Laboratory Considerations
No specific laboratory interactions or concerns were noted.

Doses
- **DOGS/CATS:**

  Note: There is very little information available regarding ertapenem use in dogs or cats and, therefore use must be considered investigational. If the drug is to be administered, it is suggested to use the human pediatric dose of 15 mg/kg IV or IM every 12 hours (not to exceed a daily dosage of 1 gram). Monitor the literature for additional data and recommendations.

Monitoring
- Clinical efficacy (WBC, fever, etc.)
- Adverse effects (potentially: GI, neurotoxicity, hypersensitivity); in humans receiving ertapenem for a prolonged period, hepatic, hematopoietic, and renal function are suggested for periodic assessment

Client Information
- Clients should understand the investigational nature of using this drug in animals and that it should be administered only by veterinary professionals

Chemistry/Synonyms
Ertapenem sodium is a synthetic 1-(beta) methyl carbapenem antibiotic that occurs as a white to off-white, hygroscopic, crystalline powder. It is soluble in water and normal saline.

Ertapenem may also be known as L-749345, ML-0826, ZD-4433, ertapenemum or *Invanz*®.

Storage/Stability/Compatibility
The 1 gram injectable product contains approximately 6 mEq of sodium and 175 mg of sodium bicarbonate (as an excipient). It should be stored at temperatures at, or below, 25°C.

For intravenous use, vial contents can be reconstituted with 10 mL of water for injection, bacteriostatic water for injection, or 0.9% sodium chloride injection. After shaking to dissolve the powder, immediately transfer to a 50 mL bag of 0.9% sodium chloride. Do not use diluents containing dextrose. Once reconstituted and diluted in normal saline for IV use, ertapenem is stable at room temperature for 6 hours. If refrigerated, it can be stored for 24 hours and used within 4 hours after removal from the refrigerator. Do not freeze reconstituted solutions.

If ertapenem is to be given IM, dilute the vial with 3.2 mL of 1% lidocaine HCl injection (*without epinephrine*). Use within one hour. Do not give IV.

Do not mix ertapenem with other medications or use IV solutions containing dextrose.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Ertapenem Sodium Powder for Injection: 1 g (as ertapenem) vials; *Invanz*® (Merck); (Rx)

ERYTHROMYCIN
ERYTHROMYCIN ESTOLATE
ERYTHROMYCIN ETHYLSUCCINATE
ERYTHROMYCIN LACTOBIONATE

(er-ith-roe-*mye*-sin) Gallimycin®

MACROLIDE ANTIBIOTIC

Prescriber Highlights
- Macrolide antibiotic; also used as a prokinetic agent
- Contraindicated in rabbits, gerbils, guinea pigs, & hamsters; oral use in ruminants, adult horses(?), hypersensitivity
- Adverse Effects: GI distress (oral), pain on IM injection; thrombophlebitis (IV), hyperthermia (foals)
- Many drug interactions possible

Uses/Indications
Erythromycin is approved for use to treat infections caused by susceptible organisms in swine, sheep, and cattle. It is often employed when an animal is hypersensitive to penicillins or if other antibiotics are ineffective against a certain organism.

Erythromycin, at present, is considered to be one of the treatments of choice (with rifampin) for the treatment of *C.* (*Rhodococcus*) *equi* infections in foals. Erythromycin estolate and microencapsulated base appear to be the most efficacious forms of the drug in foals due to better absorption and less frequent adverse effects.

Erythromycin may be used as a prokinetic agent to increase gastric emptying in dogs and cats. It may also be beneficial in treating reflux esophagitis.

Pharmacology/Actions
Erythromycin is usually a bacteriostatic agent, but in high concentrations or against highly susceptible organisms it may be bactericidal. The macrolides (erythromycin and tylosin) are believed to act by binding to the 50S ribosomal subunit of susceptible bacteria, thereby inhibiting peptide bond formation.

Erythromycin has *in vitro* activity against gram-positive cocci (staphylococci, streptococci), gram-positive bacilli, (*Bacillus anthracis*, Corynebacterium, *Clostridium* spp., (not *C. difficile*), Listeria, Erysipelothrix), and some strains of gram-negative bacilli, including Haemophilus, Pasturella, and Brucella. Some strains of Actinomyces, Mycoplasma, Chlamydia, Ureaplasma, and Rickettsia are also inhibited by erythromycin. Most strains of the family Enterobacteriaceae (Pseudomonas, *E. coli*, Klebsiella, etc.) are resistant to erythromycin.

Erythromycin is less active at low pHs and many clinicians suggest alkalinizing the urine if using the drug to treat UTI's.

At sub-antimicrobial doses, erythromycin mimics the effects of motilin (cats, humans, rabbits) or 5-hydroxytryptophan$_3$ (5-HT$_3$) and stimulates migrating motility complexes and antegrade peristalsis. By inducing antral contractions, gastric emptying is enhanced. Erythromycin also increases lower esophageal pressure. Erythromycin's prokinetic mechanism of action in dogs is not completely understood, but probably is via activation of 5-HT$_3$ receptors.

Pharmacokinetics

Erythromycin is absorbed after oral administration in the upper small intestine. Several factors can influence the bioavailability of erythromycin, including salt form, dosage form, GI acidity, food in the stomach, and stomach emptying time. Both erythromycin base and stearate are susceptible to acid degradation; enteric coatings are often used to alleviate this. Both the ethylsuccinate and estolate forms are dissociated in the upper small intestine and then absorbed. After IM or SC injection of the polyethylene-based veterinary product (*Erythro®-200; Gallimycin®-200*) in cattle, absorption is very slow. Bioavailabilities are only about 40% after SC injection and 65% after IM injection.

Erythromycin is distributed throughout the body into most fluids and tissues including the prostate, macrophages, and leukocytes. CSF levels are poor. In foals, erythromycin levels in bronchiolar lavage cells are equivalent to those found in the serum, but concentrations in pulmonary epithelial lining fluid are lower. Erythromycin may be 73–81% bound to serum proteins and the estolate salt, 96% bound. Erythromycin will cross the placenta; fetal serum levels are 5–20% of maternal levels. Erythromycin levels of about 50% of those found in the serum can be detected in milk. The volume of distribution for erythromycin in dogs is reportedly 2 L/kg; 3.7–7.2 L/kg in foals; 2.3 L/kg in mares; and 0.8–1.6 L/kg in cattle. In lactating dairy cattle, the milk to plasma ratio about 6–7.

Erythromycin is primarily excreted unchanged in the bile, but is also partly metabolized by the liver via N-demethylation to inactive metabolites. Some of the drug is reabsorbed after biliary excretion. Only about 2–5% of a dose is excreted unchanged in the urine.

The reported elimination half-life of erythromycin in various species is: 60–90 minutes in dogs and cats, 60–70 minutes in foals and mares, and 190 minutes in cattle.

Contraindications/Precautions/Warnings

Erythromycin is contraindicated in patients hypersensitive to it. In humans, the estolate form has been associated rarely with the development of cholestatic hepatitis. This effect has not apparently been reported in veterinary species, but the estolate should probably be avoided in patients with preexisting liver dysfunction.

As it may induce a toxic enterocolitis, erythromycin (and other macrolides) is contraindicated in rabbits, gerbils, guinea pigs, and hamsters.

Many clinicians believe that erythromycin is contraindicated in adult horses (see Adverse Effects below), and oral erythromycin should not be used in ruminants as severe diarrhea may result.

Adverse Effects

Adverse effects are relatively infrequent with erythromycin when used in small animals, swine, sheep, or cattle. When injected IM, local reactions and pain at the injection site may occur. Oral erythromycin may occasionally cause GI disturbances such as diarrhea, anorexia, and vomiting. Rectal edema and partial anal prolapse have been associated with erythromycin in swine. Intravenous injections must be given very slowly, as they can readily cause thrombophlebitis. Allergic reactions can occur but are thought to be rare.

Oral erythromycin should not be used in ruminants as severe diarrheas may result.

In foals treated with erythromycin, a mild, self-limiting diarrhea can occur; however, severe enterocolitis is possible. Erythromycin may alter temperature homeostasis in foals. Foals between the ages of 2–4 months old have been reported to develop hyperthermia with associated respiratory distress and tachypnea. Physically cooling off these animals has been successful in controlling this effect.

Adult horses may develop severe, sometimes fatal, diarrheas from erythromycin making the use of the drug in adults very controversial.

When used as prokinetic agent, erythromycin may actually increase clinical signs of intestinal distress as it can stimulate emptying of larger food particles into the intestine than is normal.

Reproductive/Nursing Safety

While erythromycin has not demonstrated teratogenic effects in rats, and the drug is not thought to possess serious teratogenic potential, it should only be used during pregnancy when the benefits outweigh the risks. In humans, the FDA categorizes erythromycin and its salts, except ethylsuccinate, 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), this drug 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.*)

In humans, the FDA categorizes erythromycin ethylsuccinate as category ***C*** for use during pregnancy (*Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; or there are no animal reproduction studies and no adequate studies in humans.*)

Erythromycin is excreted in milk and may concentrate (observed milk:plasma ratio of 0.5). Erythromycin is considered compatible with breastfeeding by the American Academy of Pediatrics.

Overdosage/Acute Toxicity

With the exception of the adverse effects outlined above, erythromycin is relatively non-toxic; however, shock reactions have been reported in baby pigs receiving erythromycin overdosages.

Drug Interactions

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

- **AZOLE ANTIFUNGALS** (**ketoconazole, fluconazole, itraconazole**): Possible increased erythromycin levels
- **CISAPRIDE:** Erythromycin can inhibit the metabolism of cisapride and the manufacturer states that use of these drugs together (in humans) is contraindicated
- **CHLORAMPHENICOL:** *in vitro* evidence of antagonism
- **CLINDAMYCIN, LINCOMYCIN:** *in vitro* evidence of antagonism
- **DIGOXIN:** Erythromycin may increase the serum level of digoxin
- **DILTIAZEM, VERAPAMIL:** May increase erythromycin levels
- **ERGOT ALKALOIDS:** Acute ergot toxicity possible
- **OMEPRAZOLE:** Erythromycin and omeprazole can increase the plasma levels of one another
- **WARFARIN:** Erythromycin may potentiate the effects of oral anticoagulant drugs

Erythromycin can inhibit the metabolism of other drugs that use the CYP3A subfamily of the cytochrome P450 enzyme system. Depending on the therapeutic index of the drug(s) involved, therapeutic drug monitoring and/or dosage reduction may be required if the drugs must be used together. These drugs include:

- **ALFENTANIL**
- **BROMOCRIPTINE**
- **BUSPIRONE**

- **CARBAMAZEPINE**
- **CYCLOSPORINE**
- **DISOPYRAMIDE** (also risk of increased QT interval)
- **METHYLPREDNISOLONE**
- **MIDAZOLAM, ALPRAZOLAM, TRIAZOLAM**
- **QUINIDINE** (also risk of increased QT interval)
- **SILDENAFIL**
- **TACROLIMUS** (**systemic**)
- **THEOPHYLLINE**

Laboratory Considerations

- Erythromycin may cause falsely elevated values of **AST** (SGOT), and **ALT** (SGPT) when using colorimetric assays.
- Fluorometric determinations of **urinary catecholamines** can be altered by concomitant erythromycin administration.

Doses

- **DOGS:**

  For susceptible infections:
  a) 10–20 mg/kg PO three times daily (Aucoin 2000)
  b) For localized, soft tissue infections: 10–15 mg/kg PO q8h or 15–25 mg/kg PO q12h for 7–10 days;
  For systemic, bacteremia infections: 22 mg/kg PO or IV q8h for as long as necessary (Greene and Watson 1998)

  As a prokinetic agent:
  a) 0.5–1 mg/kg PO q8h (Hall and Washabau 2000)

- **CATS:**

  For susceptible infections:
  a) 10–20 mg/kg PO three times daily (Aucoin 2000)
  b) For localized, soft tissue infections: 10–15 mg/kg PO q8h or 15–25 mg/kg PO q12h for 7–10 days;
  For systemic, bacteremia infections: 22 mg/kg PO or IV q8h for as long as necessary (Greene and Watson 1998)

  As a prokinetic agent:
  a) 0.5–1 mg/kg PO q8h (Hall and Washabau 2000)

- **FERRETS:**

  For susceptible infections:
  a) 10 mg/kg PO 4 times daily (Williams 2000)

- **BIRDS:**

  For susceptible infections:
  a) Oral suspension: 60 mg/kg PO q12h (Hoeffer 1995)
  b) Ratites: 5–10 mg/kg PO 3 times daily (Jenson 1998)

- **CATTLE:**

  For susceptible infections:
  a) 4–8 mg/kg IM q12–24h (Jenkins 1987b)
  b) For bronchopneumonia and fibrinous pneumonia in cattle associated with bacteria sensitive to erythromycin and resistant to sulfas, penicillin G and tetracyclines: Using *Erythro-200®*: 44 mg/kg IM q24h usually for a maximum of 4 days. Inject no more than 10 mL at any one site. Do not inject at any site previously used. Severe local tissue reactions may occur. Recommend a 30-day slaughter withdrawal at this dosage. (Hjerpe 1986)

  For mastitis:
  a) Dry cow (using dry cow formula): Milk out affected quarter, clean and disinfect. Infuse contents of one syringe into each affected quarter at time of drying off. Close teat orifice with gentle pressure and massage udder.
  b) Lactating cow (using lactating cow formula): As above, but repeat after each milking for 3 milkings (Label directions; *Erythro®-Dry* and *Erythro®-36*—Ceva)

- **HORSES:**

  For treatment of *C.* (*Rhodococcus*) *equi* infections in foals:
  a) Erythromycin: 15–25 mg/kg PO q12–24h daily, with Rifampin (5 mg/kg, PO q12h). Treatment may be necessary for 1–3 months. (Chaffin 2006b)
  b) Erythromycin: 25 mg/kg PO q12h with rifampin: 3–5 mg/kg PO q12h. If rifampin use becomes cost prohibitive, use erythromycin alone. Treat for 4–6 weeks or until lungs are clear of abscesses on radiographs. (Foreman 1999)

  For treatment of proliferative enteropathy caused by *L. intracellularis* infections in foals:
  a) Erythromycin estolate: 25 mg/kg PO q6–8h, with rifampin: 10 mg/kg PO q12h for a minimum of 21 days (Lavoie and Drolet 2003)

  For susceptible infections:
  a) Foals: Erythromycin estolate: 25 mg/kg PO q6h; Erythromycin gluceptate: 5 mg/kg IV q4–6h (Caprile and Short 1987); (Brumbaugh 1999)

  As a prokinetic agent:
  a) 0.1–1 mg/kg, IV or erythromycin lactobionate 2.2 mg/kg IV over a 30–60 minute period every 6 hours. Dose in a 450 kg horse is 1 gram. (Moore 1999)

- **SWINE:**

  For susceptible infections:
  a) For respiratory infections: 2.2–6.6 mg/kg IM once daily
  b) For scours in young pigs: 22 mg/kg IM in one or more daily doses (Label directions; *Erythro®-100* and *Erythro®-200*—Ceva)

- **SHEEP:**

  For susceptible infections:
  a) For respiratory infections in older animals: 2.2 mg/kg IM once daily as indicated.
  b) For prevention of "dysentery" in newborn lambs when the likely causative agent is susceptible to erythromycin: 123 mg/kg IM once soon after birth (Label directions; *Erythro®-100* and *Erythro®-200*—Ceva)

Monitoring

- Clinical efficacy
- Adverse effects (periodic liver function tests if patient receiving erythromycin estolate long-term; may not be necessary for foals receiving erythromycin and rifampin for Rhodococcus infections)

Client Information

- The intramuscular 100 mg/mL (*Erythro-100®*) product (*Erythro-200®*) has quite specific instructions on where and how to inject the drug. Refer to the label directions or package insert for more information before using.
- When administering orally to small animals, give on an empty stomach unless gastrointestinal signs (vomiting, lack of appetite, diarrhea) occur, then give with food. The estolate, ethylsuccinate or enteric-coated forms of erythromycin may be given with or without food.
- If gastrointestinal adverse effects are severe or persist, contact veterinarian.

Chemistry/Synonyms

A macrolide antibiotic, produced from *Streptomyces erythreus*, erythromycin is a weak base that is available commercially in several salts and esters. It has a pK_a of 8.9.

Erythromycin base occurs as a bitter tasting, odorless or practically odorless, white to slight yellow, crystalline powder. Approximately 1 mg is soluble in 1 mL of water; it is soluble in alcohol.

Erythromycin estolate occurs as a practically tasteless and odorless, white, crystalline powder. It is practically insoluble in water and approximately 50 mg are soluble in 1 mL of alcohol. Erythromycin estolate may also be known as erythromycin propionate lauryl sulfate.

Erythromycin ethylsuccinate occurs as a practically tasteless and odorless, white to slight yellow, crystalline powder. It is very slightly soluble in water and freely soluble in alcohol.

Erythromycin lactobionate occurs as white to slightly yellow crystals or powder. It may have a faint odor and is freely soluble in water and alcohol.

Erythromycin may also be known as: eritromicina, and erythromycinum; many trade names are available.

Storage/Stability/Compatibility

Erythromycin (base) capsules and tablets should be stored in tight containers at room temperature (15–30°C). Erythromycin estolate preparations should be protected from light. To retain palatability, the oral suspensions should be refrigerated.

Erythromycin ethylsuccinate tablets and powder for oral suspension should be stored in tight containers at room temperature. The commercially available oral suspension should be stored in the refrigerator to preserve palatability. After dispensing, the oral suspensions are stable for at least 14 days at room temperature, but individual products may have longer labeled stabilities.

Erythromycin lactobionate powder for injection should be stored at room temperature. For initial reconstitution (vials), only sterile water for injection should be used. After reconstitution, the drug is stable for 24 hours at room temperature and 2 weeks if refrigerated. To prepare for administration via continuous or intermittent infusion, the drug is further diluted in 0.9% sodium chloride, Lactated Ringer's, or Normosol-R. Other infusion solutions may be used, but first must be buffered with 4% sodium bicarbonate injection (1 mL per 100 mL of solution). At pH's of <5.5, the drug is unstable and loses potency rapidly. Many drugs are physically **incompatible** with erythromycin lactobionate; it is suggested to consult specialized references or a hospital pharmacist for more specific information.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Erythromycin 100 mg/mL for IM Injection (with 2% butyl aminobenzoate as a local anesthetic) in 100 mL vials; *Gallimycin®-100* (Bimeda); (OTC). Approved for use in cattle, sheep, and swine. Milk withdrawal (when used as labeled) = 72 hours. Slaughter withdrawal (when used as labeled) for cattle =14 days, sheep = 3 days, swine =7 days.

There may also be erythromycin premixes alone and in combination with other drugs for use in swine and/or poultry.

HUMAN-LABELED PRODUCTS:

Erythromycin Base Delayed-release Tablets enteric-coated: 250 mg, 333 mg and 500 mg; *Ery-Tab®* (Abbott); (Rx)

Erythromycin Base Tablets Film-coated: 250 mg, & 500 mg; *Erythromycin Filmtabs®* (Abbott); (Rx)

Erythromycin Base Tablets with polymer coated particles: 333 mg and 500 mg; *PCE Dispertab®* (Abbott); (Rx)

Erythromycin Base Delayed-release Capsules enteric-coated pellets: 250 mg; *Eryc®* (FH Faulding & Co. Ltd.); generic; (Rx)

Erythromycin Estolate Suspension: 125 mg (as base) per 5 mL in 473 mL and 250 mg (as base) per 5 mL in 473 mL; generic (Alpharma); (Rx)

Erythromycin Stearate Film-coated tablets: 250 mg, 500 mg; *Erythrocin Stearate®* (Abbott); (Rx)

Erythromycin Ethylsuccinate Tablets: 400 mg; *E.E.S. 400®* (Abbott); generic; (Rx)

Erythromycin Ethylsuccinate Powder for Oral Suspension: 200 mg per 5 mL when reconstituted in 60 mL (400 mg only), 100 mL, 200 mL and UD 5 mL; *E.E.S.® Granules* (Abbott), *EryPed® 200* and *400* (Abbott); (Rx)

Erythromycin Ethylsuccinate Oral Suspension: 200 mg per 5 mL in 100, 480 mL; *EES 200®* (Abbott); generic; (Rx)

Erythromycin Ethylsuccinate Oral Suspension: 400 mg per 5 mL in 100 & 480 mL; *EES 400®* (Abbott) (Rx); generic; (Rx)

Erythromycin Ethylsuccinate Oral Suspension: 100 mg per 2.5 mL in 50 mL; *EryPed Drops®* (Abbott); (Rx)

Erythromycin Lactobionate Powder for Injection: 500 mg and 1 g (as lactobionate) in vials, piggyback vials and ADD-Vantage vials; *Erythrocin®* (Abbott); (Rx); generic; (Rx)

Erythromycin & Sulfisoxazole Granules for Oral Suspension: erythromycin ethylsuccinate (equivalent to 200 mg erythromycin activity) and sulfisoxazole acetyl (equivalent to 600 mg sulfisoxazole) per 5 mL when reconstituted in 100 mL, 150 mL & 200 mL; *Eryzole®* (Alra); *Pediazole®* (Ross); generic; (Rx)

Topical and ophthalmic preparations are also available.

ESMOLOL HCL

(ess-moe-lol) Brevibloc®

BETA-1 BLOCKER

Prescriber Highlights

- **Ultra-short acting beta$_1$-blocker used IV for short-term treatment of SVT's or to determine if beta-blockers are effective for controlling arrhythmias**
- **Contraindications: Patients with overt cardiac failure, 2nd or 3rd degree AV block, sinus bradycardia, or in cardiogenic shock**
- **Caution: Patients with CHF, bronchoconstrictive lung disease, or diabetes mellitus**
- **Adverse Effects: Hypotension & bradycardia are the effects most likely seen**

Uses/Indications

Esmolol may be used as test drug to indicate whether beta-blocker therapy is warranted as an antiarrhythmic agent, particularly in cats with hypertrophic cardiomyopathy, or as an infusion in the short-term treatment of supraventricular tachyarrhythmias (*e.g.*, atrial fibrillation/flutter, sinus tachycardia).

Pharmacology/Actions

Esmolol primarily blocks both beta$_1$-adrenergic receptors in the myocardium. At clinically used doses, esmolol does not have any intrinsic sympathomimetic activity (ISA) and unlike propranolol, does not possess membrane-stabilizing effects (quinidine-like) or bronchoconstrictive effects. Cardiovascular effects secondary to esmolol include negative inotropic and chronotropic activity that can lead to reduced myocardial oxygen demand. Systolic and diastolic blood pressures are reduced at rest and during exercise. Esmolol's antiarrhythmic effect is thought to be due to its blockade of adrenergic stimulation of cardiac pacemaker potentials. Esmolol increas-