CEPHALOSPORINS (Veterinary—Systemic)

This monograph includes information on the following: Cefaclor; Cefadroxil; Cefazolin; Cefixime; Cefotaxime; Cefotetan; Cefoxitin; Cefpodoxime†; Ceftazidime; Ceftiofur; Cephalexin; Cephalothin*; Cephapirin†; Cephradine†.

Some commonly used *brand names* are:

For veterinary-labeled products—

Cefa-Drops [Cefadroxil]	*Excenel RTU* [Ceftiofur]
Excede [Ceftiofur]	*Naxcel* [Ceftiofur]
Excede for Swine [Ceftiofur]	*Simplicef* [Cefpodoxime]
Excenel [Ceftiofur]	

For selected human-labeled products—

Ancef [Cefazolin]	*Keflin* [Cephalothin]
Apo-Cefaclor [Cefaclor]	*Keftab* [Cephalexin]
Apo-Cephalex [Cephalexin]	*Kefzol* [Cefazolin]
Ceclor [Cefaclor]	*Mefoxin* [Cefoxitin]
Cefadyl [Cephapirin]	*Novo-Lexin* [Cephalexin]
Cefotan [Cefotetan]	*Nu-Cephalex* [Cephalexin]
Ceporacin [Cephalothin]	*PMS-Cephalexin* [Cephalexin]
Ceptaz [Ceftazidime]	*Suprax* [Cefixime]
Claforan [Cefotaxime]	*Tazicef* [Ceftazidime]
Fortaz [Ceftazidime]	*Velosef* [Cephradine]
Keflex [Cephalexin]	

Note: For a listing of dosage forms and brand names by country availability, see the *Dosage Forms* section(s).

*Not commercially available in the U.S.
†Not commercially available in Canada.

Category: Antibacterial (systemic).

Indications

Note: The text between [EL-US] and [EL] describes uses that are not included in U.S. product labeling. Text between [EL-CAN] and [EL] describes uses that are not included in Canadian product labeling.

The [EL-US] or [EL-CAN] designation can signify a lack of product availability in the country indicated. See the *Dosage Forms* section of this monograph to confirm availability.

General considerations

Cephalosporins are wide-spectrum antibiotics used to treat a variety of infections in animals. They have been grouped into three "generations" based primarily on their spectrum of antibacterial activity.{R-1; 2} Some of the more recently developed cephalosporins may not easily fit into one of the generations, but are usually included in the generation their antibacterial properties most closely resemble.

First-generation cephalosporins include cefadroxil, cefazolin, cephalexin, cephalothin, cephapirin, and cephradine.

First-generation cephalosporins have the highest activity of the cephalosporins against gram-positive bacteria, including most *Corynebacteria, Streptococci,* and *Staphylococci*, particularly *Staphylococcus aureus*{R-3} and *Staphylococcus intermedius.*{R-32} Cephalothin and cephapirin generally have the greatest activity against staphylococci;{R-2} *Staphylococcus epidermidis* is only variably susceptible to cephalexin and cefadroxil.{R-1} *Rhodococcus equi*, methicillin-resistant *S. aureus*, and *Enterococcus* species are usually resistant.{R-1} The first-generation cephalosporins have activity against gram-negative bacteria, including some *Actinobacillus, Escherichia coli, Haemophilus influenzae, Klebsiella pneumoniae, Pasteurella, Proteus mirabilis,* and *Salmonella;* however, *Actinobacter, Citrobacter, Enterobacter,* indole-positive *Proteus,* and *Pseudomonas* are resistant.{R-1; 3; 4; 53} Many anaerobic bacteria are susceptible to these antibacterials, with the exception of beta-lactamase–producing *Bacteroides*{R-1; 4} and *Clostridium difficile.*{R-98}

Second-generation cephalosporins include cefaclor, cefamandole, cefmetazole, cefonicid, cefotetan, cefoxitin, cefprozil, and cefuroxime.

Second-generation cephalosporins have the same efficacy as or perhaps slightly less efficacy than first-generation cephalosporins against gram-positive pathogens; however, this lack of efficacy is primarily against *S. aureus* and *S. intermedius*. Second-generation are more effective than first-generation cephalosporins in the treatment of infections caused by gram-negative bacteria such as *Enterobacter, E. coli, Klebsiella,* and *Proteus*.{R-1; 4; 7} Many anaerobic bacteria are susceptible to second-generation cephalosporins; cefoxitin{R-7-9} and cefotetan{R-80} can also be effective against *Bacteroides fragilis.* However, *Enterococcus* and *Pseudomonas* species are resistant to second-generation cephalosporins.{R-80} Use of these antimicrobials is generally reserved for infections that are resistant to first-generation cephalosporins.

Third-generation cephalosporins include cefixime, cefoperazone, cefotaxime, cefpodoxime, ceftazidime, ceftizoxime, and ceftriaxone.

Third-generation cephalosporins are the most effective of the cephalosporins against antibiotic-resistant gram-negative bacteria.{R-1; 2; 7} Ceftazidime and cefoperazone are active against *Pseudomonas*, but the majority of the third-generation cephalosporins commonly used in veterinary practice are not.{R-4; 80} Third-generation cephalosporins, in general, are no more and perhaps are less effective than other cephaosporins against gram-positive bacteria.{R-1; 4; 7} Cefotaxime, ceftazidine, ceftizoxine, and ceftriaxone are the only cephalosporins that consistently reach effective antibacterial concentrations in the central nervous system in people with inflamed meninges. Cefpodoxime remains stable in the presence of many beta-lactamase enzymes, thereby increasing its effectiveness in the treatment of beta-lactamase–producing bacteria; however, it is not active against most obligate anaerobes, *Pseudomonas* species, or enterococci.{R-110} Ceftiofur is a cephalosporin that does not clearly fit into the third-

Evidence Quality

A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Insufficient evidence to support a recommendation for use
D	Moderate evidence to support a recommendation against use
E	Good evidence to support a recommendation against use

Evidence Type

1	Species-specific evidence from at least one large randomized and controlled trial (RCT) or multiple small RCTs
2	Species-specific evidence from a small RCT, disease models, large case studies, pharmacokinetic studies using surrogate endpoints, or evidence from well-designed trials in a different species that is considered appropriate for comparison
3	Dramatic results from either well-designed, species-specific trials without controls or small case studies
4	Pharmacokinetic studies without surrogate endpoints
5	*In vitro* studies
6	Opinions of respected authorities on the basis of clinical experience or reports of expert committees

generation category and has been called a "new-generation" cephalosporin.{R-91} It has broader gram-positive activity, including good activity against *Streptococci*, and less activity against *Pseudomonas* than other third-generation cephalosporins.{R-68} It is active against beta-lactamase–producing strains as well as anaerobes, such as *Fusobacterium necrophorum* and *Bacteroides melaninogenicus.*{R-81} Ceftiofur is rapidly metabolized to desfuroylceftiofur *in vivo* and *S. aureus* is four- to eightfold less sensitive to desfuroylceftiofur than to the parent ceftiofur.{R-63; 100} *Proteus mirabilis* has a widely variable susceptibility to some metabolites of ceftiofur.{R-72}

Accepted

Escherichia coli infections (treatment)—EL,CAN*Chicks*EL and *turkey poults,* day-old: Ceftiofur for injection is indicated in the control of early mortality associated with susceptible *E. coli.*{R-11; 12}

EL,CANMetritis (treatment)EL—*Cattle:* Ceftiofur injectable suspension is indicated in the treatment of acute metritis (up to 14 days postpartum), caused by susceptible organisms.{R-81}

Pneumonia, bacterial (treatment)—

Cattle: EL,CANCeftiofur injectable oil suspension,EL ceftiofur injectable suspension, and ceftiofur for injection are indicated in the treatment of bovine respiratory disease complex (shipping fever), caused by susceptible organisms, including *Histophilus somni* (formerly *Haemophilus somnus*), *Mannheimia (Pasteurella) haemolytica,* and *Pasteurella multocida.*{R-11; 12; 81; 99; 106} EL,CANCeftiofur injectable oil suspension is also indicated in the control of these infections in animals at high risk of developing them.EL{R-106}

EL,CAN*Goats*EL: Ceftiofur for injection is indicated in the treatment of caprine respiratory disease caused by susceptible organisms, including *M. haemolytica* and *P. multocida.*{R-11}

Pigs: Ceftiofur injectable suspension and ceftiofur for injection are indicated in the treatment of swine respiratory disease caused by susceptible organisms, including *Actinobacillus pleuropneumoniae, P. multocida, Salmonella choleraesuis,* and *Streptococcus suis* type 2.{R-11; 81; 96; 99} Ceftiofur injectable oil suspension is indicated in the treatment of respiratory tract infections caused by susceptible organisms, including *Actinobacillus pleuropneumoniae, Haemophilus parasuis, P. multocida,* and *Streptococcus suis*.{R-107}

Sheep: Ceftiofur for injection is indicated in the treatment of ovine respiratory disease caused by susceptible *M. haemolytica* and *P. multocida.*{R-11; 12; 97} In Canada, ceftiofur for injection is indicated in the treatment of respiratory infection caused by *Mannheimia* species in lambs.{R-12}

Pododermatitis, acute (treatment)—*Cattle:* Ceftiofur for injection and ceftiofur injectable suspension are indicated in the treatment of acute bovine interdigital necrobacillosis associated with *F. necrophorum* and *B. melaninogenicus.*{R-11; 12; 81; 99}

Respiratory tract infections (treatment)—*Horses:* Ceftiofur for injection is indicated in the treatment of respiratory tract infections caused by susceptible organisms, including *Streptococcus zooepidemicus.*{R-11; 12}

Skin and soft tissue infections (treatment)—

Cats: Cefadroxil and EL,USA,CANcephalexinEL are indicated in the treatment of skin and soft tissue infections caused by susceptible organisms, including *P. multocida, S. aureus,* some *S. epidermidis, S. intermedius,* and *Streptococcus* species.{R-3; 32; 79}

Dogs: Cefadroxil and EL,USA,CANcephalexinEL are indicated in the treatment of skin and soft tissue infections caused by susceptible organisms, including *P. multocida, S. aureus,* some *S. epidermidis, S. intermedius,* and *Streptococcus* species.{R-3; 32; 79}

EL,CANCefpodoxime proxetil tablets are indicated in the treatment of skin infections caused by susceptible *E. coli, P. multocida, Proteus mirabilis, S. aureus, S. intermedius,* and *Streptococcus canis* (group G, *beta*-hemolytic).EL{R-110}

Urinary tract infections (treatment)—*Dogs:* Cefadroxil and ceftiofur for injection are indicated in the treatment of urinary tract infections caused by susceptible organisms, including *E. coli, P. mirabilis,* and *S. aureus.*{R-3; 11; 12}

EL,USA,CANPerioperative infections (prophylaxis)EL—*Dogs:* Cefazolin is used in the prevention of infections associated with surgery, including bone surgery, and caused by susceptible organisms when the risk of infection is high or potentially severely damaging.{R-1; 2; 6; 82; 83}

Potentially effective

Infections, bacterial (treatment)—

EL,USA,CAN*Birds*EL: There are insufficient data to establish the efficacy and safety of cephalexin and cephalothin in the treatment of bacterial infections in birds, such as cranes, ducks, emu, pigeons, and quail; however, based on pharmacokinetic studies and the apparent wide margin of safety, they have been used in the treatment of susceptible bacterial infections.{R-34}

Cats: EL,USA,CANThere are insufficient data to establish the efficacy and safety of cefotaxime{R-42} and cephalexin{R-49; 50} in the treatment of bacterial infections in cats; however, based on pharmacokinetics, pathogen sensitivities, and the apparent wide margin of safety, these medications are used to treat a variety of susceptible infections, including certain *bone, respiratory, skin, soft tissue,* and *urinary tract infections*.EL

Dogs: EL,USA,CANThere are insufficient data to establish the efficacy and safety of cefaclor, cefazolin, cefotaxime, ceftiofur (for non–urinary tract infections), cephalexin, cephalothin, cephapirin, and cephradrine for the treatment of bacterial infections in dogs; however, based on pharmacokinetic data,{R-43; 49; 50; 72; 82; 83; 133} knowledge about *in vitro* efficacy, and the apparent wide margin of safety, these medications are used to treat a variety of susceptible infections, including certain *bone, respiratory, skin, soft tissue,* and *urinary tract infections*.

Also, there are insufficient data to establish the clinical efficacy and safety of cefixime in the treatment of bacterial infections in dogs; however, pharmacokinetics and determination of minimum inhibitory concentrations against common pathogens show that cefixime is likely to be effective in the treatment of *bone, bladder, skin,* and *soft tissue infections.*{R-77}

There are insufficient data to establish the clinical efficacy and safety of cefotetan and cefoxitin in the treatment of *gram-negative* or *polymicrobial infections* (such as *Enterobacteriaceae* species and an obligate anaerobe) in dogs; however, pharmacokinetics and a determination of minimum inhibitory concentrations against common pathogens show that cefotetan and cefoxitin are likely to be effective in the treatment of these types of infections.{R-84}

In addition, although safety and efficacy have not been established, there are pharmacokinetic and minimum inhibitory concentration data that suggest ceftazidime is likely to be effective in the treatment of infections caused by *gram-negative bacteria,* including *Pseudomonas* species (Evidence rating: B-2).EL{R-147}

EL,USA,CAN*Foals*EL: There are insufficient data to establish the safety and efficacy of ceftiofur{R-48} and cephradine{R-85} in foals for the treatment of bacterial infections; however, based on the pharmacokinetics known, pathogen sensitivities, and the apparent wide margin of safety, these medications are used to treat a variety of susceptible infections, including certain *bone, joint, respiratory, skin, soft tissue,* and *urinary tract infections*.

There are insufficient data to establish the safety and efficacy of cefotaxime and other third-generation cephalosporins in the treatment of *neonatal sepsis* and secondary *bacterial meningitis* in foals; however, based on known human central nervous system distribution and clinical response in foals, cefotaxime is used to treat these infections when they are not

responsive to other antimicrobials.[EL] {R-62; 67}
There are insufficient data to establish the safety and efficacy of cefpodoxime in the treatment of bacterial infections in foals; however, pharmacokinetic data from a three-day dosing study suggest that serum concentrations of cefpodoxime proxetil necessary to treat certain bacterial infections can be reached (Evidence rating: B-2).{R-112}

Horses: [EL,US,CAN] There are insufficient data to establish the efficacy and safety of cefoxitin,{R-29} cephalothin,{R-9; 19} and cephapirin{R-18} in horses for the treatment of bacterial infections; however, based on the pharmacokinetics known, pathogen sensitivities, and the apparent wide margin of safety, these medications are used to treat a variety of susceptible infections, including certain *bone, joint, respiratory, skin, soft tissue,* and *urinary tract infections*. There are insufficient data to establish the safety and efficacy of cephalexin in the treatment of susceptible gram-positive infections in horses; however, pharmacokinetic evidence suggests that plasma concentrations of cephalexin necessary to treat certain bacterial infections can be reached with oral administration (Evidence rating: B-2).[EL] {R-131}

[EL,US,CAN] Mastitis, severe coliform (treatment adjunct) [EL]—*Cows:* Parenterally administered ceftiofur is not considered an effective treatment for mastitis in cattle.{R-69; 140-142} Pharmacokinetic studies have shown that distribution of ceftiofur into milk is insufficient to produce therapeutic concentrations when the medication is administered at recommended dosages.{R-69; 141} However, an efficacy study suggests the survival rate of cattle with severe coliform mastitis can be increased with systemic ceftiofur administration, a result attributed to controlling the effects of bacteremia (Evidence rating: B-1,2).{R-139} It should not be assumed that a milk withdrawal time is unnessary for cows receiving this treatment. See *Ceftiofur for Injection* and *Ceftiofur Injectable Suspension* in the *Dosage Forms* section of this monograph for more information.

[EL,US,CAN] Retained fetal membranes (treatment)[EL]—*Cows:* There are insufficient data to establish the safety and efficacy of the intrauterine administration of ceftiofur in improving clinical outcomes for cows with retained fetal membranes; however, one study suggests this treatment decreases a dairy cow's risk of culling and improves its chances of performing as well as other cows in the herd (Evidence rating: B-1).{R-148}

Regulatory Considerations

U.S. and Canada—{R-11; 12}

Withdrawal times have been established for ceftiofur (see the *Dosage Forms* section). Ceftiofur is not for use in horses intended for human consumption.

Chemistry

Source: Most cephalosporins are semisynthetic derivatives of the metabolic products of the fungus *Cephalosporium acremonium.*{R-1-3}

Chemical group: Beta-lactam antibiotics.{R-2; 7}

Molecular formula:{R-13}

Cefaclor—$C_{15}H_{14}ClN_3O_4S \cdot H_2O$.
Cefadroxil—$C_{16}H_{17}N_3O_5S \cdot H_2O$.
Cefazolin sodium—$C_{14}H_{13}N_8NaO_4S_3$.
Cefixime—$C_{16}H_{15}N_5O_7S_2 \cdot 3H_2O$.
Cefotaxime sodium—$C_{16}H_{16}N_5NaO_7S_2$.
Cefotetan disodium—$C_{17}H_{15}N_7Na_2O_8S_4$.
Cefoxitin sodium—$C_{16}H_{16}N_3NaO_7S_2$.
Cefpodoxime proxetil—$C_{21}H_{27}N_5O_9S_2$.
Ceftazidime—$C_{22}H_{22}N_6O_7S_2 \cdot 5H_2O$.
Ceftiofur hydrochloride—$C_{19}H_{17}N_5O_7S_3 \cdot HCl$.
Ceftiofur sodium—$C_{19}H_{16}N_5NaO_7S_3$.
Cephalexin—$C_{16}H_{17}N_3O_4S \cdot H_2O$.
Cephalexin hydrochloride—$C_{16}H_{17}N_3O_4S \cdot HCl \cdot H_2O$.
Cephalothin sodium—$C_{16}H_{15}N_2NaO_6S_2$.
Cephapirin sodium—$C_{17}H_{16}N_3NaO_6S_2$.
Cephradine—$C_{16}H_{19}N_3O_4S$.

Molecular weight:{R-13}

Cefaclor—385.82.
Cefadroxil—381.40;{R-13} 372.39 (hemihydrate); 363.4 (anhydrous).{R-14}
Cefazolin sodium—476.49.
Cefixime—507.50.
Cefotaxime sodium—477.45.
Cefotetan disodium—619.58.
Cefoxitin sodium—449.43.
Cefpodoxime proxetil—557.60.
Ceftazidime—636.65.
Ceftiofur hydrochloride—560.02.
Ceftiofur sodium—545.54.
Cephalexin—365.40.
Cephalexin hydrochloride—401.87.
Cephalothin sodium—418.42.
Cephapirin sodium—445.45.
Cephradine—349.40.

Description:{R-14}

Cefaclor USP—White to off-white, crystalline powder.
Cefadroxil USP—White to off-white, crystalline powder.
Cefazolin Sodium USP—White to off-white, practically odorless, crystalline powder, or white to off-white solid.
Cefixime USP—White to light yellow, crystalline powder.
Cefotaxime Sodium USP—Off-white to pale yellow crystalline powder.
Cefotaxime sodium injection—Solutions of cefotaxime sodium range from very pale yellow to light amber depending on the concentration and the diluent used.
Cefotetan disodium—White to pale yellow powder.
Cefotetan disodium injection—Solution varies from colorless to yellow, depending on the concentration.
Cefoxitin Sodium USP—White to off-white, granules or powder, having a slight characteristic odor. Is somewhat hydroscopic.
Cefpodoxime Proxetil USP—White to light brownish-white powder. Odorless or having a faint odor, and has a bitter taste.
Ceftazidime—White to cream-colored, crystalline powder.
Ceftiofur sodium—Off-white to tan powder. Decomposes above 190 °C without melting.{R-108}
Cephalexin USP—White to off-white, crystalline powder.
Cephalexin Hydrochloride USP—White to off-white crystalline powder.
Cephalothin Sodium USP—White to off-white, practically odorless, crystalline powder.
Cephapirin Sodium USP—White to off-white crystalline powder, odorless or having a slight odor.
Cephradine USP—White to off-white, crystalline powder.

pKa:

Cefotaxime—3.35.{R-15}
Cefoxitin—2.2.{R-16; 17}
Cephalexin—5.3 and 7.3.{R-16; 17}
Cephalothin—5.0.{R-17}
Cephapirin—2.15 and 5.44.{R-16}
Cephradine—2.6 and 7.3.{R-17}

Solubility:{R-14}

Cefaclor USP—Slightly soluble in water; practically insoluble in methanol and in chloroform.
Cefadroxil USP—Slightly soluble in water; practically insoluble in alcohol, in chloroform, and in ether.
Cefazolin Sodium USP—Freely soluble in water, in saline TS, and in dextrose solutions; very slightly soluble in alcohol; practically insoluble in chloroform and in ether.
Cefixime USP—Soluble in methanol and in propylene glycol; slightly soluble in alcohol, in acetone, and in glycerin; very slightly soluble in 70% sorbitol and in octanol; practically insoluble in ether, in ethyl acetate, in hexane, and in water.
Cefotaxime Sodium USP—Freely soluble in water; practically insoluble in organic solvents.

Cefotetan disodium—Very soluble in water.

Cefoxitin Sodium USP—Very soluble in water; soluble in methanol; sparingly soluble in dimethylformamide; slightly soluble in acetone; insoluble in ether and in chloroform.

Cefpodoxime Proxetil USP—Very slightly soluble in water; soluble in acetonitrile and in methanol; freely soluble in dehydrated alcohol; slightly soluble in ether.

Ceftazidime—Soluble in alkali and in dimethyl sulfoxide; slightly soluble in dimethylformamide, in methanol, and in water; insoluble in acetone, in alcohol, in chloroform, in dioxane, in ether, in ethyl acetate, and in toluene.

Ceftiofur sodium—Solubility is pH dependent (greater than 400 mg per mL in water at pH > 5.5),[R-68] although it gels with time.[R-108] No gelling or precipitation occurs at a concentration of 70 mg/mL.[R-108]

Cephalexin USP—Slightly soluble in water; practically insoluble in alcohol, in chloroform, and in ether.

Cephalexin Hydrochloride USP—Soluble to the extent of 10 mg per mL in water, in acetone, in acetonitrile, in alcohol, in dimethylformamide, and in methanol; practically insoluble in chloroform, in ether, in ethyl acetate, and in isopropyl alcohol.

Cephalothin Sodium USP—Freely soluble in water, in saline TS, and in dextrose solutions; insoluble in most organic solvents.

Cephapirin Sodium USP—Very soluble in water; insoluble in most organic solvents.

Cephradine USP—Sparingly soluble in water; very slightly soluble in alcohol and in chloroform; practically insoluble in ether.

Pharmacology/Pharmacokinetics

Note: See also *Table 1. Pharmacology/Pharmacokinetics* at the end of this monograph.

Mechanism of action/Effect: Cephalosporins are beta-lactam antibiotics that produce their bactericidal effect by inhibition of cell wall synthesis. The site of action for beta-lactam antibiotics is the penicillin-binding proteins (PBPs) on the inner surface of the bacterial cell membrane that are involved in synthesis of the cell wall.[R-2] In actively growing cells, the cephalosporins bind to the PBPs within the cell wall and lead to interference in production of cell wall peptidoglycans and subsequent lysis of the cell in an iso-osmotic environment.[R-7; 9] Differences in affinity for the types of PBPs by different beta-lactam antibiotics and the bacterial defense mechanisms explain the variations in bactericidal activity among cephalosporins.[R-9]

Distribution: Cephalosporins distribute into most body tissues and fluids.[R-18] They penetrate into pleural fluid, synovial fluid, pericardial fluid, and urine. Cephalosporins can be found in bile fluid if no biliary obstruction is present.[R-1] The cephalosporins penetrate aqueous humor and prostatic fluid less than other body fluids. Most of the cephalosporins have poor penetration of the blood-brain barrier.[R-2; 113] Cefuroxime is the only second-generation cephalosporin known to adequately penetrate into cerebrospinal fluid in people; also, the third-generation antibiotics cefotaxime and cefoxitin have been shown to penetrate inflamed meninges in people.[R-1] Ceftriaxone has been shown to penetrate normal meninges in horses.[R-103]

The high level of protein binding by ceftiofur in adult animals causes its distribution to differ from that of other cephalosporins.[R-91] Also, the primary metabolite of ceftiofur, desfuroylceftiofur, has a reactive sulfhydryl group that forms reversible covalent bonds with plasma and tissue proteins.[R-63] Free concentrations of ceftiofur and its active metabolites tend to be lower than expected when dosages shown to be effective in the treatment of a disease are administered, possibly because of their unique protein binding abilities.[R-63] Concentrations of ceftiofur and active metabolites in *Pasteurella*-infected tissue chambers implanted into cattle tend to be higher than concentrations in uninfected chambers.[R-73] Studies of distribution of ceftiofur into other tissues have also shown it to be unique, although the way in which this affects efficacy in the extra-label treatment of infections is not known. Ceftiofur is found in endometrial tissue within four to eight hours of subcutaneous administration to postpartum cows.[R-120] When testing tissues potentially used for residue monitoring, the highest concentrations of ceftiofur are found in kidneys after intramuscular administration to pigs and sheep, followed in pigs by the injection sites, lungs, liver, and muscle.[R-119; 121]

Biotransformation: Cefotaxime,[R-20] cephalothin,[R-19] and cephapirin undergo biotransformation in the liver to desacetyl derivatives.[R-1; 2] Cefpodoxime proxetil is a prodrug that is converted by de-esterization in the gastrointestinal tract to an active metabolite, cefpodoxime.[R-110] Ceftiofur is rapidly converted *in vivo* to desfuroylceftiofur, which is structurally similar to and, in most instances, equally active microbiologically to, ceftiofur.[R-30] The significant exceptions are that *Staphylococcus aureus* is four- to eightfold less sensitive to desfuroylceftiofur than to ceftiofur,[R-63; 100] and that *Proteus mirabilis* has a widely variable susceptibility to some ceftiofur metabolites.[R-72] The metabolites of other cephalosporins may retain some antibacterial activity.

Elimination: For most cephalosporins, elimination is by renal tubular secretion and/or glomerular filtration.

In pigs, 70 to 80% of an intramuscular ceftiofur dosage was shown to be eliminated in the urine and about 13% in the feces.[R-119] In sheep, 93% of an intramuscular dosage was found to be eliminated in the urine and 7% in the feces.[R-121]

In dogs, 86%, and in rats, 97% of an intravenous 20-mg/kg dose of ceftazidime was demonstrated to be eliminated as active drug in the urine within twenty-four hours.[R-149]

Precautions to Consider

Species sensitivity

Rabbits and *small rodents*—Cephalosporins may disturb the normal intestinal microflora, particularly when administered orally at high doses.[R-21; 80]

Cross-sensitivity

The incidence of cross-sensitivity in animals is unknown. Caution should be used when cephalosporins are administered to patients with a history of an anaphylactic reaction to other beta-lactam antibiotics because cross-reaction may occur;[R-1] however, a history of a delayed allergic reaction to penicillin does not contraindicate use of a cephalosporin.[R-2]

Pregnancy/Reproduction

Pregnancy—Cephalosporins have been shown to cross the placenta in animals. Studies in laboratory animals have not shown the cephalosporins to cause adverse effects in the fetus.[R-22-24] Studies with cefoxitin have found no evidence that the medication is teratogenic or fetotoxic in mice and rats, but a slight decrease in fetal weight has occurred.[R-21]

Lactation

Cephalosporins are distributed into milk;[R-25] however, when administered systemically at accepted doses, therapeutic concentrations are not reached in milk.[R-67; 69]

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this

medication.
Although cephalothin has been associated with an increased human risk of nephrotoxicity when administered with an aminoglycoside, this interaction may not apply to other cephalosporins.[R-98] In fact, there is some evidence that certain cephalosporins such as cefamandole, cefazolin, and cephalothin provide a protective effect against aminoglycoside-induced nephrotoxicity in rats[R-101] while others, such as cephalexin, have no effect.[R-102]

Probenecid
(probenecid administered concurrently with a cephalosporin will inhibit renal tubular secretion and in some cases increase the serum concentrations and prolong the serum half-life of the cephalosporin,[R-2] including cefadroxil,[R-3] cefoxitin,[R-26] cephalothin,[R-30] and cephapirin;[R-27] probenecid has not been shown to alter the renal tubular secretion of ceftiofur in dairy cattle[R-70] or of cefazolin in mares[R-135])

Human drug interactions[R-46]

In addition to the above drug interactions reported in animals, the following drug interactions have been reported in humans, and are included in the human monograph *Cephalosporins (Systemic)* in *USP DI Volume I;* these drug interactions are intended for informational purposes only and may or may not be applicable to the use of cephalosporins in the treatment of animals:

Antacids or
Ranitidine or
Histamine H_2-receptor antagonists, other
(concurrent use of high doses of antacids or H_2-receptor antagonists with cefpodoxime decreases absorption of cefpodoxime by 27 to 32%, and decreases peak plasma levels by 24 to 42%)
(the extent of absorption of cefaclor is decreased with concurrent use of aluminum hydroxide- or magnesium-containing antacids; cefaclor should not be taken within 1 hour of taking these antacids)

Anticoagulants, coumarin- or indandione-derivative, or
Heparin or
Thrombolytic agents
(concurrent use of these medications with cefotetan may increase the risk of bleeding because of the *N*-methylthiotetrazole [NMTT] side chain on these medications; however, critical illness, poor nutritional status, and the presence of liver disease may be more important risk factors for hypoprothrombinemia and bleeding; because all cephalosporins can inhibit vitamin K synthesis by suppressing gut flora, prophylactic vitamin K therapy is recommended when any of these medications is used for prolonged periods in malnourished or seriously ill patients; dosage adjustments of anticoagulants may be necessary during and after therapy with cefotetan; concurrent use with thrombolytic agents may increase the risk of severe hemorrhage and is not recommended)
(an increased anticoagulant effect has been reported with concurrent use of cefaclor and oral anticoagulants)

Nephrotoxic medications
(cephalothin has been associated with an increased incidence of nephrotoxicity when used concurrently with aminoglycosides; this effect has rarely been seen with other commercially available cephalosporins used at appropriate doses; the potential for increased nephrotoxicity exists when cephalosporins are used with other nephrotoxic medications, such as loop diuretics, especially in patients with pre-existing renal function impairment; renal function should be monitored carefully in patients receiving cephalosporins and aminoglycosides concurrently)

Platelet aggregation inhibitors, other
(hypoprothrombinemia induced by large doses of salicylates and/or cephalosporins, and the gastrointestinal ulcerative or hemorrhagic potential of nonsteroidal anti-inflammatory drugs [NSAIDs], salicylates, or sulfinpyrazone may increase the risk of hemorrhage)

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

With diagnostic test results
Coombs' test
(positive reactions for the Coombs' test may be seen in animals
receiving cephalosporins;[R-110] this may be due to changes in the red blood cells, but hemolytic anemia usually is not occurring[R-2])

Glucose, urine
(in dogs, cephalexin has been shown to produce false-positive and false-negative urine glucose results with some commercial tests [*Chemstrips* and *Clinitest* were used in the study]; other than being test-dependent, this problem is probably also dosage-dependent and dependent on the timing of collection after drug administration)[R-114]
(See also *Human laboratory value alterations* below in this monograph)

With physiology/laboratory test values
Ketones, urine
(values may be increased)[R-68]

Human laboratory value alterations[R-46]

The following laboratory value alterations have been reported in humans, and are included in the human monograph *Cephalosporins (Systemic)* in *USP DI Volume I;* these laboratory value alterations are intended for informational purposes only and may or may not be applicable to the use of cephalosporins in the treatment of animals:

With diagnostic test results
Coombs' (antiglobulin) tests
(a positive Coombs' reaction frequently appears in patients
who receive large doses of a cephalosporin; hemolysis rarely
occurs, but has been reported; test may be positive in neonates whose mothers received cephalosporins before delivery)

Creatinine, serum and urine
(cefotetan, cefoxitin, or cephalothin may falsely elevate test
values when the Jaffé's reaction method is used; serum samples should not be obtained within 2 hours after administration)

Glucose, urine
(most cephalosporins [cefaclor, cefazolin, cefixime, cefotetan, cefoxitin, cephalexin, cephalothin, cephapirin, cephradine] may produce false-positive or falsely elevated test results with copper-reduction tests [Benedict's, Fehling's, or *Clinitest*]; glucose enzymatic tests, such as *Clinistix* and *Tes-Tape*, are not affected)

Protein, urine
(cefamandole may produce false-positive tests for proteinuria
with acid and denaturization-precipitation tests)

Prothrombin time (PT)
(may be prolonged; cephalosporins may inhibit vitamin K synthesis by suppressing gut flora; also, ceftazidime and cephalosporins with the NMTT side chain [cefamandole, cefoperazone, cefotetan] have been associated with an increased incidence of hypoprothrombinemia; patients who are critically ill, malnourished, or have liver function impairment may be at the highest risk of bleeding)

With physiology/laboratory test values

Alanine aminotransferase (ALT [SGPT]), or
Alkaline phosphatase, or
Aspartate aminotransferase (AST [SGOT]), or
Lactate dehydrogenase (LDH)
(serum values may be increased)
Bilirubin, serum, or
Blood urea nitrogen (BUN) or
Creatinine, serum
(concentrations may be increased)
Complete blood count (CBC) or
Platelet count
(transient leukopenia, neutropenia, agranulocytosis, thrombocytopenia, eosinophilia, lymphocytosis, and thrombocytosis have been reported on rare occasions)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance).

Except under special circumstances, this medication should not be used when the following medical problems exist:

Hypersensitivity to cephalosporins
(some reactions may be much more likely to occur in animals that have had a previous reaction to a cephalosporin or to a penicillin)[R-106; 110]

Risk-benefit should be considered when the following medical problems exist:

Bleeding disorders, history of
(some of the second- and third-generation cephalosporins have been associated with an increased risk of bleeding in people[R-65] due to a decrease in prothrombin activity, and bleeding is considered a potential human risk with all the cephalosporins; there is evidence of a significant increase in bleeding time after cephalothin administration to beagles[R-28] but not outside normal reference ranges; clinical problems have not been reported in animals and the clinical significance is unknown)
Hepatic dysfunction, severe
(because cefotaxime, cephalothin, and cephapirin are hepatically metabolized before renal elimination, severe liver dysfunction can inhibit metabolism)[R-2]
Renal insufficiency
(nephrotoxicity may occur in patients with renal insufficiency who are receiving the full dosage of cephalosporin; dosage should be adjusted)[R-1]

Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and, for humans, symptoms in parentheses where appropriate)—not necessarily inclusive:

Those indicating need for medical attention

Incidence unknown

All species

Hypersensitivity reactions (acute anaphylaxis or angioedema, allergic agranulocytosis,[R-31] fever,[R-31] serum sickness, urticaria[R-2])

Dogs

Anemia; thrombocytopenia[R-11]
Note: *Anemia* and *thrombocytopenia* have been seen in dogs given ceftiofur at high doses (three to five times the labeled dose) or for long periods of time (5 to 6 weeks). These side effects appear to be reversible when treatment is discontinued.

Foals and *horses*

Colic; diarrhea
Note: There have been reports of *colic* and/or *diarrhea* in association with the administration of some cephalosporins. Colic was reported in two of six horses given a single intragastric dose of cefpodoxime proxetil.[R-112] Diarrhea was reported in foals during treatment for infection with a regimen of intravenous cefotaxime every six to eight hours.[R-62] Colic, diarrhea, and other signs were seen during tolerance testing of horses with daily intravenous administration of ≥ 5 times the labeled dose of ceftiofur.[R-11]

Although cephalosporins are considered generally safe, horses should be monitored during antibiotic therapy.

Laminitis was reported in one of six mares in association with cefoxitin administration.[R-29]

Those indicating need for medical attention only if they continue or are bothersome

All species

Anorexia;[R-10; 32] ***diarrhea and vomiting—***possibly due to local irritation from the oral dosage forms;[R-1; 3] ***diarrhea caused by altered gut flora;***[R-2; 10] ***local reactions*** (mild to moderate pain, heat, swelling)—with parenteral dosage forms, especially cephalothin and cephapirin;[R-1; 11] ***phlebitis—***with intravenous administration[R-2]

Note: *Diarrhea and vomiting* can occur with any dosage but are more common with high doses.[R-33] Administration of the antibiotic with food may decrease the incidence of gastrointestinal effects.[R-33]

Cattle

Local ear swelling—with subcutaneous administration of ceftiofur injectable oil suspension
Note: Swelling in addition to that produced by the injection volume occurs up to the fourteen days after treatment and then recedes.[R-106] Some animals may have medication leakage or bleeding from the site just after injection or may develop a transiently drooping ear.[R-106]

Human side/adverse effects[R-46]

In addition to the above side/adverse effects reported in animals, the following side/adverse effects have been reported in humans, and are included in the human monograph *Cephalosporins (Systemic)* in *USP DI Volume I;* these side/adverse effects are intended for information purposes only and may or may not be applicable to the use of cephalosporins in the treatment of animals:

Incidence more frequent
Eosinophilia
Incidence less frequent or rare
Hypersensitibity reactions—have occurred with many cephalosporins, but reported more commonly with cefazolin; ***hypoprothrombinemia***—more frequent for cefotetan; ***pseudomembranous colitis; thrombophlebitis; urticaria***
Incidence rare
Allergic reactions, specifically anaphylaxis; epidermal necrolysis, toxic; erythema multiforme; hearing loss—has occurred rarely in pediatric patients being treated for meningitis, but more frequently with cefuroxime; ***hemolytic anemia, immune, drug-induced***—has occurred with many cephalosporins, but reported more commonly with cefotetan; ***leukopenia, neutropenia, or thrombocytopenia; renal dysfunction; serum sickness–like reactions***—may be more frequent with cefaclor; ***seizures***—especially with high doses and in patients with renal function impairment

Overdose

For information in cases of overdose or unintentional ingestion, **contact the American Society for the Prevention of Cruelty to Animals (ASPCA) National Animal Poison Control Center** (888-426-4435 or 900-443-0000; a fee may be required for consultation) **and/or the drug manufacturer.**

LD_{50}—

Cefpodoxime proxetil:[R-111]

Mouse—
Intraperitoneal: 2535 mg/kg.
Oral: >8,000 mg/kg.
Subcutaneous: >10,000 mg/kg.
Rat—Intravenous: >4,000 mg/kg.

Ceftiofur: *Rat*—
Ceftiofur hydrochloride: Intraperitoneal—881 mg/kg.{R-109}
Ceftiofur sodium:
Oral—>7,760 mg/kg. {R-108}
Peritoneal—927 mg/kg.{R-108}

General Dosing Information

Except for medications labeled specifically for veterinary use, most doses listed have been derived from phamacokinetic data, rather than from clinical studies.{R-74}

Breakpoints recommended by the Clinical Laboratory and Standards Institute (CLSI; formerly NCCLS) for cefpodoxime in animals:{R-145}

Zone diameter (millimeters)	MIC (mcg/mL)	Interpretation
≥ 21	≤ 2	Susceptible
18-20	4	Intermediate
≤ 17	≥ 8	Resistant

Breakpoints recommended by CLSI, based on pharmacokinetic studies of ceftiofur after a single intramusuclar dose of 3 to 5 mg per kg of body weight (mg/kg) in pigs and 1.1 mg/kg in cattle, minimum inhibitory concentration (MIC) for common respiratory disease pathogens, and disk (30 mcg) diffusion data:{R-11; 81; 99; 104; 107}

Zone diameter (millimeters)	MIC (mcg/mL)	Interpretation
≥ 21	≤ 2	Susceptible
18-20	4	Intermediate
≤ 17	≥ 8	Resistant

Note: In cattle, the common respiratory disease pathogens used were *Histophilus somni* (formerly *Haemophilus somnus*), *Mannheimia haemolytica,* and *Pasteurella multocida*. In pigs, these were *Actinobacillus pleuropneumoniae, P. multocida, Salmonella choleraesuis,* and *Streptococcus suis*.{R-104}

Breakpoint recommended by CLSI, based on pharmacokinetic studies of ceftiofur administered by a single intramusuclar dose of 2.2 mg/kg in horses, clinical effectiveness data, and MIC data:{R-11; 104}

Zone diameter (millimeters)	MIC (mcg/mL)	Interpretation
≥ 22	≤ 0.25	Susceptible
—	—	Intermediate
—	—	Resistant

Note: The disk content was 30 mcg and the pathogen was *Streptococcus equi* subspecies *zooepidemicus*.{R-104}
The category for "susceptible only" is used for populations of organisms (usually one species) for which regression analysis (disk vs. MIC) cannot be performed.{R-104} The single breakpoint allows detection of strains with decreased susceptibility compared to the population originally tested.{R-104}

For oral dosage forms only

Administration of oral cephalosporins, such as cefadroxil, with food appears to decrease nausea in those animals prone to the side effect;{R-33} however, administration of cefixime with food can decrease the bioavailability of the antibiotic by one half.{R-77}

For parenteral dosage forms only

Many cephalosporins can be reconstituted with 1% lidocaine to decrease injection pain. See the manufacturer's package insert.{R-80}

For treatment of adverse effects

For anaphylaxis

Recommended treatment consists of the following:
- Parenteral epinephrine
- Oxygen administration and breathing support
- Parenteral fluid administration, as needed

CEFACLOR

Summary of Differences

Indications: General considerations—Second-generation cephalosporin.

Oral Dosage Forms

Note: The text between [EL-US] and [EL] describes uses not included in U.S. product labeling. Text between [EL-CAN] and [EL] describes uses that are not included in Canadian product labeling.
The [EL-US] or [EL-CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CEFACLOR CAPSULES USP

Usual dose:

Note: [EL-US,CAN]*Dogs*—Although the efficacy and safety of cefaclor in dogs have not been established, an oral dose of 4 to 20 mg per kg of body weight every eight hours has been used in the treatment of susceptible *bacterial infections* in dogs.{R-2} There is very little canine-specific information about cefaclor; therefore, dose recommendations are based primarily on human pharmacokinetics.[EL]

Strength(s) usually available:

U.S.—{R-24}
Veterinary-labeled product(s):
Not commercially available.
Human-labeled product(s):
250 mg (Rx) [*Ceclor*].
500 mg (Rx) [*Ceclor*].

Canada—{R-36}
Veterinary-labeled product(s):
Not commercially available.
Human-labeled product(s):
250 mg (Rx) [*Apo-Cefaclor; Ceclor*].
500 mg (Rx) [*Apo-Cefaclor; Ceclor*].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container.

USP requirements: Preserve in tight containers. Contain the equivalent of the labeled amount of anhydrous cefaclor, within −10% to +20%. Meet the requirements for Identification, Dissolution (80% in 30 minutes in water in Apparatus 2 at 50 rpm), Related compounds, Uniformity of dosage units, and Water (not more than 8.0%).{R-14}

CEFACLOR FOR ORAL SUSPENSION USP

Usual dose: See *Cefaclor Capsules USP*.

Strength(s) usually available: When reconstituted according to manufacturer's instructions—
U.S.:{R-24}
Veterinary-labeled product(s)—
Not commercially available.
Human-labeled product(s)—
25 mg per mL (Rx) [*Ceclor;* GENERIC].
37.4 mg per mL (Rx) [*Ceclor;* GENERIC].
50 mg per mL (Rx) [*Ceclor;* GENERIC].

75 mg per mL (Rx) [*Ceclor;* GENERIC].

Canada:[R-36]

Veterinary-labeled product(s)—

Not commercially available.

Human-labeled product(s)—

25 mg per mL (Rx) [*Apo-Cefaclor; Ceclor*].

50 mg per mL (Rx) [*Apo-Cefaclor; Ceclor*].

75 mg per mL (Rx) [*Apo-Cefaclor; Ceclor*].

Packaging and storage: Prior to reconstitution, store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container.

Stability: After reconstitution, suspensions retain their potency for 14 days if refrigerated.

Auxiliary labeling:

- Refrigerate.
- Shake well.

USP requirements: Preserve in tight containers. A dry mixture of Cefaclor and one or more suitable buffers, colors, diluents, and flavors. Contains the equivalent of the labeled amount of anhydrous cefaclor, within –10% to +20%. Meets the requirements for Identification, Uniformity of dosage units (solid packaged in single-unit containers), Deliverable volume (solid packaged in multiple-unit containers), pH (2.5–5.0, in the suspension constituted as directed in the labeling), Related compounds, and Water (not more than 2.0%).[R-14]

CEFADROXIL

Summary of Differences

Indications:

General considerations—First-generation cephalosporin.

Indicated for treatment of susceptible genitourinary tract infections in dogs and skin and soft tissue infections in cats and dogs.

Drug interactions and/or related problems: Concurrent administration of probenecid may prolong the serum half-life of cefadroxil.[R-3]

Oral Dosage Forms

CEFADROXIL FOR ORAL SUSPENSION USP

Usual dose:

Skin and soft tissue infections—

Cats: Oral, 22 mg per kg of body weight every twenty-four hours.[R-37; 38]

Dogs: Oral, 22 mg per kg of body weight every twelve hours.[R-37; 38]

Urinary tract infections—*Dogs:* Oral, 22 mg per kg of body weight every twelve hours.[R-37; 38]

Strength(s) usually available: When reconstituted according to manufacturer's instructions—

U.S.:

Veterinary-labeled product(s)—

50 mg per mL (Rx) [*Cefa-Drops*].

Canada:

Veterinary-labeled product(s)—

50 mg per mL (Rx) [*Cefa-Drops*].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container.

Stability: When reconstituted according to manufacturer's directions and refrigerated, suspensions retain their potency for 14 days.[R-37]

USP requirements: Preserve in tight containers. A dry mixture of Cefadroxil and one or more suitable buffers, colors, diluents, and flavors. Contains the equivalent of the labeled amount of anhydrous cefadroxil, within –10% to +20%. Meets the requirements for Identification, Uniformity of dosage units (solid packaged in single-unit containers), Deliverable volume (solid packaged in multiple-unit containers), pH (4.5–6.0, in the suspension constituted as directed in the labeling), and Water (not more than 2.0%).[R-14]

CEFAZOLIN

Summary of Differences

Indications: General considerations—First-generation cephalosporin.

Parenteral Dosage Forms

Note: The dosing and strengths of the dosage forms available are expressed in terms of cefazolin base (not the sodium salt).

The text between [EL US] and [EL] describes uses not included in U.S. product labeling. Text between [EL CAN] and [EL] describes uses that are not included in Canadian product labeling.

The [EL US] or [EL CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CEFAZOLIN INJECTION USP

Usual dose: Although Cefazolin Injection USP is the same antimicrobial as Cefazolin For Injection USP, it is only available frozen in premixed dilute concentrations, making it less practical for veterinary use. For dosing information, see *Cefazolin For Injection USP*.

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):

500 mg (base) in 50 mL (Rx) [*Ancef*].

1 gram (base) in 50 mL (Rx) [*Ancef*].

Canada—

Not commercially available.

Packaging and storage: Store at –10 °C (14 °F) or below, unless otherwise specified by the manufacturer.

Preparation of dosage form: Cefazolin sodium injection should be thawed at room temperature, and all ice crystals should have melted, before administration. Thawing should not be forced by immersion in water baths or by microwave irradiation.

Stability: See manufacturer's product labeling for stability information.

Incompatibilities:

The admixture of cefazolin sodium injection with other medications is not recommended.

The admixture of beta-lactam antibacterials (penicillins and cephalosporins) and aminoglycosides may result in substantial mutual inactivation; they should not be mixed in the same intravenous bag or bottle.

USP requirements: Preserve in Containers for Injections. Maintain in the frozen state. A sterile solution of Cefazolin and Sodium

Bicarbonate in a diluent containing one or more suitable tonicity-adjusting agents. It meets the requirements for Labeling under Injections. The label states that it is to be thawed just prior to use, describes conditions for proper storage of the resultant solution, and directs that the solution is not to be refrozen. Contains the labeled amount, within –10% to +15%. Meets the requirements for Identification, Bacterial endotoxins, Sterility, pH (4.5–7.0), and Particulate matter.{R-14}

CEFAZOLIN FOR INJECTION USP

Usual dose: [EL US,CAN]Perioperative infections (prophylaxis)[EL]—*Dogs:* Intravenous, 22 mg (base) per kg of body weight every two hours, or 8 mg (base) per kg of body weight every hour, starting at the beginning of surgery and continuing until the end of surgery.{R-82}

Note: The above dose is based on pharmacokinetic studies, including studies performed during surgical procedures. [EL US,CAN]Also for *dogs*, an intramuscular or intravenous dose of 20 to 35 mg (base) per kg of body weight every four to eight hours has been used for the treatment of susceptible *bacterial infections,* based on pharmacokinetics studies.[EL]{R-2; 38; 86}

Size(s) usually available:

U.S.—{R-39}

Veterinary-labeled product(s):
Not commercially available.

Human-labeled product(s):
500 mg (base) (Rx) [*Ancef; Kefzol;* GENERIC].
1 gram (base) (Rx) [*Ancef; Kefzol;* GENERIC].
5 grams (base) (Rx) [*Ancef*].
10 grams (base) (Rx) [*Ancef; Kefzol;* GENERIC].

Canada—{R-40}

Veterinary-labeled product(s):
Not commercially available.

Human-labeled product(s):
50 mg (base) (Rx) [*Kefzol*].
500 mg (base) (Rx) [*Ancef; Kefzol;* GENERIC].
1 gram (base) (Rx) [*Ancef; Kefzol;* GENERIC].
10 grams (base) (Rx) [*Ancef; Kefzol;* GENERIC].

Packaging and storage: Prior to reconstitution, store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

Preparation of dosage form: To prepare the 100 mg of cefazolin (base) per mL dilution commonly used in veterinary practice for intramuscular or intravenous administration, 9.6 mL of sterile water for injection should be added to each 1-gram vial.{R-39; 95} See manufacturer's package insert for other preparation instructions.

Stability: See manufacturer's product labeling for stability information.

Incompatibilities: The admixture of beta-lactam antibacterials (penicillins and cephalosporins) and aminoglycosides may result in substantial mutual inactivation; they should not be mixed in the same intravenous bag or bottle.

USP requirements: Preserve in Containers for Injections. Contains an amount of Cefazolin Sodium equivalent to the labeled amount of cefazolin, within –10% to +15%. Meets the requirements for Constituted solution, Identification, Specific rotation (–10° to –24°), Bacterial endotoxins, Sterility, pH (4.0–6.0, in a solution containing 100 mg of cefazolin per mL), Uniformity of dosage units, Water (not more than 6.0%), and Particulate matter, and for Labeling under Injections.{R-14}

CEFIXIME

Summary of Differences

Indications: General considerations—Third-generation cephalosporin.

Veterinary Dosing Information: Administration with food decreases the bioavailability by one half.

Oral Dosage Forms

Note: The text between [EL US]and [EL] describes uses not included in U.S. product labeling. Text between [EL CAN]and [EL] describes uses that are not included in Canadian product labeling.

The [EL US] or [EL CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CEFIXIME FOR ORAL SUSPENSION USP

Usual dose:

Note: [EL US,CAN]*Dogs*—Although the efficacy and safety of cefixime have not been established, an oral dose of 5 mg per kg of body weight every twelve to twenty-four hours has been used in the treatment of *cystitis* in dogs, based on pharmacokinetic data.{R-77}

There are also some pharmacokinetic data to suggest that the same dose, administered for two to four weeks, is likely to be effective for treatment of *bone, skin,* and *soft tissue infections* in dogs.[EL]{R-77}

Strength(s) usually available: When reconstituted according to manufacturer's directions—

U.S.—

Veterinary-labeled product(s):
Not commercially available.

Human-labeled product(s):
20 mg per mL (Rx) [*Suprax*].

Canada—

Veterinary-labeled product(s):
Not commercially available.

Human-labeled product(s):
20 mg per mL (Rx) [*Suprax*].

Packaging and storage: Prior to reconstitution, store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

Stability: After reconstitution, suspension retains its potency for 14 days at room temperature or if refrigerated.

Auxiliary labeling: • Shake well.

USP requirements: Preserve in tight containers. A dry mixture of Cefixime and one or more suitable diluents, flavors, preservatives, and suspending agents. Label it to indicate that the cefixime contained therein is in the trihydrate form. Contains the labeled amount of anhydrous cefixime, within –10% to +20%, per mL when constituted as directed in the labeling. Meets the requirements for Identification, Uniformity of dosage units (solid packaged in single-unit containers), Deliverable volume (solid packaged in multiple-unit containers), pH (2.5–4.5, in the suspension constituted as directed in the labeling), and Water (not more than 2.0%).{R-14}

CEFIXIME TABLETS USP

Usual dose: See *Cefixime for Oral Suspension USP*.

Strength(s) usually available:

U.S.—

Not commercially available.
Canada—
Veterinary-labeled product(s):
Not commercially available.
Human-labeled product(s):
200 mg (Rx) [*Suprax*].
400 mg (Rx) [*Suprax*].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

USP requirements: Preserve in tight containers. Label Tablets to indicate that the cefixime contained therein is in the trihydrate form. Contain the labeled amount of anhydrous cefixime, within ±10%. Meet the requirements for Identification, Dissolution (75% in 45 minutes in 0.05 *M* potassium phosphate buffer [pH 7.2] in Apparatus 1 at 100 rpm), Uniformity of dosage units, and Water (not more than 10.0%).{R-14}

CEFOTAXIME

Summary of Differences

Indications: General considerations—Third-generation cephalosporin.
Pharmacology/pharmacokinetics:
Biotransformation—Significant metabolism occurs with the major pathway yielding a desacetyl derivative. Desacetylcefotaxime is less active against staphylococci but acts synergistically with the parent compound against sensitive gram-negative bacteria.{R-1}
Distribution—In people, when administered at high doses, cefotaxime enters the cerebrospinal fluid in therapeutic concentrations when meninges are inflamed.{R-1}
Medical considerations/contraindications: Severe hepatic dysfunction can inhibit metabolism.{R-2}

Parenteral Dosage Forms

Note: The dosing and strengths of the dosage forms available are expressed in terms of cefotaxime free acid (not the sodium salt).
The text between EL[US] and EL describes uses not included in U.S. product labeling. Text between EL[CAN] and EL describes uses that are not included in Canadian product labeling.
The EL[US] or EL[CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CEFOTAXIME INJECTION USP

Usual dose:
Note: EL[US,CAN]*Cats*—Although the efficacy and safety have not been established, an intramuscular or intravenous dose of 20 to 80 mg (free acid) per kg of body weight every six hours has been used in the treatment of susceptible *bacterial infections* in cats, based on pharmacokinetic data.EL{R-42}
EL[US,CAN]*Dogs*—Although the efficacy and safety have not been established, a subcutaneous dose of 50 mg (free acid) per kg of body weight every twelve hours has been used in the treatment of susceptible *bacterial infections* in dogs, based on pharmacokinetic data. When administered intramuscularly, the dose should be repeated every eight hours.EL{R-43}
EL[US,CAN]*Foals*—Although the efficacy and safety have not been established, an intravenous dose of 40 mg (free acid) per kg of body weight every six hours has been used in the treatment of *neonatal sepsis* or susceptible *bacterial meningitis* in foals.EL{R-62}

Strength(s) usually available:
U.S.—{R-44}
Veterinary-labeled product(s):
Not commercially available.
Human-labeled product(s):
20 mg (free acid) per mL (Rx) [*Claforan*].
40 mg (free acid) per mL (Rx) [*Claforan*].
Canada—
Not commercially available.

Packaging and storage: Store at –20 °C (–4 °F) or below, unless otherwise specified by manufacturer.{R-44}

Preparation of dosage form: Cefotaxime sodium injection should be thawed at room temperature, and all ice crystals should have melted, before administration.{R-44}

Stability: See manufacturer's product labeling for stability information.

USP requirements: Preserve in single-dose containers. Maintain in the frozen state. A sterile solution of Cefotaxime Sodium in Water for Injection. Contains one or more suitable buffers, and it may contain Dextrose or Sodium Chloride as a tonicity-adjusting agent. It meets the requirements for Labeling under Injections. The label states that it is to be thawed just prior to use, describes conditions for proper storage of the resultant solution, and directs that the solution is not to be refrozen. Contains an amount of cefotaxime sodium equivalent to the labeled amount of cefotaxime, within ±10%. Meets the requirements for Identification, Bacterial endotoxins, Sterility, pH (5.0–7.5), Particulate matter, and Chromatographic purity.{R-14}

CEFOTAXIME FOR INJECTION USP

Usual dose: See *Cefotaxime Injection USP*.

Size(s) usually available:
U.S.—{R-44}
Veterinary-labeled product(s):
Not commercially available.
Human-labeled product(s):
500 mg (free acid) (Rx) [*Claforan*].
1 gram (free acid) (Rx) [*Claforan*].
2 grams (free acid) (Rx) [*Claforan*].
10 grams (free acid) (Rx) [*Claforan*].
Canada—
Veterinary-labeled product(s):
Not commercially available.
Human-labeled product(s):
500 mg (free acid) (Rx) [*Claforan*].
1 gram (free acid) (Rx) [*Claforan*].
2 grams (free acid) (Rx) [*Claforan*].

Packaging and storage: Prior to reconstitution, store below 30 °C (86 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

Preparation of dosage form: Dilutions should be prepared according to manufacturer's instructions.

Stability: See manufacturer's product labeling for stability information.

Additional information: A solution containing 1 gram of cefotaxime sodium in 14 mL of sterile water for injection is isotonic.{R-44}

USP requirements: Preserve in Containers for Sterile Solids. Contains an amount of Cefotaxime Sodium equivalent to the labeled amount of cefotaxime, within –10% to +15%. Meets the requirements for Constituted solution, Identification, Bacterial endotoxins, Sterility, Uniformity of dosage units, Particulate matter, and Chromatographic purity, for pH and Loss on drying under Cefotaxime Sodium, and for Labeling under Injections.{R-14}

CEFOTETAN

Summary of Differences

Indications: General considerations—Second-generation cephalosporin.

Parenteral Dosage Forms

Note: The dosing and strengths of the dosage forms available are expressed in terms of cefotetan base (not the disodium salt).

The text between [EL-US] and [EL] describes uses not included in U.S. product labeling. Text between [EL-CAN] and [EL] describes uses that are not included in Canadian product labeling.

The [EL-US] or [EL-CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CEFOTETAN FOR INJECTION USP

Usual dose:

Note: [EL-US,CAN] *Dogs*—Although the efficacy and safety have not been established, an intravenous dose of 30 mg (base) per kg of body weight every eight hours or the same dose administered subcutaneously every twelve hours has been used in the treatment of susceptible *bacterial infections* in dogs, based on pharmacokinetic data.[EL]{R-80; 84}

Size(s) usually available:

U.S.—
- Veterinary-labeled product(s):
  - Not commercially available.
- Human-labeled product(s):
  - 1 gram (base) (Rx) [*Cefotan*].
  - 2 grams (base) (Rx) [*Cefotan*].
  - 10 grams (base) (Rx) [*Cefotan*].

Canada—
- Veterinary-labeled product(s):
  - Not commercially available.
- Human-labeled product(s):
  - 1 gram (base) (Rx) [*Cefotan*].
  - 2 grams (base) (Rx) [*Cefotan*].

Packaging and storage: Prior to reconstitution, do not store above 22 °C (72 °F), unless otherwise specified by manufacturer. Protect from light.

Preparation of dosage form: Dilutions should be prepared according to manufacturer's instructions.

Stability: See manufacturer's product labeling for stability information.

Incompatibilities: The admixture of beta-lactam antibacterials and aminoglycosides may result in substantial mutual inactivation. They should not be mixed in the same intravenous bag or bottle.

USP requirements: Preserve in containers for Sterile Solids. Contains an amount of Cefotetan Disodium equivalent to the labeled amount of cefotetan, within –10 to +20%. Meets the requirements for Constituted solution, Bacterial endotoxins, Sterility, and Particulate matter, for Identification, pH, and Water under Cefotetan Disodium, for Uniformity of dosage units, and for Labeling under Injections.{R-14}

CEFOXITIN

Summary of Differences

Indications: General considerations—Second-generation cephalosporin; good activity against anaerobic organisms, but only active against some *Bacteroides fragilis*.{R-1}

Pharmacology/pharmacokinetics: Distribution—In people, when administered at high doses, cefoxitin enters the cerebrospinal fluid in therapeutic concentrations when meninges are inflamed.{R-1}

Drug interactions and/or related problems: Concurrent administration with probenecid may prolong the serum half-life of cefoxitin.{R-26}

Parenteral Dosage Forms

Note: The dosing and strengths of the dosage forms available are expressed in terms of cefoxitin base (not the sodium salt).

The text between [EL-US] and [EL] describes uses not included in U.S. product labeling. Text between [EL-CAN] and [EL] describes uses that are not included in Canadian product labeling.

The [EL-US] or [EL-CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CEFOXITIN INJECTION USP

Usual dose:

Note: [EL-US,CAN] *Dogs*—Although the efficacy and safety have not been established, an intravenous dose of 30 mg (base) per kg of body weight every six hours or the same dose administered subcutaneously every eight hours has been used in the treatment of susceptible *bacterial infections* in dogs, based on pharmacokinetic data.[EL]{R-38; 84}

[EL-US,CAN] *Horses*—Although the efficacy and safety have not been established, an intravenous dose of 20 mg (base) per kg of body weight every four to six hours has been used in the treatment of susceptible *bacterial infections* in horses, based on pharmacokinetic data.[EL]{R-29}

Strength(s) usually available:{R-45}

U.S.—
- Veterinary-labeled product(s):
  - Not commercially available.
- Human-labeled product(s):
  - 20 mg (base) per mL (Rx) [*Mefoxin*].
  - 40 mg (base) per mL (Rx) [*Mefoxin*].

Canada—
- Not commercially available.

Packaging and storage: Store at –20 °C (–4 °F) or below, unless otherwise specified by manufacturer.{R-45}

Preparation of dosage form: See manufacturer's product labeling.

USP requirements: Preserve in Containers for Injections. Maintain in the frozen state. A sterile solution of Cefoxitin Sodium and one or more suitable buffer substances in Water for Injection. Contains Dextrose or Sodium Chloride as a tonicity-adjusting agent. It meets the requirements for Labeling under Injections. The label states that it is to be thawed just prior to use, describes conditions for proper storage of the resultant solution, and directs that the solution is not to be refrozen. Contains an amount of cefoxitin sodium equivalent to the labeled amount of cefoxitin, within –10% to +20%. Meets the requirements for Identification,

Bacterial endotoxins, Sterility, pH (4.5–8.0), and Particulate matter.{R-14}

CEFOXITIN FOR INJECTION USP
Usual dose: See *Cefoxitin Injection USP*.

Size(s) usually available:
U.S.—{R-21}
Veterinary-labeled product(s):
Not commercially available.
Human-labeled product(s):
1 gram (base) (Rx) [*Mefoxin*].
2 grams (base) (Rx) [*Mefoxin*].
10 grams (base) (Rx) [*Mefoxin*].
Canada—
Veterinary-labeled product(s):
Not commercially available.
Human-labeled product(s):
1 gram (base) (Rx) [*Mefoxin;* GENERIC].
2 grams (base) (Rx) [*Mefoxin;* GENERIC].
10 grams (base) (Rx) [*Mefoxin*].

Packaging and storage: Prior to reconstitution, store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

Preparation of dosage form: Dilutions should be prepared according to manufacturer's instructions.

Stability: See manufacturer's product labeling for stability information.

USP requirements: Preserve in Containers for Sterile Solids. Contains Cefoxitin Sodium equivalent to the labeled amount of cefoxitin, within –10% to +20%. Meets the requirements for Constituted solution, Bacterial endotoxins, Sterility, and Particulate matter, for Identification tests, pH, and Water under Cefoxitin Sodium, for Uniformity of dosage units, and for Labeling under Injections.{R-14}

CEFPODOXIME PROXETIL

Summary of Differences
Indications: General considerations—Third-generation cephalosporin.
Pharmacology/pharmacokinetics: Biotransformation—De-esterification to the active antibacterial, cefpodoxime.{R-110}

Oral Dosage Forms
Note: The dosing and strengths of the dosage forms available are expressed in terms of the active cefpodoxime moiety (not the proxetil ester).{R-110}

The text between [EL-US] and [EL] describes uses not included in U.S. product labeling. Text between [EL-CAN] and [EL] describes uses that are not included in Canadian product labeling.
The [EL-US] or [EL-CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CEFPODOXIME PROXETIL TABLETS USP
Usual dose: Skin and soft tissue infections—*Dogs:* Oral, 5 to 10 mg per kg of body weight a day for five to seven days or for two to three days past the end of clinical signs, up to a maximum of twenty-eight days.{R-110}

Note: [EL-US,CAN] *Foals*—Although the safety and efficacy have not been established, pharmacokinetic data suggest an oral dose of 10 mg per kg of body weight every six to twelve hours produces plasma concentrations that would be necessary to treat infections caused by bacteria with a minimum inhibitory concentration ≤ 0.2 mcg/mL for administration every twelve hours and ≤ 0.5 mcg/mL for administration every six hours.{R-112} Although adverse effects were not reported in six foals administered cefpodoxime for three days, two of six adult horses given a single dose of cefpodoxime proxetil (10 mg/kg) developed mild colic (pelvic flexure impaction) within twenty-four to forty-eight hours. It is not known if this effect was due to the medication, change to a new diet just before the study, or other factors.[EL]{R-112}

Strength(s) usually available:
U.S.:{R-110}
Veterinary-labeled product(s)—
100 mg (Rx) [*Simplicef*].
200 mg (Rx) [*Simplicef*].
Canada:
Veterinary-labeled product(s)—
Not commercially available.

Packaging and storage: Store at controlled room temperature, 20 to 25 °C (68 and 77 °F), unless otherwise specified by the manufacturer.{R-110} Keep in a tightly closed container.{R-110}

Caution: People handling this medication should be careful to avoid repeated or prolonged exposure in order to prevent the sensitization to antimicrobials that can occur in susceptible individuals.{R-110} Direct contact with the skin or mucous membranes should be avoided.{R-110} Those with a known hypersensitivity should avoid exposure to this medication.{R-110}

USP requirements: Preserve in tight containers, at room temperature. Contains an equivalent amount of the labeled amount of cefpodoxime, within ±10%. Meets the requirements for Identification, Dissolution (70% in 30 minutes in a solution [pH 3.0 ± 0.1] in Apparatus 2 at 75 rpm), Uniformity of dosage units, and Water (not more than 5%).{R-14}

CEFTAZIDIME

Summary of Differences
Indications: General considerations—Third-generation cephalosporin. Good activity against *Pseudomonas* species.

Parenteral Dosage Forms
Note: The dosing and strengths of the dosage forms available are expressed in terms of ceftazidime base (not the sodium salt).

The text between [EL-US] and [EL] describes uses not included in U.S. product labeling. Text between [EL-CAN] and [EL] describes uses that are not included in Canadian product labeling.
The [EL-US] or [EL-CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CEFTAZIDIME FOR INJECTION USP
Usual dose:
Note: [EL-US,CAN] Bacterial infections (treatment)—*Dogs:* Although the safety and efficacy have not been established, pharmacokinetic and minimum inhibitory concentration data suggest an intramuscular or intravenous dose of 30 mg per kg of body weight every six hours or a subcutaneous dose of 30 mg per kg of body weight every four to six hours should be effective in the treatment of gram-negative bacterial infections, including *Pseudomonas* species.{R-147; 160}

Some experts believe that administration every eight hours may be sufficient for some organisms, based on established pharmacokinetic/pharmacodynamic criteria.{R-162}

Data also suggest a continuous intravenous infusion of ceftazidime beginning with a loading dose of 4.4 mg per kg of body weight followed by 4.1 mg per kg of body weight an hour, administered in intravenous fluids, should also be effective.EL{R-147}

Size(s) usually available:

U.S.:

Veterinary-labeled product(s)—

Not commercially available.

Human-labeled product(s)—

500 mg (Rx) [*Ceptaz* (L-arginine; content in products containing it is 349 mg per gram); *Fortaz* (sodium carbonate; sodium content of products with sodium carbonate is 54 mg per gram); *Tazicef* (sodium carbonate); GENERIC].

1 gram (Rx) [*Ceptaz* (L-arginine); *Fortaz* (sodium carbonate); *Tazicef* (sodium carbonate); GENERIC].

2 grams (Rx) [*Ceptaz* (L-arginine); *Fortaz* (sodium carbonate); *Tazicef* (sodium carbonate); GENERIC]

6 grams (Rx) [*Fortaz* (sodium carbonate); *Tazicef* (sodium carbonate); GENERIC].

10 grams (Rx) [*Ceptaz* (L-arginine)].

Canada:

Veterinary-labeled product(s)—

Not commercially available.

Human-labeled product(s)—

1 gram (Rx) [*Fortaz;* GENERIC].

2 grams (Rx) [*Fortaz;* GENERIC].

6 grams (Rx) [*Fortaz;* GENERIC].

Packaging and storage: Prior to reconstitution, store between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer. Protect from light.

Preparation of dosage form: After reconstitution of the sodium carbonate formulation, carbon dioxide is formed, causing positive pressure inside the vial and sometimes significant "fizzing." The pressure may require venting.

To prepare solution for intramuscular use, 1.5 mL of suitable diluent (see manufacturer's package insert) should be added to each 500-mg vial, or 3 mL of diluent should be added to each 1-gram vial.

To prepare initial dilution for intravenous use, 3 or 5 mL of suitable diluent (see manufacturer's package insert) should be added to each 500-mg vial, or 10 mL of diluent should be added to each 1- or 2-gram vial, according to manufacturer's labeling instructions. For direct intermittent intravenous use, the resulting solution should be administered slowly over a 3- to 5-minute period. For intravenous infusion, the resulting solution may be further diluted in suitable fluids according to the manufacturer's labeling instructions.

Caution—Human product labeling states that use of diluents containing benzyl alcohol is not recommended for preparation of medications for use in neonates. A fatal toxic syndrome consisting of metabolic acidosis, CNS depression, respiratory problems, renal failure, hypotension, and possibly seizures and intracranial hemorrhages has been associated with this human use.

Stability: After reconstitution for intramuscular use with sterile water for injection, bacteriostatic water for injection, or lidocaine hydrochloride injection, solutions retain their potency for at least 18 hours at room temperature or for 7 days if refrigerated. Solutions that are frozen immediately after reconstitution in the original container retain their potency for at least 3 months at –20 °C (–4 °F).

After reconstitution for intravenous use, solutions retain their potency for at least 18 hours at room temperature or for 7 days if refrigerated. Solutions that are frozen immediately after reconstitution with sterile water for injection in the original container retain their potency for at least 3 months at –20 °C (–4 °F).

Once thawed, solutions should not be refrozen. Thawed solutions retain their potency for at least 8 hours at room temperature or for at least 4 days if refrigerated.

Intravenous infusions at concentrations from 1 to 40 mg per mL retain their potency for at least 18 hours at room temperature or for 7 days if refrigerated, when stored in suitable fluids (see manufacturer's package insert). However, storage in sodium bicarbonate injection is not recommended since ceftazidime is less stable in sodium bicarbonate than in other fluids.

Solutions range in color from light yellow to amber, depending on the diluent and volume. Ceftazidime powder and solutions tend to darken, depending on storage conditions. This does not affect their potency.

Incompatibilities: The admixture of ceftazidime with other medications, including pentamidine isethionate, is not recommended.

The admixture of beta-lactam antibacterials (penicillins and cephalosporins) and aminoglycosides may result in substantial mutual inactivation. If they are administered concurrently, they should be administered in separate sites. Do not mix them in the same intravenous bag or bottle.

Vancomycin is physically incompatible with ceftazidime and a precipitate may form, depending on the concentration. Therefore, the intravenous lines should be flushed between the administration of these two medications if they are to be given through the same tubing.

USP requirements: Preserve in Containers for Sterile Solids, protected from light. A sterile mixture of Sterile Ceftazidime and Sodium Carbonate or Arginine. Contains not less than 90.0% and not more than 105.0% of ceftazidime, on the dried and sodium carbonate- or arginine-free basis, and contains the labeled amount, within –10% to +20%. Meets the requirements for Identification, Bacterial endotoxins, Sterility, pH (5.0–7.5, in a solution constituted in the sealed container, taking care to relieve the pressure inside the container during constitution, containing 100 mg of ceftazidime per mL), Loss on drying (not more than 12.5%, where it contains arginine; not more than 13.5% where it contains sodium carbonate), Particulate matter, Sodium carbonate (where present), Limit of pyridine, and Content of arginine (where present), for Uniformity of dosage units, and for Labeling under Injections.{R-14}

CEFTIOFUR

Summary of Differences

Indications: General considerations—Third-generation cephalosporin.

Pharmacology/pharmacokinetics: Biotransformation—Biotransformation to an active antibacterial metabolite, desfuroylceftiofur, occurs.{R-66}

Drug interactions and/or related problems: Probenecid has not been shown to alter the excretion of ceftiofur.{R-70}

Side/adverse effects: Often-reversible anemia and thrombocytopenia can occur in animals given three to five times the recommended dose of ceftiofur.{R-66}

Parenteral Dosage Forms

Note: The dosing and strengths of the dosage forms available are expressed in terms of ceftiofur free acid (not the sodium salt).

The text between ELUS and EL describes uses not included in U.S.

product labeling. Text between [EL-CAN] and [EL] describes uses that are not included in Canadian product labeling.
The [EL-US] or [EL-CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CEFTIOFUR FOR INJECTION

Usual dose:

Escherichia coli infections—

[EL-CAN]*Chicks*[EL], day-old: Subcutaneous, 0.08 to 0.2 mg (free acid) per chick as a single dose.{R-11}
Withdrawal times—US: Not labeled for use in chicks older than one day of age.{R-11}

Turkey poults, day-old: Subcutaneous, 0.17 to 0.5 mg (free acid) per poult as a single dose.{R-11}
Withdrawal times—US and Canada: Not labeled for use in turkey poults older than one day of age.{R-11; 12}

Pneumonia—

Cattle: Intramuscular or [EL-CAN]subcutaneous[EL], 1.1 to 2.2 mg (free acid) per kg of body weight every twenty-four hours.{R-11}
Withdrawal times—US and Canada: Meat—4 days, Milk—None.{R-11; 12} Product labeling states that treatment should not exceed five days for withdrawal times to apply.

[EL-CAN]*Goats*[EL]: Intramuscular, 1.1 to 2.2 mg (free acid) per kg of body weight every twenty-four hours.{R-11}
Withdrawal times—US: Meat—0 days, Milk—None.{R-11}

Pigs: Intramuscular, 3 to 5 mg (free acid) per kg of body weight every twenty-four hours.{R-11}
Withdrawal times—US: Meat—4 days.{R-11} Canada: Meat—24 hours.{R-12} Product labeling states that treatment should not exceed three days for withdrawal times to apply.

Sheep: Intramuscular, 1.1 to 2.2 mg (free acid) per kg of body weight every twenty-four hours for three days.{R-11; 97} If a satisfactory response is not seen, the dose may be repeated on the fourth and fifth days.{R-11; 97}
Note: Canadian product labeling lists a dose of 2 mg (free acid) per kg of body weight a day for three days for use in *lambs*.{R-12}
Withdrawal times—*Sheep:* US—Meat: 0 days, Milk: None.{R-11} *Lambs:* Canada—Meat: 24 hours.{R-12}

Pododermatitis—*Cattle:* Intramuscular or [EL-CAN]subcutaneous[EL], 1.1 to 2.2 mg (free acid) per kg of body weight every twenty-four hours.{R-11}
Withdrawal times—US and Canada: Meat—4 days, Milk—None.{R-11; 12} Product labeling states that treatment should not exceed five days for withdrawal times to apply.

Respiratory tract infections—*Horses:* Intramuscular, 2.2 to 4.4 mg (free acid) per kg of body weight every twenty-four hours.{R-11; 12}
Note: [EL-US,CAN]For treatment of susceptible infections in *foals,* a dose of 2.2 to 6.6 mg (free acid) per kg of body weight every twelve to twenty-four hours has been used, based on pharmacokinetic data.[EL]{R-48}
Withdrawal times—US and Canada: Not labeled for use in horses intended for human consumption.{R-11; 12}

Urinary tract infections—*Dogs:* Subcutaneous, 2.2 mg (free acid) per kg of body weight every twenty-four hours.{R-11}
Note: [EL-US,CAN]For treatment of *bacterial infections* other than urinary tract infections in dogs, a dose of 2.2 to 4.4 mg (free acid) per kg of body weight every twenty-four hours has been used, based on pharmacokinetic data.[EL]{R-74; 76}

Note: [EL-US,CAN]Mastitis, severe coliform (treatment adjunct)—*Cows:* Although the efficacy has not been established, there is some evidence to suggest that the labeled dose of intramuscularly administered ceftiofur, 2.2 mg per kg of body weight a day for five days, may improve survival rates for cows with severe coliform mastitis by controlling bacteremia.{R-139} Other treatment may include administration of an intramammary antimicrobial, intravenous fluids, or an anti-inflammatory medication.

Extra-label withdrawal—There are insufficient data at this time for the Food Animal Residue Avoidance Databank to estimate a milk withdrawal interval when ceftiofur is administered parenterally to cows with severe mastitis.{R-143} The medication is distributed more efficiently to inflamed mammary tissue and, while milk concentrations are not considered therapeutic, there is a possibility they could exceed residue limits in some cows. Testing the milk from each cow treated, with a drug screening test sensitive to ceftiofur, is recommended to insure ceftiofur residues are avoided. If a positive test occurs, milk is discarded until the next daily test is negative; that is, until twenty-four hours after the last positive test.[EL]

[EL-US,CAN]Retained fetal membranes (treatment)—*Cows:* Although the safety and efficacy have not been established, there is some evidence to suggest that intrauterine administration of ceftiofur, 1000 mg as a single total dose, may improve survival rates for dairy cows, by decreasing the risk of being culled from the herd.[EL]{R-148}

Extra-label withdrawal—There are insufficient data at this time for the Food Animal Residue Avoidance Databank to estimate a meat or milk withdrawal interval after single-dose intrauterine administration of ceftiofur to cows with retained fetal membranes.{R-146} Because of the lack of information regarding intrauterine ceftiofur absorption in cows with retained fetal membranes, we cannot preclude the possibility of delayed absorption and prolonged residues.
Testing the milk of each treated cow with an appropriate drug screening test is recommended to insure ceftiofur residues are avoided in milk. If a positive test occurs, milk is discarded until the next daily test is negative; that is, until twenty-four hours after the last positive test.
There is no established antemortem test for residues in meat. The urine Live Animal Swab Test (LAST, MedTox Diagnostics, Inc., www.medtox.com, 800-334-1116) may be useful to screen for the possibility of antibiotic residues after an extended withdrawal.[EL]{R-163; 164}

Strength(s) usually available: When reconstituted according to manufacturer's instructions—

U.S.:{R-11}
Veterinary-labeled product(s)—
50 mg (free acid) per mL (Rx) [*Naxcel*].

Canada:{R-12}
Veterinary-labeled product(s)—
50 mg (free acid) per mL (Rx) [*Excenel*].

Packaging and storage:

Store unreconstituted product at controlled room temperature, 20 to 25 °C (68 to 77 °F),{R-11} unless otherwise specified by manufacturer.

Store reconstituted product either in a refrigerator at 2 to 8 °C (36 to 46 °F) for up to seven days or at controlled room temperature, 20 to 25 °C (68 to 77 °F), for up to twelve hours,{R-11} unless otherwise specified by manufacturer.

Protect from light.

Caution: People handling this medication should be careful to avoid repeated or prolonged exposure to avoid the sensitization to antimicrobials that can occur in susceptible individuals.{R-106} Direct contact with eyes, mouth, or skin should be avoided.{R-106} Those with a known hypersensitivity should avoid exposure to this medication.{R-106}

Preparation of dosage form: To prepare dilution for intramuscular

use, 20 or 80 mL of sterile water for injection should be added to the 1-gram or 4-gram vial, respectively.{R-11}

Stability:{R-11}
After reconstitution, solutions retain their potency for 7 days when refrigerated at 2 to 8 °C (36 to 46 °F) or 12 hours at room temperature, 15 to 30 °C (59 to 86 °F).
After reconstitution, solutions may be frozen for up to eight weeks. Frozen ceftiofur sodium may be thawed at room temperature or under warm to hot running water. Solutions should not be refrozen.
Variations in color do not affect potency.

USP requirements: Not in USP.{R-14}

CEFTIOFUR INJECTABLE OIL SUSPENSION

Usual dose: Pneumonia—
Cattle:
Beef or nonlactating dairy cattle—Subcutaneous, 6.6 mg per kg of body weight, as a single dose administered in the middle third of the posterior aspect of the ear or in the posterior aspect of the ear where it attaches to the head.{R-106; 165} Avoid all blood vessels when administering this medication.{R-106}
Lactating dairy cattle—Subcutaneous, 6.6 mg per kg of body weight, as a single dose administered in the posterior aspect of the ear where it attaches to the head (the base of the ear).{R-165}
Withdrawal times—US: Meat—13 days, Milk—None.{R-165} This product is not labeled for use in preruminating calves intended to be processed for veal.{R-106} Using a different site of administration, such as subcutaneous administration in the neck area, or administering a higher dose than recommended on product labeling, may result in violative tissue residues.{R-106}

Note: Intra-arterial injection is likely to cause *sudden death.*{R-106} Of 6000 cattle in clinical studies, 9 died acutely; 3 of these deaths were confirmed to be due to accidental intra-arterial injection.{R-106} See the manufacturer's product labeling for more information on method of injection.{R-106}

After the subcutaneous injection is complete and the needle is being withdrawn, product labeling recommends applying pressure to the needle insertion point and massaging toward the base of the ear.{R-106}

Pigs: Intramuscular, 5 mg per kg of body weight, as a single dose administered in the postauricular region of the neck.{R-107} The volume of injection at each site should not be more than two mL.{R-107}
Withdrawal times—US: Meat—14 days.{R-106} If administered as recommended on product labeling, a transient reaction at the injection site may cause some local trim loss of edible tissue.{R-107} The administration of this medication at a dose higher than recommended, by a route of administration not recommended on product labeling, or by an injection volume of more than 2 mL in one site may result in violative tissue residues.{R-106}

Strength(s) usually available: When reconstituted according to manufacturer's instructions—
U.S.:{R-106; 107}
Veterinary-labeled product(s)—
100 mg per mL (Rx) [*Excede for Swine*].
200 mg per mL (Rx) [*Excede*].
Canada:
Veterinary-labeled product(s)—
Not commercially available.

Packaging and storage: Store at controlled room temperature, 20 to 25 °C (68 and 77 °F), unless otherwise specified by manufacturer.{R-106} Protect from freezing.

Caution: People handling this medication should be careful to avoid repeated or prolonged exposure to prevent the sensitization to antimicrobials that can occur in susceptible individuals.{R-106} Direct contact with eyes, mouth, or skin should be avoided.{R-106} Those with a known hypersensitivity should avoid exposure to this medication.{R-106; 107}

Stability: Labeling on the suspension for use in cattle states that the product should be used within 30 days of removing the first dose.{R-106} Labeling on the suspension for use in pigs states that the product should be used within 12 weeks of removing the first dose.{R-107}

Auxiliary labeling:{R-106; 107}
Shake well before using.
Keep out of the reach of children and pets.

USP requirements: Not in USP.{R-14}

CEFTIOFUR INJECTABLE SUSPENSION

Usual dose:
EL,CANMetritisEL—*Cattle:* Intramuscular or subcutaneous, 2.2 mg per kg of body weight every twenty-four hours for five days.{R-81}
Pododermatitis—*Cattle:* Intramuscular or subcutaneous, 1.1 to 2.2 mg per kg of body weight every twenty-four hours.{R-81}
Pneumonia—
Cattle: Intramuscular or subcutaneous, 1.1 to 2.2 mg per kg of body weight every twenty-four hours.{R-81} Alternatively, the clinician may choose, based on the severity of disease, pathogen susceptibility, and the clinical response, to administer intramuscularly or subcutaneously, 2.2 mg per kg of body weight every forty-eight hours for two doses.{R-81}
Withdrawal times—US: Meat—3 days, Milk—None.{R-81; 99} Product labeling states that treatment should not exceed five days for withdrawal times to apply for cattle.{R-81} This product is not labeled for use in preruminating calves. Discoloration of local edible tissues may persist beyond 11 days of neck injections and beyond 28 days of intramuscular injection in the rear leg, resulting in trim loss at slaughter.{R-81} Administration by unapproved routes of administration, such as intramammary, may cause illegal residues in edible tissues or milk.{R-81; 99}
Canada—Meat: 3 days, Milk: None.{R-99} Product labeling states that treatment should not exceed five days for withdrawal times to apply for cattle.{R-99} Trim-out of edible tissue may occur within 11 days of subcutaneous administration and 28 days of intramuscular administration. Administration by unapproved routes, such as intramammary administration, may cause illegal residues in edible tissues or milk.{R-81; 99}

Pigs: Intramuscular, 3 to 5 mg per kg of body weight every twenty-four hours for three days{R-81; 96}
Withdrawal times—US: Meat—4 days.{R-81} Canada: Meat—2 days.{R-99} US and Canada: *Pigs*—Trim-out of edible tissue at slaughter may occur within 11 days of injection because of areas of discoloration associated with the injection site.{R-81; 99} Product labeling states that treatment should not exceed three days for withdrawal times to apply to pigs.{R-81; 99} Administration by unapproved routes may cause illegal residues in edible tissues or milk.{R-81; 99}

Note: Mastitis, severe coliform (treatment adjunct); or retained fetal membranes (treatment)—*Cows:* See *Ceftiofur for Injection* above in this monograph.

Strength(s) usually available:{R-81; 96; 99}
U.S.—
Veterinary-labeled product(s):
50 mg per mL (Rx) [*Excenel RTU*].
Note: Be aware that this product differs from *Excenel* available in Canada.
Canada—
Veterinary-labeled product(s):
50 mg per mL (Rx) [*Excenel RTU*].

Packaging and storage: Store at controlled room temperature, 20 to 25 °C (68 and 77 °F), unless otherwise specified by manufacturer.{R-81} Protect from freezing.

Caution: People handling this medication should be careful to avoid repeated or prolonged exposure to avoid the sensitization to antimicrobials that can occur in susceptible individuals.{R-106} Direct contact with eyes, mouth, or skin should be avoided.{R-106} Those with a known hypersensitivity should avoid exposure to this medication.{R-106}

Auxiliary labeling:
- Shake well before using.{R-35; 81} Canadian product labeling recommends shaking the bottle for a minimum of ten seconds or until contents are resuspended.{R-99}
- Keep out of reach of children.{R-81}

USP requirements: Not in USP.{R-14}

CEPHALEXIN

Summary of Differences
Indications: General considerations—First-generation cephalosporin.

Oral Dosage Forms
Note: The text between EL(US) and EL describes uses not included in U.S. product labeling. Text between EL(CAN) and EL describes uses that are not included in Canadian product labeling.

The EL(US) or EL(CAN) designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CEPHALEXIN CAPSULES USP
Usual dose:
Note: EL(US,CAN)*Birds*—Although the efficacy and safety have not been established, an oral dose of 35 to 50 mg per kg of body weight every two to six hours has been used in the treatment of susceptible *bacterial infections* in birds, based on pharmacokinetic studies.{R-34}
In general, larger birds maintain measurable serum concentrations of cephalexin longer than do smaller birds; adequate concentrations may be achieved in larger birds with a six-hour dosing interval.EL{R-34}
EL(US,CAN)*Cats and dogs*—Although the safety and efficacy have not been established, an oral dose of 15 to 30 mg per kg of body weight every six to twelve hours has been recommended in the treatment of susceptible *bacterial infections,* based on pharmacokinetic data.{R-49; 50; 129; 130} However, the lowest dose in the range, 15 mg per kg of body weight every twelve hours or 30 mg per kg of body weight a day, has only been clinically investigated for *superficial pyodermas,* with evidence of efficacy.{R-145; 161} For other infections, many clinicians consider 22 mg per kg of body weight to be the low end of the range, when administered every twelve hours. Dosing every six to eight hours is recommended for gram-negative infections while less frequent administration is considered appropriate for more susceptible organisms.EL
EL(US,CAN)*Horses*—Although the safety and efficacy have not been established, pharmacokinetic data suggest an oral dose of 30 mg per kg of body weight every eight hours produces plasma concentrations that would be necessary to treat infections caused by bacteria with a minimum inhibitory concentration $\leq$ 0.5 mcg/mL.{R-131} Investigations have only used single-dose administration, leaving the safety of multiple-dose regimens unknown.EL

Strength(s) usually available:
U.S.—{R-23}
Veterinary-labeled product(s):
Not commercially available.
Human-labeled product(s):
250 mg (Rx) [*Keflex;* GENERIC].
500 mg (Rx) [*Keflex;* GENERIC].
Canada—
Veterinary-labeled product(s):
Not commercially available.
Human-labeled product(s):
250 mg (Rx) [*Novo-Lexin*].
500 mg (Rx) [*Novo-Lexin*].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container.

USP requirements: Preserve in tight containers. Contain the equivalent of the labeled amount of anhydrous cephalexin, within –10% to +20%. Meet the requirements for Identification, Dissolution (80% in 30 minutes in water in Apparatus 1 at 100 rpm), Uniformity of dosage units, and Water (not more than 10.0%).{R-14}

CEPHALEXIN FOR ORAL SUSPENSION USP
Usual dose: See *Cephalexin Capsules USP*.

Strength(s) usually available: When reconstituted according to manufacturer's instructions—
U.S.:{R-23}
Veterinary-labeled product(s)—
Not commercially available.
Human-labeled product(s)—
25 mg per mL (Rx) [*Keflex;* GENERIC].
50 mg per mL (Rx) [*Keflex;* GENERIC].
Canada:
Veterinary-labeled product(s)—
Not commercially available.
Human-labeled product(s)—
25 mg per mL (Rx) [*Keflex; Novo-Lexin; PMS-Cephalexin*].
50 mg per mL (Rx) [*Keflex; Novo-Lexin; PMS-Cephalexin*].

Packaging and storage: Prior to reconstitution, store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container.

Stability: After reconstitution, suspensions retain their potency for 14 days if refrigerated.{R-23}

Auxiliary labeling:
- Refrigerate.

- Shake well.

USP requirements: Preserve in tight containers. A dry mixture of Cephalexin and one or more suitable buffers, colors, diluents, and flavors. Contains the equivalent of the labeled amount of anhydrous cephalexin per mL when constituted as directed in the labeling, within –10% to +20%. Meets the requirements for Identification, Uniformity of dosage units (solid packaged in single-unit containers), Deliverable volume (solid packaged in multiple-unit containers), pH (3.0–6.0, in the suspension constituted as directed in the labeling), and Water (not more than 2.0%).{R-14}

CEPHALEXIN TABLETS USP

Usual dose: See *Cephalexin Capsules USP*.

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):

250 mg (Rx) [GENERIC].

500 mg (Rx) [GENERIC].

Canada—

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):

250 mg (Rx) [*Apo-Cephalex; Keflex; Novo-Lexin; Nu-Cephalex; PMS-Cephalexin*].

500 mg (Rx) [*Apo-Cephalex; Keflex; Novo-Lexin; Nu-Cephalex; PMS-Cephalexin*].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container.

USP requirements: Preserve in tight containers. They are prepared from Cephalexin or Cephalexin Hydrochloride. The label states whether the Tablets contain Cephalexin or Cephalexin Hydrochloride. Contain the equivalent of the labeled amount of anhydrous cephalexin, within –10% to +20%. Meet the requirements for Identification, Dissolution (80% in 30 minutes in water in Apparatus 1 [use 40-mesh cloth] at 100 rpm for cephalexin and 75% in 45 minutes in water in Apparatus 1 [use 10-mesh cloth] at 150 rpm for cephalexin hydrochloride), Uniformity of dosage units, and Water (not more than 9.0% where Tablets contain cephalexin; not more than 8.0% where Tablets contain cephalexin hydrochloride).{R-14}

CEPHALEXIN HYDROCHLORIDE TABLETS USP

Usual dose: See *Cephalexin Capsules USP*.

Strength(s) usually available:

U.S.—{R-51}

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):

500 mg (Rx) [*Keftab*].

Canada—

Not commercially available.

Packaging and storage: Store between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container.

USP requirements: Preserve in tight containers. They are prepared from Cephalexin or Cephalexin Hydrochloride. The label states whether the Tablets contain Cephalexin or Cephalexin Hydrochloride. Contain the equivalent of the labeled amount of anhydrous cephalexin, within –10% to +20%. Meet the requirements for Identification, Dissolution (80% in 30 minutes in water in Apparatus 1 [use 40-mesh cloth] at 100 rpm for cephalexin and 75% in 45 minutes in water in Apparatus 1 [use 10-mesh cloth] at 150 rpm for cephalexin hydrochloride), Uniformity of dosage units, and Water (not more than 9.0% where Tablets contain cephalexin; not more than 8.0% where Tablets contain cephalexin hydrochloride).{R-14}

CEPHALOTHIN

Summary of Differences

Indications: General considerations—First-generation cephalosporin.

Drug interactions and/or related problems: Concurrent administration with probenecid may prolong the serum half-life of cephalothin.{R-30}

Medical considerations/contraindications: Severe hepatic dysfunction may inhibit metabolism.{R-2}

Side/adverse effects: Local irritation may occur.{R-1}

Parenteral Dosage Forms

Note: The dosing and strengths of the dosage forms available are expressed in terms of cephalothin base (not the sodium salt).

The text between [EL-US] and [EL] describes uses not included in U.S. product labeling. Text between [EL-CAN] and [EL] describes uses that are not included in Canadian product labeling.

The [EL-US] or [EL-CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CEPHALOTHIN FOR INJECTION USP

Usual dose:

Note: [EL-US,CAN] *Birds*—Although the efficacy and safety have not been established, an intramuscular dose of 100 mg (base) per kg of body weight every two to six hours has been used in the treatment of susceptible *bacterial infections* in birds, based on pharmacokinetic studies.{R-34}

In general, larger birds maintain measurable serum concentrations of cephalothin longer than do smaller birds; adequate concentrations may be achieved in larger birds with a six-hour dosing interval.[EL]{R-34}

[EL-US,CAN] *Dogs*—Although the efficacy and safety have not been established, an intramuscular or intravenous dose of 10 to 30 mg (base) per kg of body weight every four to eight hours has been used in the treatment of susceptible *bacterial infections* in dogs, based on pharmacokinetic data.[EL]{R-38}

[EL-US,CAN] *Horses*—Although the efficacy and safety have not been established, an intramuscular or intravenous dose of 10 to 25 mg (base) per kg of body weight every four hours has been used in the treatment of susceptible *bacterial infections* in horses, based on pharmacokinetic data.[EL]{R-9; 19}

Size(s) usually available:

U.S.—

Not commercially available.

Canada—{R-54}

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):

1 gram (base) (Rx) [*Ceporacin; Keflin*].

Packaging and storage: Prior to reconstitution, store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer.

Preparation of dosage form: Dilutions should be prepared according to the manufacturer's instructions.{R-22; 53}

Stability:{R-22}

After reconstitution, solutions retain their potency for 96 hours if refrigerated. Solutions for intramuscular use retain their potency for 12 hours at room temperature.

A precipitate may form in the solution. Upon being warmed to room temperature and shaken, the precipitate will dissolve.

Concentrated solutions will darken in color, especially at room temperature. However, slight discoloration does not affect potency.

If frozen immediately after reconstitution with sterile water for injection, 5% dextrose injection, or 0.9% sodium chloride injection, solutions retain their potency in the original container up to 12 weeks at –20 °C (–4 °F). Once thawed, solutions should not be refrozen.

Incompatibilities:

The admixture of other medications with cephalothin sodium injection is not recommended.

The admixture of beta-lactam antibiotics (penicillins and cephalosporins) and aminoglycosides may result in substantial mutual inactivation; they should not be mixed in the same intravenous bag or bottle.

USP requirements: Preserve in Containers for Sterile Solids. Contains an amount of Cephalothin Sodium equivalent to the labeled amount of cephalothin, within –10% to +15%. May contain Sodium Bicarbonate. Meets the requirements for Constituted solution, Specific rotation (+124° to +134°, calculated on the dried and sodium bicarbonate-free basis), Content of sodium bicarbonate (if present), Bacterial endotoxins, Sterility, pH (6.0–8.5, in the solution constituted as directed in the labeling), Uniformity of dosage units, and Particulate matter, for Identification test A and Loss on drying under Cephalothin Sodium, and for Labeling under Injections.{R-14}

CEPHAPIRIN

Summary of Differences

Indications: General considerations—First-generation cephalosporin.

Pharmacology/pharmacokinetics: Human biotransformation—Hepatic metabolism to the desacetyl form occurs.{R-2}

Drug interactions and/or related problems: Concurrent administration with probenicid may prolong the serum half-life of cephapirin.{R-30}

Medical considerations/contraindications: In people, severe hepatic dysfunction can inhibit metabolism.{R-2}

Side/adverse effects: Local reactions may occur.{R-1}

Parenteral Dosage Forms

Note: The dosing and strengths of the dosage forms available are expressed in terms of cephapirin base (not the sodium salt).

The text between EL[US] and EL describes uses not included in U.S. product labeling. Text between EL[CAN] and EL describes uses that are not included in Canadian product labeling.

The EL[US] or EL[CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CEPHAPIRIN FOR INJECTION USP

Usual dose:

Note: EL[US,CAN]*Dogs*—Although the efficacy and safety have not been established, an intramuscular or intravenous dose of 10 to 30 mg (base) per kg of body weight every four to eight hours has been used in the treatment of susceptible *bacterial infections* in dogs, based on pharmacokinetic data.EL{R-2; 38; 86}

EL[US,CAN]*Horses*—Although the efficacy and safety have not been established, an intramuscular or intravenous dose of 20 to 30 mg per kg of body weight every four to eight hours has been used in the treatment of susceptible *bacterial infections* in horses, based on pharmacokinetic data.EL{R-18}

Size(s) usually available:

U.S.—{R-55}

Veterinary-labeled product(s):
Not commercially available.

Human-labeled product(s):
500 mg (base) (Rx) [*Cefadyl*].
1 gram (base) (Rx) [*Cefadyl*].
2 grams (base) (Rx) [*Cefadyl*].
4 grams (base) (Rx) [*Cefadyl*].
20 grams (base) (Rx) [*Cefadyl*].

Canada—
Not commercially available.

Packaging and storage: Prior to reconstitution, store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

Preparation of dosage form: Dilutions should be prepared according to manufacturer's instructions.

Stability: See manufacturer's product labeling for stability information.

Incompatibilities: The admixture of beta-lactam antibiotics (penicillins and cephalosporins) and aminoglycosides may result in substantial mutual inactivation; they should not be mixed in the same intravenous bag or bottle.

USP requirements: Preserve in Containers for Sterile Solids. Contains an amount of Cephapirin Sodium equivalent to the labeled amount of cephapirin, within –10% to +15%. Meets the requirements for Constituted solution, Bacterial endotoxins, Sterility, and Particulate matter, for Identification, Crystallinity, pH, and Water under Cephapirin Sodium, and for Uniformity of dosage units and Labeling under Injections.{R-14}

CEPHRADINE

Summary of Differences

Indications: General considerations—First-generation cephalosporin.

Oral Dosage Forms

Note: The text between EL[US] and EL describes uses not included in U.S. product labeling. Text between EL[CAN] and EL describes uses that are not included in Canadian product labeling.

The EL[US] or EL[CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CEPHRADINE CAPSULES USP

Usual dose:

Note: EL[US,CAN]*Dogs*—Although the efficacy and safety have not been established, an oral dose of 10 to 25 mg per kg of body weight every six to twelve hours has been used in the treatment of susceptible *bacterial infections* in dogs, based on pharmacokinetic data.EL{R-2; 38}.

EL[US,CAN]*Foals*—Although the efficacy and safety have not been established, an oral dose of 25 mg per kg of body weight every six to eight hours has been used in the treatment of susceptible *bacterial infections* in foals, based

on pharmacokinetic data.[EL]{R-85}

Strength(s) usually available:
U.S.—
Veterinary-labeled product(s):
Not commercially available.
Human-labeled product(s):
250 mg (Rx) [*Velosef;* GENERIC].
500 mg (Rx) [*Velosef;* GENERIC].
Canada—
Not commercially available.

Packaging and storage: Store below 30 °C (86 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container.

USP requirements: Preserve in tight containers. The quantity of cephradine stated in the labeling is in terms of anhydrous cephradine. Contain the labeled amount of cephradine, within –10% to +20%, calculated as the sum of cephradine and cephalexin. Meet the requirements for Identification, Dissolution (75% in 45 minutes in 0.12 *N* hydrochloric acid in Apparatus 1 at 100 rpm), Uniformity of dosage units, and Loss on drying (not more than 7.0%).{R-14}

CEPHRADINE FOR ORAL SUSPENSION USP
Usual dose: See *Cephradine Capsules USP*.

Strength(s) usually available: When reconstituted according to manufacturer's instructions—
U.S.:
Veterinary-labeled product(s)—
Not commercially available.
Human-labeled product(s)—
25 mg per mL (Rx) [*Velosef;* GENERIC].
50 mg per mL (Rx) [*Velosef;* GENERIC].
Canada:
Not commercially available.

Packaging and storage: Prior to reconstitution, store below 40° C (104° F), preferably between 15 and 30° C (59 and 86° F), unless otherwise specified by manufacturer. Store in a tight container.

Stability: After reconstitution, suspensions retain their potency for 7 days at room temperature or for 14 days if refrigerated.

Auxiliary labeling:
- Refrigerate.
- Shake well.

USP requirements: Preserve in tight containers. A dry mixture of Cephradine and one or more suitable buffers, colors, diluents, and flavors. Contains the labeled amount of cephradine, within –10% to +25%, calculated as the sum of cephradine and cephalexin. Meets the requirements for Identification, Uniformity of dosage units (solid packaged in single-unit containers), Deliverable volume (solid packaged in multiple-unit containers), pH (3.5–6.0, in the suspension constituted as directed in the labeling), and Water (not more than 1.5%).{R-14}

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Interim revision: 07/08/98; 11/5/99; 09/30/02; 04/04/03

Table 1. Pharmacology/Pharmacokinetics*

Drug	Protein Binding (%)	Half-life of Elimination (hr)	Vol_D, Steady State (L/kg)	Clearance (mL/min/kg)	Route; Dose (mg/kg)	T_{max} (min)	C_{max} (mcg/mL)	Bioavailability (%)
First-Generation								
Cefadroxil								
Cats{R-3}	20				Oral; 22	60–120	17.4	
Dogs{R-3}	20				Oral; 22	60–120	18.6	
Horses								
Adult{R-78}		0.8	0.46	7	IV; 25			
Foal{R-56}		1.4			Oral; ~100	90	23.4	37–100
Foal{R-134}		1.1	0.37	5.2	IV; 5–20			
(2 weeks)					Oral; 10	126	7.0	99
(1 mo)					Oral; 5	84	3.2	68
					Oral; 10	96	5.8	68
					Oral; 20	120	12.2	71
					Oral; 40	133	19.7	66
(2 mo)					Oral; 10	96	3.7	35
(3 mo)					Oral; 10	58	3.0	19
(5 mo)					Oral; 20	54	3.6	15
Cefazolin								
Dogs{R-5}		0.8-1.2			IV; 15			
Horses{R-57}	8	0.6-0.8	0.19	5.51	IV; 11			
Pigs{R-5}		0.27			IV; 15			
Cephalexin								
Birds{R-34}					Oral; 25–50	30–60	20	
Cats{R-50}					Oral; 15	120	11–29	
{R-49}					Oral; 20	156	19	
					SQ; 20	66	54	
					IM; 20	42	61.8	
Dogs{R-2; 49}					Oral; 10–15	108	18.6	
					SQ; 10	72	24.9	
					IM; 10	54	31.9	

{R-129}		1.4	0.22	2.5	IV; 20			
					IM; 20	90	24.2	63
					Oral; 20	90	20.3	57
Horses{R-132}		1.6	0.29	4	IV; 10			
					IM; 10	60	10.1	
{R-131}		2	0.25	3.4	IV; 10			
					Oral; 30	58	3.5	5
Pigs{R-5}		1			IV; 15			
Cephalothin								
Birds{R-34}					IM; 100	30	18	
Dogs{R-5}		0.7			IV; 15			
Horses{R-19}	18	0.25	0.15	13.6	IV; 11			
					IM; 11	47	11.3	65
Cephapirin								
Calves{R-58} (3–16 wks)					IM; 10	20	6.3	
Cows{R-25}					IM; 10	10	13.3	
Dogs{R-2}		0.4						
Foals{R-59} (4–6 days)					IM; 20	10	21.2	
Horses{R-18}		0.9	0.17	10	IV; 20			
					IM; 20	25	14.8	95
Cephradine								
Dogs{R-2}		1.4						
Foals{R-85}		1.6	0.4	6.7	IV; 25			
					Oral; 25	90	13.2	
Second-Generation								
Cefaclor								
Dogs{R-5}		2			IV; 3.75			
Cefotetan								
Dogs{R-84}		1.1			IV; 30			
					SC; 30	30-60		84
Cefoxitin								
Calves{R-26}	42-55	1.1	0.32	4.9	IV; 20			
					IM; 20			74
Dogs{2; 84}		0.7; 1.3						
Horses{R-29}		0.8	0.12	4.32	IV; 20			
					IM; 20			77
Third-Generation								
Cefixime								
Calves{R-78}	90	3.5–4	0.34		Oral; 5	240	3.4	Fed; 20–28
Dogs{R-77; 87-89}	82–92	7 to 8	0.22		Oral; 5	360	2	55
					Oral; 5 (6 days)	144	4.8	
Cefotaxime								
Calves{R-137}		3.5		13.5	IV; 10			
{R-138}	26–34				IM; 10			64
Cats{R-42}		1	0.18	2.8	IV; 10			
					IM; 10	42	36	93–98
					IM; 50	24–36	47	86.5
					SQ; 50	36–60	30	100
Dogs{R-2; 43}		0.8	0.4	10.5	IV; 50			
					IM; 50	30	47	85
					SQ; 50	48	30	100
Goats{R-15}		0.4			IV			
Foals{R-136}		0.6§		5.2	IV; 40			
(1 week)								
Sheep{R-20; 60}		0.3–04	0.78	2.9	IV			
Cefpodoxime proxetil								
Dogs{R-110}		4.7	0.13	0.38	IV; 10			
					Oral; 10	133	164	63
Horses{R-112}					Oral; 10	48	1.3	
Foals{R-112} (7 days–4 mo.)					Oral; 10	102–120	0.74–0.81	
Pigs{R-113}					Oral; 10	234	23.3	
Ceftazidime								
Calves{R-157}		2.3	0.29	1.8	IV; 10			
Cows{R-158}		1.4	0.39	3.1	IV; 10			
					IM; 10	0.7	11.6	77

Cows, lactating[R-158]		1.1	0.49	1.2	IV; 10			
					IM; 10	0.7	35.7	99
Dogs[R-149; 150] [R-147]		0.86	0.21	3.2	IV; 20			
					SC; 30	60	42	
Mice[R-150]		0.17		14.2	IV; 20			
Rabbits[R-154] [R-153]		0.75			IV; 50			
	17	2.22	0.51	6.7	IV; 50			
					IM; 50	47	66.3	97
Rats[R-149] [R-155; 156]		0.2			IV; 20			
		0.3–0.7	0.22	7.1–8.7	IV; 50			
Sheep[R-159]		1.6	0.36	3.55	IV; 50			
					IM; 50	120	75.5	86
					SC; 50	120	67.8	81
Snakes (30 °C; with bacterial infection)[R-151]		24			IM; 20	60–480	26–70	
Turtles, loggerhead (at 24 °C)[R-152]		20.6	0.42	0.22	IV; 20			
					IM; 20		70	90
Ceftiofur†								
Alpacas[R-124]		5.6	0.54	1.36	IV; 1			
					IM; 1	33	2.4	
Calves[R-116]								
(7 days)		16	0.35	0.30	IV; 2.2			
					IM; 2.2	60–120	9.4	
(1 mo.)		17	0.33	0.28	IV; 2.2			
					IM; 2.2	20–120	9.3	
(3 mo.)		8	0.28	0.51	IV; 2.2			
					IM; 2.2	20–120	8.4	
(6 mo.)		6	0.26	0.66	IV; 2.2			
					IM; 2.2	40–90	8.7	
(9 mo.)		7	0.30	0.55	IV; 2.2			
					IM; 2.2	40–120	9.3	
Calves[R-61]					IM; 2.2	120	8.8	
(136–160 kg)					IM; 4.4	120	17.3	
Calves[R-115] (5 to 9 mo.)		3.2		1.8	IV; 1			
Cattle[R-117]					IM; 2.2	40–120	13.9	
					SC; 2.2	40–180	13.5	
Cows[R-70]		7.1	0.2	0.5	IV; 2			
Cows, lactating[R-71]		3.6	0.39	1.27	IV; 2			
					IM; 2	60	4.6	
Chicks,[R-127] (2 to 3 days)					SC; 1–1.3	70	0.86	
					SC; 2–2.6	50	1.67	
					SC; 4–5.3	50	2.74	
Cockatiels[R-127]					IM; 10	30	5.3	
Deer[R-126]					IM; 2.7	32	4	
Dogs[R-72]		5 to 7			SQ; 0.22	45	1.7	
					SQ; 2.2	60	8.9	
					SQ; 4.4	90	26.7	
Elephants, Asian[R-125]		3.8	0.51	1.15	IV; 1.1			
					IM; 1.1	33	1.6	19
Foals[R-48]					IM; 2.2	45	3.6	
Goats[R-122]								
Adult		4.2§	0.25	1.11	IV; 2.2			
					IM; 1.1	70	2.7	
					IM; 2.2	70	4.6	
Lactating		2.9§	0.26	1.49	IV; 1.1			
		3.9§	0.31	1.38	IV; 2.2			
Horses[R-93]		3–5[R-75]			IM; 2.2	60	4.4	
Iguanas, green[R-128]					IM; 5	20	28.6	
					SC; 5	38	18.9	
Llamas[R-123] [R-124]		2.2	0.19	0.98	IV; 2.2			
					IM; 2.2	44	5.6	
Parrots, Amazon[R-127]					IM; 10	30	11	
Pigs[R-75] [R-118]		12-13			IM; 3	35	19.2	
					IM; 3	30–240	15.8	
					IM; 5	20–120	28.3	
Sheep[R-97]		5-6			IV; 1.1–2.2			

	IM; 1.1–2.2	30	4.1–6.2
Turkey poults{R-127}	SC; 1.4–2.9	160	2.1
	SC; 2.8–5.8	24	4.4
	SC; 5.9–11.6	29	9.0
Ceftiofur crystalline free acid			
Cattle{R-106}	SC; 6.6	720	6.9
Pigs{R-107}	IM; 5	1320	4.2

*****Abbreviations: IM = Intramuscular, IV = Intravenous, SQ = Subcutaneous, Vol_D = Volume of distribution, T_{max} = Time to peak concentration, C_{max} = Peak serum concentration.

†Assays for the serum concentrations of ceftiofur listed generally include ceftiofur and either active metabolites or desfuroylceftiofur-related metabolites.

‡Data is from administration of ceftiofur sodium, which this study concluded, based on nearly equivalent results, would have comparable therapeutic efficacy to ceftiofur hydrochloride.

§Results were reported as harmonic mean.

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