Monitoring
- Efficacy for the infection treated (CBC, clinical signs, etc.)

Client Information
- Limited experience in veterinary medicine
- Best suited for inpatient use

Chemistry/Synonyms
Piperacillin sodium/tazobactam sodium occurs as a white or almost white, cryodessicated powder. Tazobactam is structurally related to sulbactam and a penicillanic acid sulfone derivative. The commercially available piperacillin/tazobactam injection contains 2.79 mEq of sodium and 0.25 mg of EDTA per gram of piperacillin.

Tazobactam may also be known as: CL 298741, or YTR 830H. Piperacillin may also be known as piperacillinum, BL-P 1908, Cl 867, CL 227193, T 12220, and TA 058. International trade names for piperacillin/tazobactam include: *Tazobac*®, *Tazocin*®, *Zosyn*® and others.

Storage/Stability/Compatibility
Piperacillin/tazobactam injection vials and *ADD-Vantage* vials should be stored at controlled room temperature (20–25°C).

Conventional vials should be reconstituted with 5 mL of diluent per gram of piperacillin. Suitable diluents include 0.9% sodium chloride, sterile water for injection, and bacteriostatic saline or water for injection. Once reconstituted, further dilute for intravenous infusion with 50–150 mL of 0.9% sodium chloride, LRS (reformulated product only—see below) or D5W. IV infusion should be over at least 30 minutes.

Once reconstituted, vials should be used immediately. It is recommended to discard after 24 hours if kept at room temperature or 48 hours if stored in the refrigerator. The manufacturer recommends not freezing reconstituted vials. IV bags (50–150 mL) containing further diluted product are stable for up to 24 hours at room temperature and one week if refrigerated. As no preservatives are used, sterility is not assured in stored reconstituted products.

Zosyn® (piperacillin/tazobactam) injection underwent a formulation change in 2006. Sodium citrate (buffer) and EDTA (metal chelator) were added that made it **compatible** with lactated Ringer's injection and via simultaneous Y-site administration at specific concentrations of gentamicin and amikacin (but not tobramycin). This reformulated product has a yellow background behind the *Zosyn*® name on the label. Refer to the package insert for specific information on diluent and concentration compatibility.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Piperacillin Sodium & Tazobactam Injection (lyophilized powder for injection); *Zosyn*® (Wyeth); (Rx):

2.25 g (piperacillin 2 g/tazobactam 0.25 g) in vials and *ADD-Vantage*® vials; contains 4.69 mEq sodium

3.375 g (piperacillin 3 g/tazobactam 0.375 g) in vials and *ADD-Vantage*® *vials*; contains 7.04 mEq sodium

4.5 g (piperacillin 4 g/tazobactam 0.5 g) in vials and *ADD-Vantage*® vials; contains 9.36 mEq sodium

40.5 g bulk vials (piperacillin 36 g/ tazobactam 4.5 g); in bulk vials; contains 84.5 mEq sodium

Also available in 3.375 g/50 mL and 4.5 g/100 mL premixed, frozen *Galaxy*® containers.

PIPERAZINE

(pi-per-a-***zeen***) Pipa-Tabs®

ANTIPARASITIC (ASCARIDS)

Prescriber Highlights
- Anthelmintic for ascarids in a variety of species
- Contraindications: Chronic liver, kidney disease, & gastrointestinal hypomotility.
- Caution: Seizure disorders, horses with heavy infestations of *P. equorum*
- Adverse Effects: Unlikely, but diarrhea, emesis, or ataxia possible

Uses/Indications
Piperazine is used for the treatment of ascarids in dogs, cats, horses, swine and poultry. Piperazine is considered safe to use in animals with concurrent gastroenteritis and during pregnancy.

Pharmacology/Actions
Piperazine is thought to exert "curare-like" effects on susceptible nematodes, thereby paralyzing or narcotizing the worm and allowing it to be passed out with the feces. The neuromuscular blocking effect is believed to be caused by blocking acetylcholine at the myoneural junction. In ascarids, succinic acid production is also inhibited.

Pharmacokinetics
Piperazine and its salts are reportedly readily absorbed from the proximal sections of the GI tract and the drug is metabolized and excreted by the kidneys. Absorptive, distribution, and elimination kinetics on individual species were not located.

Contraindications/Precautions/Warnings
Piperazine should be considered contraindicated in patients with chronic liver or kidney disease, and those with gastrointestinal hypomotility. There is some evidence in humans that high-dose piperazine may provoke seizures in patients with a history of seizures, or with renal disease.

If used in horses with heavy infestations of *P. equorum*, rupture or blockage of intestines is possible due to the rapid death and detachment of the worm.

Adverse Effects
Adverse effects are uncommon at recommended doses, but diarrhea, emesis, and ataxia may be noted in dogs or cats. Horses and foals generally tolerate the drug quite well, even at high dosage rates, but a transient softening of the feces may be seen. Other adverse effects have been seen at toxic dosages; refer to the Overdosage section below for more information.

Reproductive/Nursing Safety
In a system evaluating the safety of drugs in canine and feline pregnancy (Papich 1989), this drug is categorized as class: ***A*** (*Probably safe. Although specific studies may not have proved he safety of all drugs in dogs and cats, there are no reports of adverse effects in laboratory animals or women.*)

No information was located on use during nursing, but it probably is safe to use.

Overdosage/Acute Toxicity

Acute massive overdosage can lead to paralysis and death, but the drug is generally considered to have a wide margin of safety. The oral LD_{50} of piperazine adipate in mice is 11.4 g/kg.

In cats, adverse effects occur within 24 hours after a toxic dose is ingested. Emesis, weakness, dyspnea, muscular fasciculations of ears, whiskers, tail and eyes, rear limb ataxia, hypersalivation, depression, dehydration, head-pressing, positional nystagmus and slowed pupillary responses have all been described after toxic ingestions. Many of these effects may also be seen in dogs after toxic piperazine ingestions.

Treatment is symptomatic and supportive. If ingestion was recent, use of activated charcoal and a cathartic has been suggested. Intravenous fluid therapy and keeping the animal in a quiet, dark place is recommended. Recovery generally takes place within 3–4 days.

Drug Interactions

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

- **CHLORPROMAZINE:** Although data conflicts, piperazine and chlorpromazine may precipitate seizures if used concomitantly
- **LAXATIVES:** The use of purgatives (laxatives) with piperazine is not recommended as the drug may be eliminated before its full efficacy is established
- **PYRANTEL/MORANTEL:** Piperazine and pyrantel/morantel have antagonistic modes of action and should generally not be used together

Laboratory Considerations

- Piperazine can have an effect on **uric acid** blood levels, but references conflict with regard to the effect. Both falsely high and low values have been reported; interpret results cautiously.

Doses

CAUTION: Piperazine is available in several salts that contain varying amounts of piperazine base (see Chemistry below). Many of the doses listed below do not specify what salt (if any) is used in the dosage calculations. If the dose is in question, refer to the actual product information for the product you are using.

- **DOGS:**

  For treatment of ascarids (**Note:** Because larval stages in the host's tissues may not be affected by the drug, many clinicians recommend retreating about 2–3 weeks after the first dose):

  a) 45–65 mg of base/kg PO; for pups less than 2.5 kg: 150 mg maximum. (Cornelius and Roberson 1986)
  b) 110 mg/kg PO (Chiapella 1988)
  c) 100 mg/kg PO; repeat in 3 weeks (Morgan 1988)
  d) 20–30 mg/kg PO once (Davis 1985)
  e) 110 mg/kg PO; repeat in 21 days (Kirk 1989)
  f) 45–65 mg/kg (as base) PO (Roberson 1988b)

- **CATS:**

  For treatment of ascarids (**Note:** Because larval stages in the host's tissues may not be affected by the drug, many clinicians recommend retreating about 2–3 weeks after the first dose):

  a) 45–65 mg of base/kg PO; 150 mg maximum (Cornelius and Roberson 1986)
  b) 110 mg/kg PO (Chiapella 1988)
  c) 100 mg/kg PO; repeat in 3 weeks (Morgan 1988)
  d) 20–30 mg/kg PO once (Davis 1985)
  e) 110 mg/kg PO; repeat in 21 days (Kirk 1989)
  f) 45–65 mg/kg (as base) PO (Roberson 1988b)

- **RABBITS, RODENTS, SMALL MAMMALS:**

  a) Mice, rats, hamsters, gerbils, and rabbits: For pinworms: Piperazine citrate in drinking water at 3 grams/liter for 2 weeks. (Burke 1999)
  b) Rabbits: For Pinworms: Piperazine citrate 100 mg/kg PO q24h for 2 days. Piperazine adipate: Adults: 200–500 mg/kg PO q24h for 2 days. Young rabbits: 750 mg/kg, PO once daily for 2 days. Wash the perianal area. (Ivey and Morrisey 2000)
  c) Mice, Rats, Gerbils, Hamsters, Guinea pigs, Chinchillas: For pinworms/tapeworms using piperazine citrate: 2–5 mg/mL drinking water for 7 days, off 7 days and repeat (Adamcak and Otten 2000)

- **HORSES:**

  There are combination products available for use in horses (see Dosage Forms/Preparations section) that contain piperazine with increased efficacy against nematodes and other helminths. Refer to the individual products' package insert for more information.

  a) 110 mg/kg (base) PO; repeat in 3–4 weeks. Retreating at 10-week intervals for P. equorum infections in young animals is recommended. (Roberson 1988b)
  b) 200 mg/kg, PO. Maximum of 80 grams in adults, 60 grams in yearlings, and 30 grams in foals. (Brander, Pugh, and Bywater 1982)

- **CATTLE, SHEEP & GOATS:**

  Because of high resistance of many nematode species to piperazine, it is rarely used alone in these species.

- **SWINE:**

  For *Ascaris suum* and *Oesophagostomum*:

  a) 0.2–0.4% in the feed, or 0.1–0.2% in the drinking water. All medicated water or feed must be consumed within 12 hours, so fasting or withholding water overnight may be beneficial to ensure adequate dosing; retreat in 2 months. Safe in young animals, and during pregnancy. Drug withdrawal times not determined for swine. (Paul 1986)
  b) 110 mg/kg (as base). Citrate salt usually used in feed as a one-day treatment, and hexahydrate in drinking water. Dose must be consumed in 8–12 hours. Withholding water or feed the previous night may be beneficial. (Roberson 1988b)

- **BIRDS:**

  a) For ascarids in poultry (not effective in psittacines): 100–500 mg/kg PO once; repeat in 10–14 days (Clubb 1986)
  b) For nematodes: Piperazine citrate: 45–100 mg/kg single dose or 6–10 grams/gallon for 1–4 days. In raptors: 100 mg/kg. In parakeets and canaries: 0.5 mg/gram (Stunkard 1984)
  c) For *Ascaridia galli* in poultry: 32 mg/kg (as base) (approximately 0.3 grams for each adult) given in each of 2 successive feedings or for 2 days in drinking water. Citrate or adipate salts are usually used in feed and the hexahydrate in drinking water. (Roberson 1988b)

Monitoring

- Clinical and/or laboratory efficacy
- Adverse effects

Client Information

- Clients should be instructed to administer only the amount prescribed and to relate any serious adverse effects to the veterinarian.

Chemistry/Synonyms
Piperazine occurs as a white, crystalline powder that may have a slight odor. It is soluble in water and alcohol. Piperazine is available commercially in a variety of salts, including citrate, adipate, phosphate, hexahydrate, and dihydrochloride. Each salt contains a variable amount of piperazine (base): adipate (37%), chloride (48%), citrate (35%), dihydrochloride (50–53%), hexahydrate (44%), phosphate (42%), and sulfate (46%).

Piperazine may also be known as diethylendiamin, dispermin, hexahydropropyrazin, piperazinum, and *Pipa-Tabs*®.

Storage/Stability
Unless otherwise specified by the manufacturer, piperazine products should be stored at room temperature (15–30°C).

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS:

Piperazine Dihydrochloride tablets equivalent to 50 mg or 250 mg base. *Pipa-Tabs*® (Vet-A-Mix); (Rx). Approved for use in dogs and cats.

Additional OTC products and combination products may be available for a variety of species. Products and/or trade names include: *Alfalfa Pellet Horse Wormer, Tasty Paste® Dog & Puppy Wormer, Wonder Wormer™ for Horses, D-Worm™ Liquid Wormer for Cats and Dogs, Wazine®-17, Wazine®-34, Hartz® Advanced Care™ Liquid Wormer, Hartz® Advanced Care™ Once-a-Month® Wormer for Kittens and Cats, Hartz® Advanced Care™ Once-a-Month® Wormer for Dogs, Sergeant's® Vetscription® Worm-Away® for Cats, Sergeant's® Vetscription® Sure Shot® Liquid Wormer for Cats & Kittens, Piperazine-17 Medicated, WormEze™ Canine Anthelmintic, WormEze™ Feline Anthelmintic Paste, WormEze™ Canine & Feline Anthelmintic Liquid.*

HUMAN-LABELED PRODUCTS: None

PIRLIMYCIN HCL

(per-li-***mye***-sin) Pirsue®

INTRAMAMMARY LINCOSAMIDE ANTIBIOTIC

Prescriber Highlights

- Lincosamide antibiotic for intramammary use in dairy cattle
- Milk withdrawal (at labeled doses) = 36 hours after last treatment; Meat withdrawal (at labeled doses) = 9 days

Uses/Indications
Pirlimycin mastitis tubes are indicated for the treatment of clinical and subclinical mastitis caused by susceptible organisms in lactating dairy cattle.

Pharmacology/Actions
Like other lincosamides, pirlimycin acts by binding to the 50S ribosomal subunit of susceptible bacterial RNA, thus interfering with bacterial protein synthesis. It is primarily active against gram-positive bacteria, including a variety of species of staphylococcus (*S. aureus, S. epidermidis, S. chromogenes, S. hyicus, S. xylosus*), streptococcus (*S. agalactiae, S. dysgalactiae, S. uberis, S. bovis*) and *Enterococcus faecalis*.

Organisms with a MIC of ≤2 mcg/mL are considered susceptible, and organisms with a MIC value of 4 mcg/mL are considered resistant. If using a 2 microgram disk for Kirby-Bauer plate testing, a zone diameter of ≤12mm indicates resistance and a diameter of ≥13mm indicates susceptibility.

Pharmacokinetics
Little information is available; the manufacturer states that the drug penetrates the udder well and is absorbed systemically from the udder and then secreted into the milk of all four quarters. Tissue levels in treated quarters of pirlimycin are approximately 2–3 times those found in the extracellular fluid.

Contraindications/Precautions/Warnings
No information was noted.

Adverse Effects
No adverse affects, including udder irritation have been reported thus far.

Milk from untreated quarters must be disposed of during withdrawal time as residues may be detected from untreated quarters.

Reproductive/Nursing Safety
No information was noted.

Overdosage/Acute Toxicity
No data was located.

Drug Interactions
Because **erythromycin** and clindamycin have shown antagonism *in vitro*, this could also occur with pirlimycin.

Laboratory Considerations
- The established tolerance of pirlimycin in milk is 0.4 ppm.

Doses
- **CATTLE:**
  a) Lactating Dairy Cattle: Infuse one syringe into each affected quarter; repeat one time in 24 hours. See label directions for more specific information on administrative techniques. (Package Insert; *Pirsue*®—Upjohn)

Monitoring
- Efficacy
- Withdrawal periods

Client Information
- Be sure clients understand dosage recommendations and withdrawal periods.
- Milk from untreated quarters must be disposed of during withdrawal time as residues may be detected from untreated quarters.

Chemistry/Synonyms
Pirlimycin HCl is a lincosamide antibiotic. It has a molecular weight of 465.4.

Pirlimycin HCl may also be known as U-57930E and *Pirsue*®.

Storage/Stability
Store syringes at or below 25°C (77°F); protect from freezing.