■ **CATS:**

a) For UTI: 2.2 mg/kg SC once daily for 5–14 days
For systemic, soft tissue infections: 2.2 mg/kg q12h or 4.4 mg/kg q24h SC for 5–14 days
For sepsis, bacteremia: 4.4 mg/kg q12h SC for 2–5 days (Greene and Watson 1998)

■ **BIRDS:**

a) Day-Old Turkey Poults: Administer by SC injection in the neck region of day-old turkey poults at the dosage of 0.17 to 0.5 mg ceftiofur/poult. One mL of the 50 mg/mL reconstituted solution will treat approximately 100 to 294 day-old poults.
Day Old Chicks: Administer by SC injection in the neck region of day-old chicks at the dosage of 0.08 to 0.20 mg ceftiofur/chick. One mL of the 50 mg/mL reconstituted solution will treat approximately 250 to 625 day-old chicks. A sterile 26 gauge needle and syringe or properly cleaned automatic injection machine should be used. (Package Insert; *Naxcel*®—Pfizer)

b) Ratites: 10–20 mg/kg IM twice daily (Jenson 1998)

■ **REPTILES:**

a) For chelonians: 4 mg/kg IM once daily for 2 weeks. Commonly used in respiratory infections. (Gauvin 1993)

b) Green iguanas: for microbes susceptible at > 2 µg/mL, 5 mg/kg, IM or SC, every 24 hours (Bensen, Lee et al. 2003)

c) For bacterial pneumonia: 2.2 mg/kg IM q24–48h; keep patient at upper end of ideal temperature range (Johnson 2004b)

■ **EXOTICS/WILDLIFE:**

a) Captive Female Asian Elephants: 1.1 mg/kg IM given two to three times a day or, alternatively 1.1 mg/kg IV once daily, depending upon the MIC of the pathogen (Dumonceax, Isaza et al. 2005)

Treatment Monitoring

Because cephalosporins usually have minimal toxicity associated with their use, monitoring for efficacy is usually all that is required. Some clinicians recommend weekly CBC monitoring of small animals receiving ceftiofur. Patients with diminished renal function may require intensified renal monitoring. Serum levels and therapeutic drug monitoring are not routinely done with these agents.

Chemistry/Synonyms

Ceftiofur sodium is a semisynthetic 3rd generation cephalosporin. Ceftiofur sodium is a weak acid and is acid stable and water-soluble.

Ceftiofur sodium may also be known as CM 31-916, U 64279E, ceftiofen sodium, *Excenel*® (not *Excenel*® *RTU*), *Naxcel*®, or *Accent*®.

Storage/Stability

Unreconstituted ceftiofur sodium powder for reconstitution should be stored at room temperature. Protect from light. Color of the cake may vary from off-white to tan, but this does not affect potency.

After reconstitution with bacteriostatic water for injection or sterile water for injection, the solution is stable up to 7 days when refrigerated and for 12 hours at room temperature (15–30°C). According to the manufacturer, if a precipitate should form while being stored refrigerated during this time, the product may be used if it goes back into solution after warming. If not, contact the manufacturer. Frozen reconstituted solutions are stable up to 8 weeks. Thawing may be done at room temperature or by swirling the vial under running warm or hot water.

One-time salvage procedure for reconstituted product: At the end of the 7-day refrigeration or 12-hour room temperature storage period following reconstitution, any remaining reconstituted product may be frozen up to 8 weeks without loss in potency or other chemical properties. This is a one-time only salvage procedure for the remaining product. To use this salvaged product at any time during the 8-week storage period, hold the vial under warm running water, gently swirling the container to accelerate thawing, or allow the frozen material to thaw at room temperature. Rapid freezing or thawing may result in vial breakage. Any product not used immediately upon thawing should be discarded.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Ceftiofur Sodium Powder for Injection 50 mg ceftiofur/mL when reconstituted in 1 g and 4 g vials; *Naxcel*® (Pfizer); (Rx). Withdrawal times: Cattle: 4-day slaughter withdrawal time is required. No milk discard time is required. Swine: A 4-day slaughter withdrawal time is required. Sheep/Goats: No slaughter withdrawal time or milk discard time is required. Not to be used in horses intended for human consumption.

HUMAN-LABELED PRODUCTS: None

CEFTRIAXONE SODIUM

(sef-try-***ax***-ohn) Rocephin®

3rd GENERATION CEPHALOSPORIN

Prescriber Highlights

- 3rd generation cephalosporin; achieves high levels in CNS; long half life
- Potentially could cause hypersensitivity reactions, granulocytopenia/thrombocytopenia, diarrhea, mild azotemia, biliary "sludging"
- Causes pain on IM injection; Give IV over 30 minutes (or more)
- May need to reduce dose in renal failure; avoid with icterus

Uses/Indications

Ceftriaxone is used to treat serious infections, particularly against susceptible Enterobacteriaceae that are not susceptible to other less expensive agents or when aminoglycosides are not indicated (due to their potential toxicity). Its long half life, good CNS penetration, and activity against *Borrelia burgdorferi* also has made it a potential choice for treating Lyme's disease.

Pharmacology/Actions

Ceftriaxone is a third generation injectable cephalosporin agent. The third generation cephalosporins retain the gram-positive activity of the first and second-generation agents, but, have much expanded gram-negative activity. As with the 2nd generation agents, enough variability exists with individual bacterial sensitivities that susceptibility testing is necessary for most bacteria. Because of the excellent gram-negative coverage of these agents and when compared to the aminoglycosides and their significantly less toxic potential, they have been used on an increasing basis in veterinary medicine.

Pharmacokinetics

Ceftriaxone is not absorbed after oral administration and must be given parenterally. It is widely distributed throughout the body; CSF levels are higher when meninges are inflamed. Ceftriaxone crosses the placenta and enters maternal milk in low concentrations; no documented adverse effects to offspring have been noted. Ceftriaxone is excreted by both renal and non-renal mechanisms; in humans, elimination half-lives are approximately 6–11 hours.

In dogs, ceftriaxone bioavailability after IM or SC administration equal that of IV, but peak levels occur much faster after IM (approximately 30 minutes) than SC (80 minutes). Peak levels are higher with IM administration than SC, but total area under the curve is similar for both routes. Elimination half-life is longer after SC administration (1.73 hrs) than either IM (1.17 hrs) or IV administration (0.88 hrs). The authors of the study (Rebuelto, Albarellos et al. 2002) concluded that once or twice daily IM or SC injections of 50 mg/kg should be adequate to treat most susceptible infections in dogs.

Contraindications/Precautions/Warnings

Only prior allergic reaction to cephalosporins contraindicates ceftriaxone's use. In humans documented hypersensitive to penicillin, up to 16% may also be allergic to cephalosporins. The veterinary significance of this is unclear.

Although bleeding times have only been reported rarely in humans, ceftriaxone should be used with caution in patients with vitamin K utilization or synthesis abnormalities (*e.g.*, severe hepatic disease).

Patients in renal failure may need dosage adjustments; but are not generally required unless severely uremic, or with concomitant hepatic impairment.

Adverse Effects

Because veterinary usage of ceftriaxone is very limited, an accurate adverse effect profile has not been determined. The following adverse effects have been reported in humans and may or may not apply to veterinary patients: hematologic effects, including eosinophilia (6%), thrombocytosis (5%), leukopenia (2%) and, more rarely, anemia, neutropenia, lymphopenia and thrombocytopenia. Approximately 2–4% of humans get diarrhea. Very high dosages (100 mg/kg/day) in dogs have caused a "sludge" in bile. Hypersensitivity reactions (usually a rash) have been noted. Increased serum concentrations of liver enzymes, BUN, creatinine, and urine casts have been described in about 1–3% of patients. When given IM, pain may be noted at the injection site.

Reproductive/Nursing Safety

No teratogenic effects were demonstrated in studies in pregnant mice and rats given up to 20X labeled doses of ceftriaxone. In humans, the FDA categorizes this drug 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.*)

Ceftriaxone is distributed into milk in low concentrations and is unlikely to pose much risk to nursing offspring.

Overdosage/Acute Toxicity

Limited information available; overdoses should be monitored and treated symptomatically and supportively if required.

Drug Interactions

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

- **AMINOGLYCOSIDES/NEPHROTOXIC DRUGS**: The concurrent use of parenteral aminoglycosides or other nephrotoxic drugs (*e.g.*, amphotericin B) with cephalosporins is somewhat controversial. Potentially, cephalosporins could cause additive nephrotoxicity when used with these drugs, but this interaction has only been well documented with cephaloridine (no longer marketed). *In vitro* studies have demonstrated that cephalosporins can have synergistic or additive activity against certain bacteria when used with aminoglycosides.
- **CALCIUM**: Concomitant use with calcium containing solutions have caused fatal calcium-ceftriaxone precipitates in lungs and kidneys of neonatal humans. Do not mix with calcium or administer calcium-containing solutions or products within 48 hours of ceftriaxone administration.

Laboratory Considerations

- When using Kirby-Bauer disk diffusion procedures for testing susceptibility, a specific 30 micrograms ceftriaxone disk should be used. A cephalosporin-class disk containing cephalothin should not be used to test for ceftriaxone susceptibility. An inhibition zone of 18 mm or more indicates susceptibility; 14–17 mm, intermediate; and 13 mm or less, resistant.
- When using a dilution susceptibility procedure, an organism with a MIC of 16 micrograms/mL or less is considered susceptible and 64 micrograms/mL or greater is considered resistant. With either method, infections caused by organisms with intermediate susceptibility may be effectively treated if the infection is limited to tissues where the drug is concentrated or if a higher than normal dose is used.
- Ceftriaxone, like most other cephalosporins, may cause a **false-positive urine glucose** determination when using the cupric sulfate solution test (*e.g.*, *Clinitest*®).
- Ceftriaxone in very high concentrations (50 micrograms/mL or greater) may cause falsely elevated **serum creatinine** levels when manual methods of testing are used. Automated methods do not appear to be affected.

Doses

- **DOGS:**
  a) For meningitis/borreliosis: 15–50 mg/kg (maximum single dose in humans is 1 gram) IV or IM q12h for 4–14 days
  For preoperative/intraoperative use: 25 mg/kg (maximum single dose in humans is 1 gram) IM or IV one time
  For skin, genitourinary infections: 25 mg/kg IM once daily (q24h) for 7–14 days (Greene and Watson 1998)
  b) For infectious endocarditis and documented resistance against or other contraindications for fluoroquinolones and aminoglycosides in dogs: 20 mg/kg IV q12h (DeFrancesco 2000)
  c) 15–50 mg/kg (route not specified) once daily (Trepanier 1999)
- **CATS:**
  For systemic infections:
  a) 25–50 mg/kg IV, IM or Intraosseous q12h as long as necessary (Greene and Watson 1998)
- **HORSES:**
  For susceptible infections:
  a) 25–50 mg/kg q12h IV or IM (**Note:** This is a human dose and should be used as a general guideline only) (Walker 1992)
  b) 20 mg/kg IV q12h (Brumbaugh 1999)

Monitoring
- Efficacy
- If long-term therapy, occasional CBC, renal function (BUN, Serum Creatinine, urinalysis) and liver enzymes (AST, ALT) may be considered.

Chemistry/Synonyms
A third generation cephalosporin, ceftriaxone sodium occurs as a white to yellowish-orange crystalline powder. It is soluble in water (400 mg/mL at 25°C). Potencies of commercial products are expressed in terms of ceftriaxone. One gram of ceftriaxone sodium contains 3.6 mEq of sodium.

Ceftriaxone Sodium may also be known as: ceftriaxonum natricum, Ro-13-9904, or Ro-13-9904/000; many trade names are available.

Storage/Stability/Compatibility
The sterile powder for reconstitution should be stored at or below 25°C and protected from light.

After reconstituting with either 0.9% sodium chloride or D_5W, ceftriaxone solutions (at concentrations of approximately 100 mg/mL) are stable for 3 days at room temperature and for 10 days when refrigerated. Solutions of concentrations of 250 mg/mL are stable for 24 hours at room temperature and 3 days when refrigerated. At concentrations of 10–40 mg/mL solutions frozen at -20°C are stable for 26 weeks. The manufacturer does not recommend admixing any other anti-infective drugs with ceftriaxone sodium, but amikacin and metronidazole are reported **compatible**.

Do not mix with calcium or calcium-containing solutions, or administer calcium-containing solutions or products within 48 hours of ceftriaxone administration (see Drug Interactions).

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Ceftriaxone Powder for Injection: 250 mg, 500 mg, 1 g, & 2g (as base) in vials, piggyback vials, *ADD-Vantage vials,* duplex bags and in bulk; *Rocephin*® (Roche); generic; (Rx)

Ceftriaxone Injection: in 5% dextrose in Water 1 g and 2 g in frozen, premixed 50 mL containers; *Rocephin*® (Roche); generic; (Rx)

CEFUROXIME AXETIL
CEFUROXIME SODIUM

(sef-yoor-*ok*s-eem) Ceftin®, Zinacef®

2nd GENERATION CEPHALOSPORIN

Prescriber Highlights
- **Oral & parenterally administered 2nd generation cephalosporin that is more active against some gram-negative bacteria than first generation (*e.g.,* cephalexin, cefazolin) cephalosporins**
- **Potentially useful in small animals when a cephalosporin is desired to treat bacterial infections susceptible to cefuroxime, but resistant to first generation cephalosporins, when enhanced gram-negative coverage is desired for surgery prophylaxis, or when high CNS levels are necessary**
- **Limited clinical experience in veterinary medicine**
- **Adverse effects most likely seen in small animals would be GI-related**

Uses/Indications
Cefuroxime is a semi-synthetic 2nd generation cephalosporin with enhanced activity against some gram-negative pathogens when compared to the first generation agents. Cefuroxime is available in both oral and parenteral dosage forms. It potentially may be useful in small animals when a cephalosporin is desired to treat bacterial infections susceptible to cefuroxime, but resistant to first generation cephalosporins, when enhanced gram-negative coverage is desired for surgery prophylaxis, or when high CNS levels are necessary. Little information is available with regard to its clinical use in small animals, however.

Pharmacology/Actions
Cefuroxime, like other cephalosporins, is bactericidal and acts by inhibiting cell wall synthesis. Its spectrum of activity is similar to that of cephalexin, but it is more active against gram-negative bacteria including strains of *E. coli*, *Klebsiella pneumoniae,* Salmonella and Enterobacter. It is not effective against methicillin-resistant Staphylococcus, Pseudomonas, Serratia or Enterococcus. For more information on cephalosporin pharmacology and spectrums of activity, refer to the Cephalosporin monograph.

Pharmacokinetics
No information was located for the pharmacokinetics of cefuroxime in dogs, cats or horses.

In humans, cefuroxime axetil is well absorbed after oral administration and is rapidly hydrolyzed in the intestinal mucosa and circulation to the parent compound. Bioavailability ranges on average from 37% (fasted) to 52% (with food). Peak serum levels occur in about 2–3 hours after oral dosing. When the sodium salt is administered IM, peak levels occur within 15 minutes to 1 hour. Cefuroxime is widely distributed after absorption, including to bone, aqueous humor and joint fluid. Therapeutic levels can be attained in the CSF if meninges are inflamed. Binding to human plasma proteins ranges from 35–50%. Cefuroxime is primarily excreted unchanged in the urine; elimination half-life in patients with normal renal function is between 1–2 hours.