

ONE AND DONE Cefovecin sodium's convenient one-time dosing eliminates reliance on owner compliance while providing efficacy similar to that of traditional oral antibiotic regimens.

FOCUS ON

Cefovecin Sodium for Skin and Soft Tissue Infections

Emily Sorah, PharmD, RPh, DICVP, FSVHP, FACVP, and Hafiz Tayebali, PharmD, RPh, FSVHP
North Carolina State Veterinary Hospital Pharmacy

Cefovecin sodium (Convenia; Zoetis, zoetis.com) is a broad-spectrum, third-generation cephalosporin antibiotic administered by subcutaneous injection. It was developed to relieve pet owners of the responsibility of giving pills orally to their pets over an extended period, making compliance easier and thus giving the pet the best chance for treatment success.

In the United States, Convenia was approved by the U.S. Food and Drug Administration (FDA) in 2008 for the treatment of skin infections (secondary superficial pyoderma, abscesses, and wounds) caused by *Staphylococcus intermedius* and *Streptococcus canis* (Group G) in dogs and for the treatment of skin infections (wounds and abscesses) caused by *Pasteurella multocida* in cats.¹ In the United Kingdom, European Union, and Australia, Convenia is approved for treatment of urinary tract infections and as adjunctive treatment for periodontal disease.

SKIN INFECTIONS IN DOGS AND CATS

The most common skin infections in dogs include pyoderma, infected wounds, and abscesses, often secondary to allergies or parasite infestations that cause the animal to scratch, lick, or bite the affected area, making it susceptible to bacterial invasion. In cats, skin

infections are usually related to wounds or abscesses from trauma or a bite.

Skin infections can be caused by a variety of bacterial pathogens, with the most prevalent being *S intermedius*.² *Staphylococcus schleiferi*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* have also been identified in canine pyoderma. Organism coverage, side effect profile, and caregiver compliance need to be considered when selecting an appropriate antibiotic, and cefovecin sodium is likely to be appropriate in many instances; therefore, it is important for clinicians to be knowledgeable about its use.

MECHANISM OF ACTION

As a third-generation cephalosporin antibiotic, cefovecin sodium, like other β -lactam agents, binds to penicillin-binding proteins in the bacterial cell wall, thereby blocking cell wall synthesis and resulting in cell death. However, cefovecin is not effective against *Pseudomonas* species or enterococci.¹

EFFECTIVENESS

Dogs

Efficacy studies showed noninferiority of cefovecin

Cefovecin Sodium at a Glance

- **Mechanism of action:** Cefovecin sodium is a third-generation cephalosporin antibiotic. Its effects are due to the drug binding to penicillin-binding proteins in the bacterial cell wall, blocking cell wall synthesis and resulting in cell death.
- **Place in therapy:** Treatment of skin infections (secondary superficial pyoderma, abscesses, and wounds) caused by *Staphylococcus intermedius* and *Streptococcus canis* (Group G) in dogs and of skin infections (wounds and abscesses) caused by *Pasteurella multocida* in cats.
- **Adverse effects:** Vomiting, diarrhea, lethargy, decreased appetite, and injection-site irritation may occur; effects may be prolonged. Transient edema has occurred, generally with repeat injections.
- **Cautions/monitoring parameters:** Monitor for efficacy and resolution of skin conditions.

sodium compared with an oral active control antibiotic in 320 dogs with superficial secondary pyoderma, abscesses, or infected wounds. Of the dogs treated with cefovecin, 14% required a second dose administered 14 days after the first dose.¹

Another study of 354 dogs compared subcutaneous cefovecin sodium at 14-day intervals with oral amoxicillin–clavulanic acid twice daily for 14 days. Cases were evaluated for clinical efficacy at 28 days after the final dose by scoring the clinical signs typical of skin infections. Cefovecin demonstrated statistical noninferiority compared with amoxicillin–clavulanic acid for all clinical diagnoses (up to 96.9% efficacy versus 92.5%, respectively).³

Cats

A study of 291 cats with infected wounds or abscesses found that a single 8 mg/kg subcutaneous dose of cefovecin sodium was as effective as an oral active control drug given once daily for 14 days. In this particular study, cefovecin was 96.6% effective; the active control was 90.9% effective.¹ A similar study conducted in cats found that cefovecin was as efficacious as amoxicillin–clavulanic acid, and efficacy was 100% for both treatments.⁴

PHARMACOKINETICS

After subcutaneous injection, cefovecin sodium is rapidly and completely absorbed.¹ Peak plasma

concentrations are reached about 6 hours after administration in dogs and about 2 hours after administration in cats.^{1,5,6} The half-life in dogs and cats has been shown to be approximately 133 hours and 166 hours, respectively.^{1,5,6} Cefovecin is not metabolized hepatically and is eliminated unchanged in urine and bile.¹ It takes approximately 65 days to eliminate 97% of the administered dose.¹

DOSING AND ADMINISTRATION

In both dogs and cats, cefovecin sodium should be administered subcutaneously as a one-time dose of 8 mg/kg.¹ Product labeling suggests that a second dose may be administered in dogs after susceptibility data, integrity of the dog's immune system, and clinical resolution have been considered, but should not exceed 2 doses.¹ A recommended dosing interval for a second dose is not given; however, therapeutic concentrations are maintained for 7 days when treating *S intermedius* in dogs or *P multocida* infections in cats and 14 days when treating *S canis* infections in dogs.¹

Cefovecin requires aseptic reconstitution with 10 mL of sterile water for injection and inspection to ensure that all material is dissolved, resulting in an 80 mg/mL solution. Vials should be stored under refrigeration in the original package and protected from light. Any unused portions should be used or discarded 56 days after reconstitution.¹ Users should be aware of the potential for solution to darken over time, even when stored protected from light. However, if the solution is used within the 56-day period, the manufacturer states that color does not adversely affect potency.¹

ADVERSE EFFECTS

Short Term

Cefovecin sodium is generally well tolerated, but commonly reported side effects include vomiting, diarrhea, lethargy, and inappetence. These effects appear to be less frequent subsequent to cefovecin administration when compared with active controls.¹ However, due to the long-acting nature of cefovecin, adverse effects such as diarrhea have been noted to last up to 28 days in dogs and 42 days in cats. Because it can take up to 65 days to clear the drug from the body, patients should be monitored for side effects for this duration. Injection-site irritation and transient edema have also occurred in a dose-related manner and with repeat injections.¹

Mild to moderate increases in liver enzymes (e.g., alanine aminotransferase [ALT], γ -glutamyl transferase) are possible in dogs treated with cefovecin sodium. Of 147 treated cats, 4 had mild increases in ALT concentrations, 24 had increases in blood urea nitrogen, and 6 had moderately elevated serum creatinine values.¹

The Convenia package insert notes the potential for cephalosporin-associated myelotoxicity leading to toxic neutropenia. Since the drug's approval by the FDA, there have also been reports of severe myelotoxicity, neutropenia, and anemia resulting in death in dogs and cats. While not all cases can be directly linked to the use of cefovecin, it is especially important to note that due to cefovecin's prolonged activity, severe adverse effects could require prolonged treatment. While the long-activity characteristics of cefovecin are largely considered convenient from an administration standpoint, the risk of prolonged adverse effects must be considered.

Long Term

Safety has not been established with long-term use, as cefovecin sodium dosing should not exceed 1 single dose in cats and 2 doses in dogs. This dose restriction may limit its use in difficult-to-treat abscesses.

CONTRAINDICATIONS AND WARNINGS

Known allergy to cefovecin sodium or to β -lactam group antimicrobials is a contraindication to cefovecin administration, and anaphylaxis has been reported with the use of this product. Cefovecin should not be administered again to patients that experience an allergic reaction. Anaphylactic reactions may require emergency therapy (e.g., epinephrine, oxygen, fluid therapy, antihistamine, corticosteroids).¹ Human caregivers with penicillin or cephalosporin allergies should also avoid handling or administering cefovecin or handling waste from treated patients.

Additionally, European labeling cautions against the use of cefovecin in patients with renal dysfunction, which could have practical implications when considering its use in diabetic patients, cats with chronic urinary tract infections, or patients with other renal diseases.⁷

Safety Precautions

The safety of use in dogs or cats younger than 4 months has not been determined and therefore should be avoided.^{1,7} Similarly, cefovecin sodium should not be used in pregnant/lactating dogs or cats, and treated animals should not be used for breeding for 12 weeks after the last injection of cefovecin.⁷

Care should be taken to ensure that cefovecin sodium is appropriately distinguished from other injectable cephalosporins or other drugs with similar names to avoid medication errors. The FDA Center for Veterinary Medicine received a report of a veterinary medication error that occurred when Convenia was mistaken for Cerenia (maropitant). In this case, the error was realized before the drugs were administered, but it highlights the importance of awareness of "look-alike, sound-alike" drugs and the potential for error when administering cefovecin.⁸

Cefovecin sodium is approved only for subcutaneous administration, and safe use has not been established with intravenous or intramuscular administration. These routes of administration should be avoided.

Safety has not been established with long-term use, as cefovecin sodium dosing should not exceed 1 single dose in cats and 2 doses in dogs.

Drug Interactions

Cefovecin sodium is highly protein-bound (98.5% in dogs and 99.8% in cats) and therefore may result in high free (active) concentrations of cefovecin or competing drugs when administered concurrently with other highly protein-bound drugs. For example, experimental in vitro systems demonstrated that when given concomitantly, cefovecin could increase the free concentrations of carprofen, furosemide, doxycycline, and ketoconazole.¹ However, the clinical significance of this has not been shown, and it is thought that a clinically significant drug interaction is unlikely, specifically from concurrent administration of carprofen and cefovecin.

Fluoroquinolones have not only been shown to be compatible with cephalosporins, but also synergistic against *Pseudomonas* species. Concomitant use of fluoroquinolones and cefovecin has not yet been studied.

Monitoring

Monitoring subsequent to cefovecin sodium administration should include efficacy and resolution of clinical signs. Owners should be counseled on the expected side effects and note the occurrence of these or any other, more severe reactions. Monitoring of renal function may be warranted in patients with known renal dysfunction. Patients experiencing more severe side effects may require further monitoring, including a complete blood count or serum biochemistry panel.

OFF-LABEL USE

Urinary Tract Infections

The product package insert for Convenia states that although it is as effective as other cephalosporins against *Escherichia coli* in vitro, its high affinity for protein binding keeps its in vivo free concentration from reaching the MIC₉₀ for *E coli*.¹ However, other studies have evaluated the efficacy of cefovecin for the treatment of urinary tract infections in both cats and dogs. Overall cure rates for dogs with *E coli* infections were 79.1% for those treated with cefovecin and 36.4%

for those treated with cephalexin.⁹ In cats, cefovecin demonstrated statistical noninferiority compared with cephalexin for bacterial elimination.¹⁰

Parvovirus

A 2017 study found cefovecin sodium administered at the labeled dose to be a reasonable option as part of an outpatient regimen, including subcutaneous fluids and maropitant, for the treatment of canine parvoviral enteritis in patients that cannot receive standard inpatient therapy.¹¹

CONCLUSION

Cefovecin sodium provides reliable efficacy for the treatment of canine and feline skin infections, abscesses, and wounds. Its convenient one-time dosing eliminates reliance on owners to maintain medication compliance for days to weeks while providing efficacy similar to that of traditional oral antibiotic regimens. Cefovecin is generally well tolerated in both cats and dogs, with adverse effects being mild. However, risk should always be weighed against benefit due to its long-acting nature and, therefore, potential for long-lasting adverse effects. **TVP**

References

1. Convenia [package insert]. Kalamazoo, MI: Zoetis; January 2013.
2. Wang N, Neilan AM, Klompas M. *Staphylococcus intermedius* infections: case report and literature review. *Infect Dis Rep* 2013;5(1):e3.
3. Stegemann MR, Coati N, Passmore CA, Sherington J. Clinical efficacy and safety of cefovecin in the treatment of canine pyoderma and wound infections. *J Small Anim Pract* 2007;48(7):378-386.
4. Stegemann MR, Sherington J, Passmore C. The efficacy and safety of cefovecin in the treatment of feline abscesses and infected wounds. *J Small Anim Pract* 2007;48(12):683-689.
5. Stegemann MR, Sherington J, Blanchflower S. Pharmacokinetics and pharmacodynamics of cefovecin in dogs. *J Vet Pharmacol Ther* 2006;29(6):501-511.
6. Stegemann MR, Sherington J, Coati N, et al. Pharmacokinetics of cefovecin in cats. *J Vet Pharmacol Ther* 2006;29(6):513-524.
7. European Medicines Agency. European Public Assessment Report Convenia (cefovecin). ema.europa.eu/en/documents/overview/convenia-epar-summary-public_en.pdf. Accessed September 2020.
8. Veterinary Medication Errors. Food and Drug Administration Center for Veterinary Medicines. fda.gov/animal-veterinary/product-safety-information/veterinary-medication-errors. Accessed September 2020.
9. Passmore CA, Sherington J, Stegemann MR. Efficacy and safety of cefovecin (Convenia) for the treatment of urinary tract infections in dogs. *J Small Anim Pract* 2007;48(3):139-144.
10. Passmore CA, Sherington J, Stegemann MR. Efficacy and safety of cefovecin for the treatment of urinary tract infections in cats. *J Small Anim Pract* 2008;49(6):295-301.
11. Venn EC, Preisner K, Boscan PL, et al. Evaluation of an outpatient protocol in the treatment of canine parvoviral enteritis. *J Vet Emerg Crit Care* 2017;27(1):52-65.

Emily Sorah

Dr. Sorah received her Doctor of Pharmacy degree from East Tennessee State University's Bill Gatton College of Pharmacy in 2014. She then completed the clinical veterinary pharmacy residency program at NC State before accepting a staff pharmacist position. Dr. Sorah now serves as director of Clinical Pharmacy Services at NC State College of Veterinary Medicine. She also serves as an adjunct professor, teaching veterinary pharmacology at Campbell University School of Pharmacy and UNC Eshelman School of Pharmacy.



Hafiz Tayebali

Dr. Tayebali received his Doctor of Pharmacy degree from the University of North Carolina Eshelman School of Pharmacy in 2019. He then completed the Clinical Veterinary Pharmacy Residency program at the NC State College of Veterinary Medicine in 2020.

