# ZOETIS | AIF PRODUCT COMPARISON

## CHOOSE THE ONLY ANTI-INFECTIVES BACKED BY THE RESIDUE FREE GUARANTEE.

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>ACTIVE INGREDIENT</th>
<th>INDICATIONS</th>
<th>APPROVED DOSAGE</th>
<th>LABELED TREATMENT AND ROUTE OF ADMINISTRATION†</th>
<th>MEAT WITHDRAWAL</th>
<th>MILK DISCARD</th>
</tr>
</thead>
</table>
| EXCEDE® | Ceftiofur crystalline free acid | Treatment of acute metritis, BRD†† and foot rot, and control of BRD†† in heifers | 1.5 mL/100 lbs. (6.6 mg CE/kg) | **Acute postpartum metritis:** 2 doses, administered 72 hours apart  
**BRD and foot rot:** 1 dose only  
Route of administration: Base of opposite ears | 13 days | 0 days |
| EXCENEL® RTU EZ | Ceftiofur hydrochloride | Treatment of acute metritis, BRD†† and foot rot | Acute metritis: 2 mL/100 lbs.  
BRD and foot rot: 1-2 mL/100 lbs. | **Acute postpartum metritis:** Once daily for 5 consecutive days  
**BRD and foot rot:** 3-5 consecutive days  
Route of administration: Sub-Q or IM††† | 4 days | 0 days |
| NAXCEL® | Ceftiofur sodium | Treatment of BRD†† and foot rot | 1-2 mL/100 lbs. (0.5-1.0 mg/lb.) | Once daily for 3-5 consecutive days  
Route of administration: Sub-Q or IM††† | 4 days | 0 days |
| Polyflex® | Ampicillin | Bacterial pneumonia | 2-5 mg/lb. | Once daily for 3-7 consecutive days  
Route of administration: IM††† | 6 days | 48 hours |
| Penicillin | Penicillin G procaine | Bacterial pneumonia | 1 mL/100 lbs. (300,000 units/mL) | Once daily for up to 4 consecutive days  
Route of administration: IM††† | 10 days | 48 hours |
| Tetracycline | Oxytetracycline 200 | Pneumonia, shipping fever, foot rot, pinkeye, scours, wooden tongue, Leptospira pomona | 3-5 mL/100 lbs. (9 mg/lb.) | Once daily for up to 4 consecutive days  
Route of administration: IV†† | 28 days | 96 hours |

Choose the only anti-infectives backed by the residue free guarantee.

Pneumonia, shipping fever, foot rot, pinkeye, scours, wooden tongue, Leptospira pomona
You have our unwavering support.

Zoetis is committed to you, the health and profitability of your dairy operation, and the quality and safety of the food you produce. In fact, no other animal health company stands behind its products with this kind of promise.

**OUR GUARANTEE: NO MILK OR MEAT RESIDUES.**

You won’t have to worry about a violative residue for ceftiofur in milk or meat when you use any of these anti-infectives from Zoetis:

- EXCENEL® RTU EZ (ceftiofur hydrochloride) Sterile Suspension
- EXCEDE® (ceftiofur crystalline free acid) Sterile Suspension
- NAXCEL® (ceftiofur sodium) Sterile Powder

That’s because only Zoetis offers the Residue Free Guarantee™. When you use these products according to label indications,** you have our assurance that you will not have a violative milk or meat residue for ceftiofur. If a violative residue occurs from on-label use, Zoetis will compensate you for the beef market value of the animal, or purchase the tanker of milk. It’s that simple.

For more details on the Residue Free Guarantee, visit [www.AvoidResidues.com](http://www.AvoidResidues.com), consult your veterinarian or Zoetis representative, or call 888-ZOETIS1 (888-963-8471).

*Excludes off-label use prescribed by a veterinarian.
Important Safety Information for EXCEDE: The use of EXCEDE is contraindicated in animals with known allergy to ceftiofur or to the β-lactam group (penicillins and cephalosporins) of antimicrobials. Though safe in cattle when properly administered, inadvertent intra-arterial injection is possible and fatal. EXCEDE has a pre-slaughter withdrawal time of 13 days following the last dose in cattle. Do not use in calves to be processed for veal.

Important Safety Information for EXCENEL RTU EZ: EXCENEL RTU EZ should not be used in animals found to be hypersensitive to the product. EXCENEL RTU EZ has a pre-slaughter withdrawal period of four days following the last dose.

Important Safety Information for NAXCEL: NAXCEL should not be used in animals found to be hypersensitive to the product. NAXCEL has a pre-slaughter withdrawal time of four days.

Effective. On-label. No risk of meat or milk residues. We guarantee it.

DAIRY WELLNESS MAKES A DIFFERENCE™

*Residue Free Guarantee: If you use a Zoetis-branded ceftiofur product according to label indications, and experience a violative ceftiofur milk or meat residue, Zoetis will compensate you for the beef market value of the animal or purchase the tanker of milk at fair market value. You must purchase the product from a Zoetis-approved supplier, use the product according to label indications, have documentation of the product purchase and treatment records, and have conducted training on appropriate use to ensure proper dose and route of administration of the product. Extra-label use as prescribed by a veterinarian is excluded from the guarantee. If you experience a ceftiofur residue violation after following label indications and the above steps, contact Zoetis VMIPS (Veterinary Medical Information and Product Support) at 888-ZOETIS1 (888-963-8471) to report the situation.

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In lactating dairy cattle the injection techniques for subcutaneous (SC) injection in the base of the ear are:

- **ADMINISTRATION FOR BASE OF THE EAR**

  • Adjust the needle insertion point to avoid any blood vessels, previous implants, ear tags or ear skin exposure. Use of antibacterial drugs in the absence of a susceptible bacterial infection is unlikely to be therapeutically effective and may increase the risk of resistance development.

  • Intra-arterial injection may occur during administration of EXCEDE Sterile Suspension if the needle is inserted too far and is directed toward the base of the ear for SC injection. This may result in death and must be avoided. Additionally, intravenous injection is an unacceptable injection route.

  • Do not use needle to puncture or pierce skin.

### ADMINISTRATION FOR THE NOSE/TONSIL

- Do not inject subcutaneously. Use EXCEDE Sterile Suspension in the NOSE/TONSIL for only 14 days for 7 to 9 month old feeder calves and for 28 days for 6 to 7 month old feeder calves.

  • Injections of EXCEDE Sterile Suspension in the NOSE/TONSIL of cattle are non-therapeutic; they are given for identification purposes. EXCEDE Sterile Suspension is available in the following package sizes:

**Table 4. Ceftiofur minimum inhibitory concentration (MIC) values of indicated pathogens from 1996 to 2007.**

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Pasteurella multocida</td>
<td>0.004</td>
<td>0.002 to 0.015</td>
</tr>
<tr>
<td>Mannheimia haemolytica</td>
<td>0.002</td>
<td>0.004 to 0.015</td>
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**Figure 2. Diagram of the approximate locations of the major thirds of the ear in cattle.**

**Figure 3. Diagram showing the directions of base of the ear injection when administered normally over the base of the ear.**

**Figure 4. Diagram showing the directions of base of the ear injection when administered normally over the middle third of the ear.**

**Figure 5. Diagram showing the directions of base of the ear injection when administered normally over the middle third of the ear.**

**Figure 6. Diagram showing the directions of base of the ear injection when administered normally over the middle third of the ear.**

**Figure 7. Diagram of ear showing the directions of base of the ear injection when administered normally over the base of the ear.**

### WARNINGS

- Excessive skinfold thickness prior to injection may make injection into the base of the ear difficult or impossible by the SC administration route.

- Injection site safety for base of the ear administration was evaluated in the metritis trials. The dermatological characteristics of the ear were assessed 24 hours post-injection and were normal. The site was not scored for severity.

- Injection site safety for middle third of the ear administration was evaluated in the ketosis trials. Topical exposures to such antimicrobials, including ceftiofur, may elicit mild to severe dermatitis in sensitive animals. If contact with such drug is made, wash with soap and water. Remove contaminated clothing. If allergic reaction occurs, discontinue therapy.

- Topical dermatitis has been observed in cattle treated systemically with EXCEDE Sterile Suspension. Some practitioners have administered this medication topically, which is not a recommended route of administration.

### ADJUVANTS

- EXCEDE Sterile Suspension contains no additional adjuvants.

### ADDITIONAL INFORMATION

- Injection site safety for the middle third of the ear administration was evaluated in the metritis trials. All treatment groups were compared with a control group for treatment success, which was based on defined decreases in lesion, swelling and temperature. Following treatment, all treated animals showed a decrease in lesion size, swelling and temperature, which was confirmed and adjusted significantly (p < 0.05) in treatment groups compared to controls. Post treatment, each cow remaining in the study was examined and rectal temperature recorded. In 1996, 93.8% and 58.6% of animals, and in 2006, 94.1% and 60.7% of animals, respectively, had a normal temperature (≤ 103 °F) and did not require alternate ("escape") therapy during the 14-day post-treatment period. Treatment success was based on each cow having a normal rectal temperature (< 103 °F), and that did not require alternate ("escape") therapy during the 14-day post-treatment period. In addition, the following criteria were used: reduction in lesion size and swelling of ≥ 25%, resolution of redness and swelling, and rectal temperature < 103 °F. Treatment efficacy was determined at 14 days post-injection.

- The efficacy of ceftiofur sodium in the prevention of bovine respiratory disease (BRD) has been determined by the U.S. Department of Agriculture and supported by the National Research Council, which recommended the use of ceftiofur sodium for the prevention of BRD in feedlots. The use of ceftiofur sodium for the prevention of BRD in feedlots is supported by the results of numerous studies that have demonstrated the efficacy of ceftiofur sodium in the prevention of BRD.

### RECOMMENDATIONS

- EXCEDE Sterile Suspension should be used according to the label under the supervision of an animal health professional.

- Intra-arterial injection may occur during administration of EXCEDE Sterile Suspension if the needle is inserted too far and is directed toward the base of the ear for SC injection. This may result in death and must be avoided. Additionally, intravenous injection is an unacceptable injection route.

### CLINICAL PHARMACOLOGY

- Ceftiofur sodium is a cephalosporin antibiotic that is active against a wide range of Gram-negative and Gram-positive bacteria, including some β-lactamase-producing strains. It is metabolized rapidly to desfuroylceftiofur, the primary metabolite.

**Table 5. Microbiological activity of EXCEDE Sterile Suspension.**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>MIC (μg/mL)</th>
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<td>Pasteurella multocida</td>
<td>≤ 0.25</td>
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**Table 6. Average (± standard deviation) plasma concentration-time profiles following two subcutaneous administrations of EXCEDE Sterile Suspension in cattle.**

<table>
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<th>Parameter</th>
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<td>Cmax (μg/mL)</td>
<td>4.75 ± 1.94</td>
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### DOSAGE

- Most animals will respond to treatment within three to five days. If no improvement is observed, the diagnosis should be reevaluated.

- Injection site safety for middle third of the ear administration was evaluated in the metritis trials. All treatment groups were compared with a control group for treatment success, which was based on defined decreases in lesion, swelling and temperature. Following treatment, all treated animals showed a decrease in lesion size, swelling and temperature, which was confirmed and adjusted significantly (p < 0.05) in treatment groups compared to controls. Post treatment, each cow remaining in the study was examined and rectal temperature recorded. In 1996, 93.8% and 58.6% of animals, and in 2006, 94.1% and 60.7% of animals, respectively, had a normal temperature (≤ 103 °F) and did not require alternate ("escape") therapy during the 14-day post-treatment period. Treatment success was based on each cow having a normal rectal temperature (< 103 °F), and that did not require alternate ("escape") therapy during the 14-day post-treatment period. In addition, the following criteria were used: reduction in lesion size and swelling of ≥ 25%, resolution of redness and swelling, and rectal temperature < 103 °F. Treatment efficacy was determined at 14 days post-injection.

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Naxcel®
brand of ceftiofur sodium sterile powder

For treatment of and babesiosis in calves, and for treatment of respiratory disease associated with Pasteurella multocida, Haemophilus somnus, Streptococcus suis, and Betahemolytic streptococci.

Naxcel® is also indicated for treatment of bacterial infections due to organisms susceptible to ceftiofur, including E. coli, Pasteurella multocida, Haemophilus influenzae, Haemophilus somnus, Streptococcus suis, Actinobacillus pleuropneumoniae, and Beta-hemolytic streptococci.

Naxcel® is a sterile powder for intramuscular injection, containing 50 mg ceftiofur sodium per mL of sterile solution. It is a white to off-white powder in 4 gram vials. The reconstituted solution is a clear or slightly opalescent solution of 50 mg/mL ceftiofur sodium. The product contains hydroxide and monobasic potassium phosphate.

CONTRAINDICATIONS
- Naxcel® is contraindicated for use in horses with a known sensitivity to penicillins or cephalosporins.
- Naxcel® is not recommended for use in animals with known hypersensitivity to ceftiofur or its metabolites.

INDICATIONS
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ADMINISTRATION
- Naxcel® is administered by intramuscular injection at the dosage of 0.5 to 1.0 mg/lb of body weight (1 mL of reconstituted sterile solution per 22 to 37 lbs body weight). For intramuscular injection in swine, sheep, goats, and cattle, the recommended dosage is 0.5 to 1.0 mg/lb of body weight (1 mL of reconstituted sterile solution per 22 to 37 lbs body weight). For intramuscular injection in swine, sheep, goats, and cattle, the recommended dosage is 0.5 to 1.0 mg/lb of body weight (1 mL of reconstituted sterile solution per 22 to 37 lbs body weight).

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RECOMMENDATIONS
- Naxcel® is reconstituted with sterile water for injection to provide a final concentration of 50 mg/mL ceftiofur sodium per mL of sterile solution. The reconstituted solution is clear or slightly opalescent and should be used immediately. The solution is stable for at least 24 hours at room temperature.

ADVERSE REACTIONS
- In the 15-day tolerance study in dogs, high subcutaneous dosages (5.0 to 6.0 mg/kg of body weight) were administered at the maximum recommended level (1.0 mg/lb) for 42 consecutive days. The results indicated that Naxcel® is well tolerated in dogs at high subcutaneous dosages.

ANIMAL SAFETY
- Naxcel® is well tolerated for 15 days which is 0, 1, 3 and 5 times the highest recommended dose. The results indicated that Naxcel® is well tolerated in dogs at high subcutaneous dosages.

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EXCENEL RTU EZ Sterile Suspension is a ready to use formulation that contains the hydrochloride salt of ceftiofur, which is a broad-spectrum, semi-synthetic cephalosporin antibiotic. Ceftiofur is a member of the 3rd generation cephalosporins. The antibiotic core structure consists of 5-thia-1-azabicyclo [4,2,0] oct-2-ene (TBA) substituted with a 2-carboxy-3-dimethyl-l-valyl residue (desfuroylceftiofur). Ceftiofur is a broad-spectrum antibiotic effective against a wide range of Gram-positive and Gram-negative bacteria.

PRECAUTIONS

The effects of ceftiofur on cattle and swine reproductive performance, fertility and gestation have not been determined.

CLINICAL PHARMACOLOGY

Cattle: Administered as either oral or subcutaneous bolus injection. The parent antibiotic ceftiofur is rapidly metabolized to desfuroylceftiofur by liver microsomal cytochrome P-450 enzymes in cattle and swine. Desfuroylceftiofur is then further metabolized to inactive metabolites. The primary metabolite, desfuroylceftiofur, is excreted in the urine and feces.

Comparative Bioavailability Summary

The current EXCENEL RTU (Z) Sterile Suspension formulation was compared to the previous EXCENEL RTU Sterile Suspension formulation. The current EXCENEL RTU EZ product was demonstrated to be a reformulation of another hydrochloride salt formulation. Comparative bioavailability studies were performed under NADA 140-890. Comparative plasma concentrations of ceftiofur administered as EXCENEL RTU EZ Sterile Suspension or EXCENEL RTU Sterile Suspension were demonstrated to be bioequivalent. Analysis of plasma concentrations after intramuscular administration demonstrated mean urinary recoveries of 0.4% of the administered dose. In both studies, ceftiofur, when administered in an approved dose range of 2.27 mg CE/lb (5 mg CE/kg) BW, as either EXCENEL RTU Sterile Suspension or EXCENEL RTU EZ Sterile Suspension, was demonstrated to be bioequivalent to a corresponding IM injection of ceftiofur (1.0 mg CE/100 lbs) at the approved dose range (Table 3).

INTEGRAL RESIDUE DEPLETION

Injection site tissue tolerance and resolution were evaluated after intramuscular or subcutaneous administration of the reformulated EXCENEL RTU EZ Sterile Suspension by intramuscular and subcutaneous injections to 16 center-fed steers (both females and males, ranging in BW from 1,000 to 1,400 lbs). Each steer received 3 subcutaneous injections of 1.0 mL (1 mg CE/100 lbs) per injection site, once daily for three consecutive days. Each injection site was scored for tissue reaction on a scale of 1 to 4 for tissue reaction (redness and swelling, edema, discoloration, nodule formation) at the time of injection and 1 day after injection. The mean tissue reaction scores that included edema and swelling were 0.0 (0/4) for the first day after injection and 0.4 (1/4) for the 4th day after injection. Tissue reaction scores for the reformulated EXCENEL RTU EZ Sterile Suspension were demonstrated to be bioequivalent to the previous EXCENEL RTU Sterile Suspension when administered either IM or SC at a dose of 2.27 mg CE/lb BW (Table 5)."