* are not generally inhibited by sulbactam or clavulanic acid. Ampicillin/sulbactam is ineffective against practically all strains of *Pseudomonas aeruginosa*.

In dogs and cats, ampicillin/sulbactam therapy may be considered when oral amoxicillin/clavulanate treatment is not viable (patient NPO, critically ill) or when large parenteral doses would be desirable (sepsis, pneumonia, other severe infections) for treating susceptible bacterial infections or prophylaxis.

Ampicillin/sulbactam has been used successfully to treat experimentally induced *Klebsiella* pneumonia in foals.

Pharmacology/Actions

When sulbactam is combined with ampicillin it extends its spectrum of activity to those bacteria that produce beta-lactamases of Richmond-Sykes types II-VI that would otherwise render ampicillin ineffective. Sulbactam binds to beta-lactamases thereby "protecting" the beta-lactam ring of ampicillin from hydrolysis.

Sulbactam has some intrinsic antibacterial activity against some bacteria (*Neisseria*, *Moraxella*, *Bacteroides*) at achievable levels. Sulbactam binding to certain penicillin-binding proteins (PBPs) may explain its activity. For most bacteria, sulbactam alone does not achieve levels sufficient to act alone as an antibacterial but when used in combination with ampicillin, synergistic effects may result.

On a mg for mg basis, clavulanic acid is a more potent beta-lactamase inhibitor than is sulbactam, but sulbactam has advantages of reduced likelihood of inducing chromosomal beta-lactamases, greater tissue penetration and greater stability.

For further information on the pharmacology of ampicillin, refer to that monograph.

Pharmacokinetics
As sulbactam sodium is not appreciably absorbed from the GI tract, this medication must be given parenterally. A covalently linked double ester form of ampicillin/sulbactam (sultamicillin) is orally absorbed, but this combination is not commercially available in the USA. When administered parenterally (IV/IM), sulbactam's pharmacokinetic profile closely mirrors that of ampicillin in most species studied. During the elimination phase in calves, plasma concentrations of sulbactam were consistently higher than those of ampicillin, leading the authors of the study to propose using a higher ratio (than 2:1 ampicillin/sulbactam) if the combination is used in calves.

Contraindications/Precautions/Warnings
Penicillins are contraindicated in patients with a history of severe hypersensitivity (*e.g.,* anaphylaxis) to them. Because there may be cross-reactivity, use penicillins cautiously in patients who are documented hypersensitive to other beta-lactam antibiotics (*e.g.*, cephalosporins, cefamycins, carbapenems).

Patients with severe renal dysfunction may require increased periods of time between doses.

Adverse Effects
Intramuscular injections may be painful. Intravenous injections may cause thrombophlebitis. Hypersensitivity reactions to penicillins occur infrequently in animals, but can be severe (anaphylaxis), particularly after IV administration.

High doses or very prolonged use of penicillins have been associated with neurotoxicity (*e.g.*, ataxia in dogs). Although the penicillins are not considered hepatotoxic, elevated liver enzymes have been reported. Other effects reported in dogs include tachypnea, dyspnea, edema and tachycardia.

Reproductive/Nursing Safety
Penicillins have been shown to cross the placenta and safe use during pregnancy has not been firmly established, but neither have there been any documented teratogenic problems associated with these drugs; however, use only when the potential benefits outweigh the risks. In humans, the FDA categorizes ampicillin as category ***B*** for use during pregnancy (*Animal studies have not yet demonstrated risk to the fetus, but there are no adequate studies in pregnant women; or animal studies have shown an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.*) In a separate system evaluating the safety of drugs in canine and feline pregnancy (Papich 1989), ampicillin is categorized as in class: ***A*** (*Probably safe. Although specific studies may not have proved the safety of all drugs in dogs and cats, there are no reports of adverse effects in laboratory animals or women.*)

It is unknown if sulbactam crosses the placenta and safe use during pregnancy has not been established.

Both ampicillin and sulbactam are distributed into human breast milk in low concentrations. For humans, the World Health Organization (WHO) rates ampicillin as being **compatible** with breastfeeding and the American Academy of Pediatrics lists sulbactam as **compatible** with breastfeeding.

Overdosage/Acute Toxicity
Neurological effects (ataxia) have rarely been reported in dogs receiving very high dosages of penicillins; should these develop, weigh the risks of continued use versus those of dosage reduction or using a different antibiotic. In humans, very high dosages of parenteral penicillins, especially in those with renal disease, have induced CNS effects.

Drug Interactions
The following drug interactions have either been reported or are theoretical in humans or animals receiving ampicillin/sulbactam and may be of significance in veterinary patients:

- **AMINOGLYCOSIDES** (**amikacin, gentamicin, tobramycin**): *In vitro* studies have demonstrated that penicillins can have synergistic or additive activity against certain bacteria when used with aminoglycosides. However, beta-lactam antibiotics can inactivate aminoglycosides *in vitro* and *in vivo* in patients in renal failure or when penicillins are used in massive dosages. Amikacin is considered the most resistant aminoglycoside to this inactivation.
- **PROBENECID**: Can reduce the renal tubular secretion of both ampicillin and sulbactam, thereby maintaining higher systemic levels for a longer period of time. This potential "beneficial" interaction requires further investigation before dosing recommendations can be made for veterinary patients.

Laboratory Considerations
- Ampicillin may cause false-positive **urine glucose** determinations when using cupric sulfate solution (Benedict's Solution, *Clinitest*®). Tests utilizing glucose oxidase (*Test-Tape*®, *Clinistix*®) are not affected by ampicillin.
- As penicillins and other beta-lactams can inactivate **aminoglycosides** *in vitro* (and *in vivo* in patients in renal failure or when penicillins are used in massive dosages), serum concentrations of aminoglycosides may be falsely decreased particularly when the serum is stored prior to analysis. It is recommended that if the aminoglycoside assay is delayed, samples be frozen and, if possible, drawn at times when the beta-lactam antibiotic is at a trough.

Doses
- **DOGS:**

  For susceptible infections:
  a) For respiratory infections: 50 mg/kg (combined) IV q8h (Hawkins 2003)
  b) For respiratory infections: 20 mg/kg IV or IM q6–8h (Greene and Reinero 2006)
  c) As adjunctive treatment of serious bite wounds: 30–50 mg/kg q8h IV (Bateman 2005b)
  d) For intra-abdominal infections: 20 mg/kg IV or IM q6–8h (Extrapolation of human dose with limited studies in dogs and cats) (Greene 2006)

- **CATS:**

  For susceptible infections:
  a) For respiratory infections using ampicillin/sulbactam (*Unasyn*®): 50 mg/kg (combined) IV q8h (Hawkins 2003)
  b) As adjunctive treatment of serious bite wounds: 30–50 mg/kg q8h IV (Bateman 2005b)
  c) For intra-abdominal infections: 20 mg/kg IV or IM q6–8h (Extrapolation of human dose with limited studies in dogs and cats) (Greene 2006)

Monitoring
- Because penicillins usually have minimal toxicity associated with their use, monitoring for efficacy is usually all that is required unless toxic signs or symptoms develop
- Serum levels and therapeutic drug monitoring are not routinely performed with these agents

Client Information
- Because of the dosing intervals required this drug is best administered to inpatients only

Chemistry/Synonyms
Ampicillin sodium and sulbactam sodium for injection occurs as a white to off-white powder that is freely soluble in water or other aqueous solutions.

Ampicillin/Sulbactam may also be known as: *Ampibactan®, Bacimex®, Begalin-P®, Bethacil®, Comabactan®, Galotam®, Loricin®, Sulam®, Sulperazon®, Synergistin®, Unacid®, Unacim®, Unasyn®* or *Unasyna®*.

Storage/Stability/Compatibility
The unreconstituted powder should be stored at temperatures at, or below, 30°C.

Diluents for reconstituting the powder for injection for IV use that are reported **compatible** with ampicillin/sulbactam include sterile water for injection, and 0.9% sodium chloride. If reconstituted to a concentration of 45 mg/mL (30/15), the resulting solution is stable for 8 hours at room temperature and for 48 hours at 4°C. If reconstituted to a concentration of 30 mg/mL (20/10), the resulting solution is stable for 72 hours at 4°C. After reconstitution and before administering, the solution should be further diluted into a 50 or 100 mL bag of 0.9% sodium chloride and administered IV over 15–30 minutes. Diluted solutions for IV administration are stable at room temperature for 8 hours.

When reconstituting for IM use, sterile water for injection or 0.5% or 2% lidocaine HCl injection may be used. 3.2 mL of diluent is added to the 1.5 g vial; 6.4 mL of diluent to the 3 g vial. After reconstituting, the solution should be administered within 1 hour.

Ampicillin/sulbactam injection is **not compatible** with aminoglycoside antibiotics (*e.g.*, gentamicin, amikacin) and should not be mixed with these agents.

Ampicillin/sulbactam is **compatible** with vancomycin when mixed at concentrations of 50/25 mg/mL of ampicillin/sulbactam and 20 mg/mL or less of vancomycin.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Ampicillin Sodium/Sulbactam Sodium Powder (injection): 1.5 g (1 g ampicillin sodium/0.5 g sulbactam sodium), 3 g (2 g ampicillin sodium/1 g sulbactam sodium) in vials, piggyback bottles and ADD-Vantage vials, and 10 g (10 g ampicillin sodium/5 g sulbactam sodium) in bulk; *Unasyn®* (Roerig); (Rx)

AMPROLIUM HYDROCHLORIDE

(am-proe-*lee*-um) **Amprovine®, Corid®**

ANTICOCCIDIAL

Prescriber Highlights
- Thiamine analog antiprotozoal (coccidia)
- Prolonged high dosages may cause thiamine deficiency; treatment is usually no longer than 14 days
- Occasionally may cause GI or neurologic effects
- May be unpalatable

Uses/Indications
Amprolium has good activity against *Eimeria tenella* and *E. acervulina* in poultry and can be used as a therapeutic agent for these organisms. It only has marginal activity or weak activity against *E. maxima, E. mivati, E. necatrix*, or *E. brunetti*. It is often used in combination with other agents (*e.g.*, ethopabate) to improve control against those organisms.

In cattle, amprolium has approval for the treatment and prevention of *E. bovis* and *E. zurnii* in cattle and calves.

Amprolium has been used in dogs, swine, sheep, and goats for the control of coccidiosis, although there are no approved products in the USA for these species.

Pharmacology/Actions
By mimicking its structure, amprolium competitively inhibits thiamine utilization by the parasite. Prolonged high dosages can cause thiamine deficiency in the host; excessive thiamine in the diet can reduce or reverse the anticoccidial activity of the drug.

Amprolium is thought to act primarily upon the first generation schizont in the cells of the intestinal wall, preventing differentiation of the metrozoites. It may suppress the sexual stages and sporulation of the oocysts.

Pharmacokinetics
No information was located for this agent.

Contraindications/Precautions/Warnings
Not recommended to be used for more than 12 days in puppies.

Adverse Effects
In dogs, neurologic disturbances, depression, anorexia, and diarrhea have been reported but are rare and are probably dose-related. See Overdosage section below for treatment recommendations. The undiluted liquid or pastes are reportedly unpalatable.

Overdosage/Acute Toxicity
Amprolium has induced polioencephalomalacia (PEM) in sheep when administered at 880 mg/kg PO for 4–6 weeks and at 1 gram/kg for 3–5 weeks. Erythrocyte production also ceased in lambs receiving these high dosages.

It is reported that overdoses of amprolium will produce neurologic clinical signs in dogs. Treatment should consist of stopping amprolium therapy and administering parenteral thiamine (1–10 mg/day IM or IV).

Drug Interactions
The following drug interactions have either been reported or are theoretical in animals receiving amprolium and may be of significance in veterinary patients:

- **THIAMINE:** Exogenously administered thiamine in high doses may reverse or reduce the efficacy of amprolium

Doses
- **DOGS:**

For coccidiosis:

a) Small Pups (< 10 kg adult weight): 100 mg (using the 20% powder) in a gelatin capsule PO once daily for 7–12 days. Large pups (>10 kg adult weight): 200 mg (using the 20% powder) in a gelatin capsule PO once daily for 7–12 days. *In food,* for pups or bitches: 250–300 mg total dose using the 20% powder on food once daily for 7–12 days. *In water,* for pups or bitches: 30 mL of the 9.6% solution in one gallon of water (no other water provided) for 7–10 days (Greene, Hartmannn et al. 2006)

b) Prophylaxis: 30 mL of 9.6% solution in one gallon (3.8 L) of drinking water or 1.25 grams of 20% powder in food to feed 4 pups daily. Give as sole source of food or water for 7 days prior to shipping. Bitches may be given medicated water (as above) as the sole source of water for 10 days prior to whelping. (USPC 1989)