



# discoveries

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- **The efficacy of Excede<sup>®</sup> for Swine (ceftiofur crystalline free acid) suggested by *in vitro* pharmacokinetic analyses has been substantiated in a challenge study and field trial.**
- **Absorption from the injection site with Excede for Swine takes at least 7 days because of the antimicrobial's unique, extended-release properties.**
- **Recent data demonstrate the swine respiratory disease pathogens targeted by Excede for Swine remain extremely sensitive to this antimicrobial.**

## Scientific foundation explains efficacy of Excede<sup>®</sup> for Swine against SRD pathogens

A robust body of research explains the efficacy of Excede<sup>®</sup> for Swine (ceftiofur crystalline free acid) against four of the bacterial pathogens associated with swine respiratory disease (SRD).

A third-generation cephalosporin, Excede for Swine is approved for treatment or control of SRD associated with *Actinobacillus pleuropneumoniae* (APP), *Streptococcus suis*, *Pasteurella multocida* and *Haemophilus parasuis*.

To be clinically effective, explains Eva Jablonski, DVM, senior technical services veterinarian, Zoetis, the levels of Excede for Swine in plasma and tissues need to stay above the minimum inhibitory concentration (MIC) of the target pathogens. MICs are the lowest concentration of a drug needed to prevent visible growth of a bacterium, and they are determined by pharmacokinetic analyses.

### Plasma levels

In one of the initial pharmacokinetic analyses Jablonski cites, investigators administered a single intramuscular (IM) dose of Excede for Swine to pigs as recommended on the label.<sup>1</sup> Next they assayed plasma samples for ceftiofur and for metabolites related to desfuroylceftiofur (DFC), which Jablonski says is the major active metabolite of ceftiofur. These assays were performed before administration of Excede for Swine and from 1 to 240 hours afterward.

Therapeutic plasma levels of ceftiofur and the DFC-related metabolites were reached within 1 hour of administration —  $2.23 \pm 1.08$  ug/ml — which was the earliest time point evaluated (Figure 1). The levels remained above established MICs for more than 7 days for the target pathogens APP, *P. multocida*, *H. parasuis* and *S. suis*.<sup>2</sup> That's substantially longer than for a full, 3-day dosing regimen for ceftiofur sodium (Naxcel<sup>®</sup>) at 3 mg/kg bodyweight, the investigators noted. "These MIC values are still relevant," Jablonski notes.<sup>3</sup>

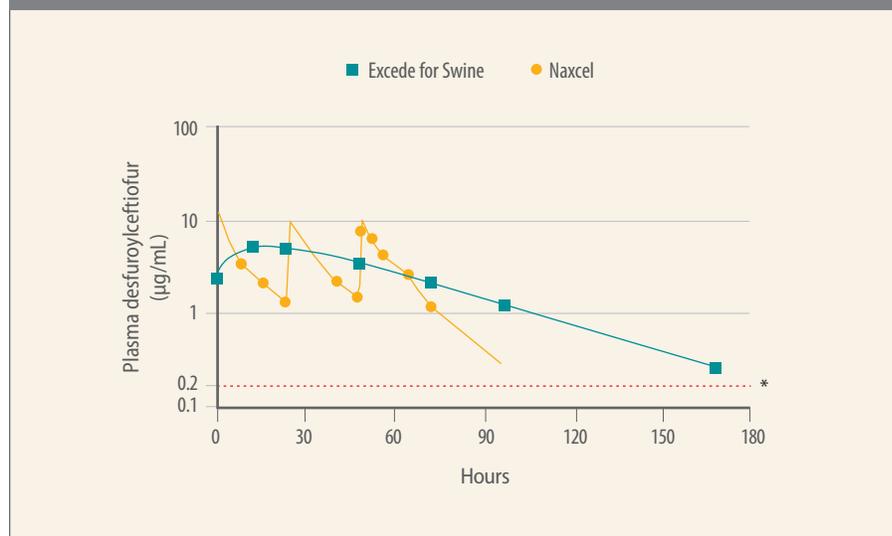
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Zoetis continues to collect hundreds of swine bacterial isolates from laboratories in the US and Canada and test them for pathogen sensitivity.

Figure 1. Plasma profile for single IM dose of 5 mg/kg bodyweight of Excede for Swine compared with three consecutive daily IM doses of 3 mg/kg bodyweight of ceftiofur sodium (Naxcel)



\* Note: 0.2 ug/mL is the concentration that is above MICs for nearly 100% of target respiratory pathogens isolated and tested over the years. \*

### Tissue concentration

An earlier, pivotal pharmacokinetic study focused on tissue levels in pigs after an IM injection of Excenel® (ceftiofur hydrochloride).<sup>4</sup> The study is relevant, Jablonski says, because Excenel, now sold as Excenel RTU EZ, has the same principal active metabolite — DFC — as Excede for Swine.

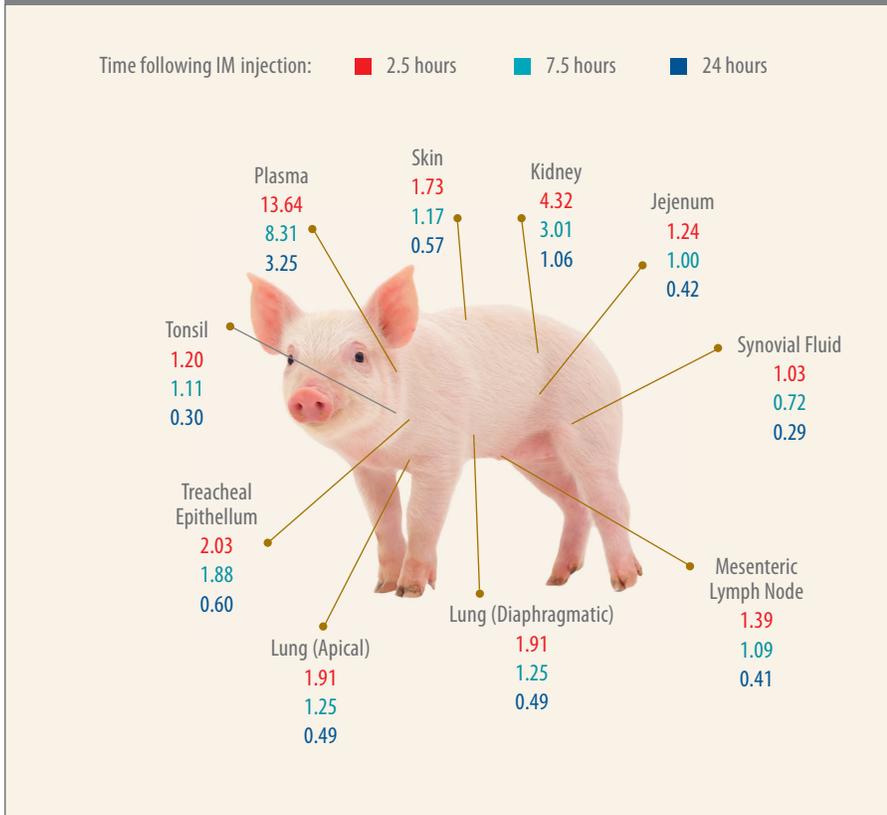
When investigators tested tissue levels for up to 24 hours after injection, the concentration of DFC was once again greater than the MICs for the pathogens tested, which in this study were APP, *P. multocida* and *S. suis* (Figure 2).

“Veterinarians often want to know about the tissue levels of an antibiotic,” Jablonski says. “*H. parasuis*, for example, is a cause of respiratory disease but can also lead to other problems like arthritis. *S. suis*, which is often secondary to viral infections such as porcine reproductive and respiratory syndrome disease, is a cause of pneumonia, but it can also cause arthritis as well as polyserositis and a host of other clinical conditions.”

### Absorption rates

The levels of Excenel or Naxcel peak and diminish from the site of injection within 24 hours. In contrast, absorption from the injection site with Excede for Swine is sustained — for at

Figure 2. Concentration of ceftiofur and desfuroylceftiofur-related metabolites (µg/mL) in selected tissues at various time points (3 mg/kg bodyweight, IM)



Since antibiotic resistance is a concern to both veterinary and human medicine, surveilling the susceptibility of pathogens to various antimicrobials is of paramount importance.

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least 7 days — because of the antimicrobial’s unique, extended-release properties, Jablonski says.

Which of the three ceftiofur products to choose depends on the pathogens involved. The indications for the three antimicrobials differ somewhat, but there is also overlap. All three, for example, are indicated for APP. A producer therefore might choose one over the other based on the required withdrawal time, which is 4 or 6 days for Excenel RTU EZ depending on the regimen used, 4 days for Naxcel and 14 days for Excede for Swine.

### Antimicrobial-susceptibility surveillance

Since antibiotic resistance is a concern to both veterinary and human medicine, surveilling the susceptibility of pathogens to various antimicrobials is of paramount importance, Jablonski continues. As part of an antibiotic-surveillance program that was initiated in 1997, Zoetis continues to collect hundreds of swine bacterial isolates from laboratories in the US and Canada and test them for pathogen sensitivity.

*continued*



...Excede for Swine demonstrated efficacy for control of *S. suis* as well as *H. parasuis* in pigs at weaning.

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“The most recent data from 2019 demonstrate that MIC values for ceftiofur against the SRD pathogens — APP, *P. multocida* and *S. suis* — remain very low. The results are consistent with those from the previous 2 decades, which tells us that these ceftiofur-targeted SRD pathogens are still extremely sensitive to this antimicrobial,”<sup>5,6</sup> Jablonski says.

Canadian researchers have had similar results, according to a study published in 2019.<sup>7</sup> For ceftiofur, enrofloxacin, florfenicol, tilmicosin and tulathromycin, they determined MIC values as well as the “mutant prevention concentration” against APP, *P. multocida* and *S. suis*.

Mutant bacterial cells are believed to arise spontaneously when there is a high density of bacteria — bacterial densities of 10<sup>7</sup> to 10<sup>9</sup> or greater colony forming units/ml. “Antibiotic drug concentration inhibiting the growth of the least susceptible [cells] in these high-density populations has been termed the mutant prevention concentration (MPC),” the investigators say.

Ceftiofur and enrofloxacin had lower MIC and MPC values than did the other drugs.<sup>8</sup> “Dosing to achieve or exceed the MPC...prevents growth of bacterial cells with reduced susceptibility,” say the investigators, and add that “optimization of therapy while minimizing the potential for antimicrobial resistance are major principles for antimicrobial stewardship.”

### Comparative APP challenge

The efficacy of Excede for Swine suggested by *in vitro* pharmacokinetic analyses has been substantiated in a challenge study and field trial. As an example, Jablonski cites a comparative study with pigs that were treated with either Excede for Swine or enrofloxacin either 3, 5 or 7 days before investigators administered a challenge with APP.<sup>9</sup>

Pigs that received Excede for Swine had significantly ( $P \leq 0.05$ ) lower mortality and total lung lesion scores compared to the enrofloxacin groups, which she says can likely be attributed to Excede for Swine’s extended duration of activity. They also had significantly less growth of *S. suis* compared to those treated with enrofloxacin.

### Multiple-site field efficacy study

The field trial with Excede for Swine involved more than 700 pigs and was conducted at multiple sites in several states.<sup>10</sup> Excede for Swine or saline was administered to mixed-sex commercial pigs. Multiple SRD pathogens were isolated from the lung tissues of pigs in the study: APP, *H. parasuis*, *P. multocida* and *S. suis*.

Figure 3. Mortality by treatment groups



Note: Percentages with different superscripts differ significantly ( $P = 0.01$ )

Pigs treated with Excede for Swine had significantly less mortality and fewer lung lesions compared to the saline control group, and there were no adverse events attributed to treatment with Excede for Swine (Figure 3).<sup>11</sup>

“Pharmacokinetic analyses, challenge studies and field trials as well as antimicrobial-sensitivity surveillance provide a solid scientific foundation for Excede for Swine,” Jablonski says. “Used wisely and judiciously, this valuable antimicrobial should continue to provide an effective treatment for SRD well into the future.”

*continued*

Pigs that received Excede for Swine had significantly ( $P \leq 0.05$ ) lower mortality and total lung lesion scores compared to the enrofloxacin groups...

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#### IMPORTANT SAFETY INFORMATION

People with known hypersensitivity to penicillin or cephalosporins should avoid exposure to EXCEDE FOR SWINE. Do not use in swine found to be hypersensitive to the product. Pre-slaughter withdrawal time is 14 days following the last dose. See Full Prescribing Information on pages 6-7.

# EXCEDE<sup>®</sup> FOR SWINE

(Ceftiofur Crystalline Free Acid)  
Sterile Suspension 100 mg/mL

For intramuscular administration in the post-auricular region of the neck of swine.

## CAUTION

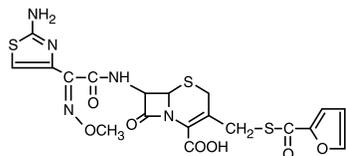
Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian. Federal Law prohibits extra-label use of this drug in swine for disease prevention purposes; at unapproved doses; frequencies, durations, or routes of administration; and in unapproved major food producing species/production classes.

## DESCRIPTION

EXCEDE FOR SWINE Sterile Suspension 100 mg/mL is a ready-to-use formulation that contains the crystalline free acid of ceftiofur, which is a broad spectrum cephalosporin antibiotic active against gram-positive and gram-negative bacteria including  $\beta$ -lactamase-producing strains. Like other cephalosporins, ceftiofur is bactericidal *in vitro*, resulting from inhibition of cell wall synthesis.

Each mL of this ready-to-use sterile suspension contains ceftiofur crystalline free acid equivalent to 100 mg ceftiofur, in a Miglyol<sup>®</sup> and cottonseed oil based suspension.

Figure 1. Structure of ceftiofur crystalline free acid:



Chemical name of ceftiofur crystalline free acid:

7-[[2-(2-Amino-4-thiazolyl)-2-(methoxyimino)acetyl]amino]-3-[[[2-(furfurylcarbonyl)thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid

## INDICATIONS

EXCEDE FOR SWINE Sterile Suspension 100 mg/mL is indicated for the treatment of swine respiratory disease (SRD) associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Haemophilus parasuis*, and *Streptococcus suis*; and for the control of SRD associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Haemophilus parasuis*, and *Streptococcus suis* in groups of pigs where SRD has been diagnosed.

## DOSAGE

Administer by intramuscular (IM) injection in the post-auricular region of the neck as a single dosage of 2.27 mg ceftiofur equivalents (CE)/lb (5.0 mg CE/kg) body weight (BW). This is equivalent to 1 mL sterile suspension per 44 lb (20 kg) BW. No more than 2 mL should be injected in a single injection site. Injection volumes in excess of 2 mL per injection site may result in violative residues. Pigs heavier than 88 lb (40 kg) will require more than one injection.

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

## ADMINISTRATION

**Shake well before using.** EXCEDE FOR SWINE Sterile Suspension 100 mg/mL is to be administered by intramuscular injection in the post-auricular region of the neck.

## CONTRAINDICATIONS

As with all drugs, the use of EXCEDE FOR SWINE Sterile Suspension 100 mg/mL is contraindicated in animals previously found to be hypersensitive to the drug.

## WARNINGS

**FOR USE IN ANIMALS ONLY.  
NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN.**

Penicillins and cephalosporins can cause allergic reactions in sensitized individuals. Topical exposures to such antimicrobials, including ceftiofur, may elicit mild to severe allergic reactions in some individuals. Repeated or prolonged exposure may lead to sensitization. Avoid direct contact of the product with the skin, eyes, mouth and clothing. Sensitization of the skin may be avoided by wearing protective gloves.

Persons with a known hypersensitivity to penicillin or cephalosporins should avoid exposure to this product.

In case of accidental eye exposure, flush with water for 15 minutes. In case of accidental skin exposure, wash with soap and water. Remove contaminated clothing. If allergic reaction occurs (e.g., skin rash, hives, difficult breathing), seek medical attention.

The material safety data sheet contains more detailed occupational safety information. To report adverse effects in users, to obtain more information or to obtain a material safety data sheet, call 1-888-963-8471.

## RESIDUE WARNINGS

- A maximum of 2 mL of formulation should be injected at each injection site. Injection volumes in excess of 2 mL per injection site may result in violative residues.
- Following label use as a single treatment, a 14-day pre-slaughter withdrawal period is required.
- **Use of dosages in excess of 5.0 mg ceftiofur equivalents (CE)/kg or administration by an unapproved route may result in illegal residues in edible tissues.**

## PRECAUTIONS

The safety of ceftiofur has not been demonstrated for pregnant swine or swine intended for breeding. Administration of EXCEDE FOR SWINE Sterile Suspension 100 mg/mL as directed may induce a transient reaction at the site of injection and underlying tissues that may result in trim loss of edible tissue at slaughter.

## ADVERSE REACTIONS

An injection site tolerance study demonstrated that EXCEDE FOR SWINE Sterile Suspension 100 mg/mL is well tolerated in pigs. Half of the injection sites at both 3 and 7 days post-injection were scored as "negative" for irritation and the other half were scored as "slight irritation". All gross observations and measurements of injection sites qualified the sites at 10 days post-injection as "negative" for irritation.

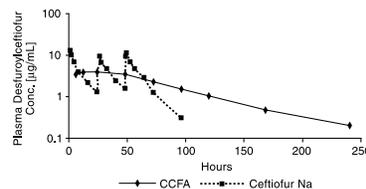
No adverse effects were observed in multi-location field efficacy studies involving more than 1000 pigs.

## CLINICAL PHARMACOLOGY

Ceftiofur administered as either ceftiofur sodium (NAXCEL<sup>®</sup> Sterile Powder), ceftiofur hydrochloride (EXCENEL<sup>®</sup> RTU Sterile Suspension) or ceftiofur crystalline free acid (EXCEDE FOR SWINE Sterile Suspension 100 mg/mL) is metabolized rapidly to desfuroylceftiofur, the primary metabolite. Administration of ceftiofur to swine as ceftiofur crystalline free acid (CCFA) at a single IM dosage of 2.27 mg CE/lb (5.0 mg CE/kg) BW provides concentrations of ceftiofur and desfuroylceftiofur-related metabolites in plasma that are multiples above the MIC<sub>90</sub>\* for the SRD label pathogens *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Haemophilus parasuis* and *Streptococcus suis* for an extended period of time (see Figure 2 and Tables 1–2).

The average plasma concentrations of ceftiofur- and desfuroylceftiofur-related metabolites for CCFA (EXCEDE FOR SWINE Sterile Suspension 100 mg/mL) after IM administration of 2.27 mg CE/lb (5.0 mg CE/kg) BW and those for ceftiofur sodium (NAXCEL Sterile Powder) after IM administration at 1.36 mg CE/lb (3 mg CE/kg) BW for three consecutive days are presented in Figure 2 below.

Figure 2. Average plasma concentrations of ceftiofur- and desfuroylceftiofur-related metabolites for CCFA (EXCEDE FOR SWINE Sterile Suspension 100 mg/mL) after IM administration of 2.27 mg CE/lb (5.0 mg CE/kg) BW and those for ceftiofur sodium (NAXCEL Sterile Powder) after IM administration at 1.36 mg CE/lb (3 mg CE/kg) BW for three consecutive days



Pharmacokinetic parameters measured after a single IM administration of 2.27 mg CE/lb (5.0 mg CE/kg) BW of EXCEDE FOR SWINE Sterile Suspension 100 mg/mL in the post-auricular region of the neck of swine are presented in the following table (Table 1).

\* Minimum inhibitory concentration for 90% of the isolates

Table 1. Pharmacokinetic parameters in swine after a single IM administration of EXCEDE FOR SWINE Sterile Suspension 100 mg/mL at 2.27 mg CE/lb (5.0 mg CE/kg) BW

Pharmacokinetic Parameter	Mean Value ± Standard Deviation (non-compartmental analyses)
C <sub>max</sub> (µg/mL)	4.17 ± 0.92
t <sub>max</sub> (h)	22.0 ± 12.2
AUC <sub>0-100</sub> (µg•h/mL)	373.0 ± 56.1
t <sub>1/2</sub> (h)	49.6 ± 11.8

C<sub>max</sub> = maximum plasma concentration (in µg CE/mL)

t<sub>max</sub> = the time after injection when C<sub>max</sub> occurs (in hours)

AUC<sub>0-100</sub> = the area under the plasma concentration vs. time curve from time of injection to the limit of quantitation of the assay (0.15 µg CE/mL)

t<sub>1/2</sub> = terminal phase biological half-life (in hours)

Table 2. Ceftiofur minimum inhibitory concentration (MIC) values\* of indicated pathogens isolated from SRD treatment and control field studies conducted in the U.S.

Indicated Pathogens	Year(s) of Isolation	Field Study	Number of Isolates	MIC <sub>50</sub> ** (µg/mL)	MIC <sub>90</sub> ** (µg/mL)	MIC Range (µg/mL)
<i>Actinobacillus pleuropneumoniae</i>	2000 to 2001	Treatment	5	NA	NA	≤0.03 to 0.06
	2009	Control	34	0.03	0.06	0.015 to 0.06
<i>Pasteurella multocida</i>	2000 to 2001	Treatment	20	≤0.03	≤0.03	≤0.03 <sup>†</sup>
	2009	Control	67	≤0.004	≤0.004	≤0.004 <sup>†</sup>
<i>Streptococcus suis</i>	2000 to 2001	Treatment	30	0.06	0.12	≤0.03 to 0.5
	2009	Control	141	0.25	1	0.03 to >2

\* The correlation between *in vitro* susceptibility data and clinical effectiveness is unknown.

\*\* The lowest MIC to encompass 50% and 90% of the most susceptible isolates, respectively.

<sup>†</sup> No range; all isolates yielded the same value.

## MICROBIOLOGY

Ceftiofur has demonstrated *in vitro* activity against *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Haemophilus parasuis*, and *Streptococcus suis*, four major pathogenic bacteria associated with SRD.

The minimum inhibitory concentrations (MICs) of ceftiofur against indicated SRD pathogens were determined using methods recommended by the Clinical and Laboratory Standards Institute (CLSI) using the M31-A and M31-A3 standards for the SRD treatment (2000-2001) and control (2009) studies, respectively. Isolates from the SRD treatment study were obtained from lung tissue collected from non-treated pigs prior to enrollment and saline-treated pigs that died or were euthanized during the study. Isolates from the SRD control study were obtained from lung tissue from non-treated pigs euthanized prior to enrollment and from saline- and ceftiofur-treated pigs that died or were euthanized during the study. The susceptibility results for the treatment and control studies are presented in Table 2.

Based on pharmacokinetic data from studies of ceftiofur in swine after a single intramuscular injection of 2.27 mg CE/lb (5.0 mg CE/kg) BW, the following interpretive criteria are recommended by CLSI:

Table 3. CLSI-accepted interpretive criteria for ceftiofur against swine respiratory disease pathogens\*

Pathogens	Disk Potency	Zone Diameter (mm)	MIC (µg/mL)	Interpretation
<i>Actinobacillus pleuropneumoniae</i>	30 µg	≥21	≤2.0	(S) Susceptible
<i>Pasteurella multocida</i>		18-20	4.0	(I) Intermediate
<i>Streptococcus suis</i>		≤17	≥8.0	(R) Resistant

\* These interpretive criteria should only be used when the CLSI M31-A3 performance standard is used to determine antimicrobial susceptibility to ceftiofur.

## EFFECTIVENESS

The effectiveness of a single dose of 2.27 or 3.18 mg CE/lb BW (5.0 or 7.0 mg CE/kg BW) EXCEDE FOR SWINE Sterile Suspension 100 mg/mL for the treatment of SRD was confirmed in a well-controlled, multi-location field study. A total of 706 pigs with clinical signs of bacterial respiratory disease were enrolled and treated with a placebo injection or EXCEDE FOR SWINE Sterile Suspension 100 mg/mL administered as a single IM injection in the post-auricular region of the neck. Clinical observations were performed on Days 1-7 and rectal temperatures were taken on Days 1, 3, and 6 following treatment (Day 0). Necropsies were performed on all pigs that died during the study and after euthanasia of all remaining study pigs at the end of the 14-day post-enrollment study period. Lung lesions were scored and lungs were submitted for bacterial identification. Mortality rates were numerically lower (but not statistically different) for the EXCEDE FOR SWINE Sterile Suspension 100 mg/mL-treated groups (4.3% for the 5.0 mg CE/kg BW group and 4.2% for the 7.0 mg CE/kg BW group) compared with the placebo-treated control group (6.3%). There was a statistically significant ( $p < 0.05$ ) improvement in clinical cure rates for the EXCEDE FOR SWINE Sterile Suspension 100 mg/mL-treated groups (24.8% for the 5.0 mg CE/kg BW group and 26.4% for the 7.0 mg CE/kg BW group) compared with the placebo-treated control group (17.7%). Lung lesion scores were numerically higher (but not statistically different) for the EXCEDE FOR SWINE Sterile Suspension 100 mg/mL-treated groups (10.4% for both the 5.0 mg CE/kg BW and the 7.0 mg CE/kg BW group) compared with the placebo-treated control group (9.2%). Bacteriological culture of the lungs of study pigs identified the following respiratory pathogens: *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Haemophilus parasuis*, and *Streptococcus suis*.

The effectiveness of a single dose of 2.27 CE/lb BW (5.0 mg CE/kg BW) EXCEDE FOR SWINE for the control of SRD was evaluated in a multi-location natural infection field study. At each site, when at least 15% of the study candidates in a pen showed clinical signs of SRD, all pigs in the pen were enrolled and treated with EXCEDE FOR SWINE ( $n = 346$ ) or saline ( $n = 347$ ). Responses to treatment were evaluated 7 days post-treatment. Success was defined as a pig that survived to Day 7 and had normal attitude, normal respiration, and a rectal temperature of  $< 104$  °F. The treatment success rate was significantly higher ( $p = 0.0188$ ) for EXCEDE FOR SWINE-treated pigs (59.6%) compared to the saline-treated pigs (41.4%). Bacteriological culture of the lungs of study pigs identified the following respiratory pathogens: *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Haemophilus parasuis*, and *Streptococcus suis*.

Table 4. Acceptable quality control ranges for ceftiofur against CLSI recommended American Type Culture Collection (ATCC) reference strains

Organism Name (ATCC No.)	MIC (µg/mL)	Zone Diameter, mm (Disk Content 30 µg)
<i>E. coli</i> ATCC 25922	0.25–1.0	26–31
<i>S. aureus</i> ATCC 29213	0.25–1.0	—
<i>S. aureus</i> ATCC 25923	—	27–31
<i>P. aeruginosa</i> ATCC 27853	16.0–64.0	14–18

## ANIMAL SAFETY

After parenteral administration, CCFa, ceftiofur sodium, and ceftiofur hydrochloride are metabolized to the same principal metabolite, desfuroylceftiofur. Plasma levels achieved are similar after recommended dosing (Figure 2). Therefore, studies conducted with ceftiofur sodium are adequate to evaluate the systemic safety of CCFa. Results from a five-day tolerance study in normal feeder pigs indicated that ceftiofur sodium produced no overt adverse signs of toxicity and was well tolerated when administered at 57 mg CE/lb (125 mg/kg) BW (more than 25 times the recommended dosage of CCFa) for five consecutive days. An additional dose toxicity study was conducted to determine the safety margin of ceftiofur in swine. Five barrows and five gilts per group were administered ceftiofur sodium IM at 0, 2.27, 6.81 and 11.36 mg CE/lb (0, 5, 15, 25 mg CE/kg) BW (0, 1, 3 and 5 times the recommended dosage for CCFa) for 15 consecutive days. There were no adverse systemic effects observed, indicating that ceftiofur sodium has a wide margin of safety when administered intramuscularly in feeder pigs.

A separate study evaluated the injection site tissue tolerance of EXCEDE FOR SWINE Sterile Suspension 100 mg/mL in swine when administered intramuscularly as a single injection at the maximum recommended dose volume of 2 mL (approximately 5 mg CE/kg BW) per injection site. Because injection site volumes greater than 2 mL may result in violative residues, only injection volumes of 2 mL were evaluated in this study. EXCEDE FOR SWINE Sterile Suspension 100 mg/mL was injected intramuscularly into each side of the neck of six swine at a dose volume of 2 mL/injection site. Clinical observations were made daily. At 3, 7 and 10 days post-injection, pairs of animals were euthanized and the neck injection sites were dissected for pathological examination (4 injection sites per time point). The injections were well tolerated in all pigs. Clinically, injection site reactions ranged from nondetectable (6 of 12 sites) to a transitory (up to 4 days post-injection) palpable, nonvisible swelling (2 of 12 sites) or a small, visible, reddened nodule at the needle insertion point (4 of 12 sites; 3 of 4 nodules were barely detectable by 3 to 7 days post-injection). There was no clinical evidence of the injections at 10 days post-injection. At necropsy, half of the injection sites at both 3 and 7 days post-injection were scored as “negative” for irritation and the other half were scored as “slight irritation”. One animal had a visible lesion described as an area of tan with red speckles present in the deep muscle fascia, less than 6 cm<sup>2</sup>, at 10 days post-injection; this lesion and the remaining injection sites evaluated at 10 days post-injection were scored as “negative” for irritation.

## STORAGE CONDITIONS

Store at controlled room temperature 20° to 25°C (68° to 77°F). Shake well before using. Contents should be used within 12 weeks after the first dose is removed.

## HOW SUPPLIED

EXCEDE FOR SWINE Sterile Suspension 100 mg/mL is available in the following package size: 100 mL vial

NADA #141-235, Approved by FDA

**zoetis**

Distributed by:  
Zoetis Inc.  
Kalamazoo, MI 49007

www.excede.com or call  
1-888-963-8471

Revised: November 2013

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- <sup>1</sup> Hibbard B, et al. Pharmacokinetics of Ceftiofur Crystalline Free Acid in Swine. Proceedings of the 18th IPVS Congress, Hamburg, Germany, 2004. Volume 2.
- <sup>2</sup> Ibid.
- <sup>3</sup> Sweeney M, et al. Antimicrobial susceptibility of *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Streptococcus suis*, and *Bordetella bronchiseptica* isolated from pigs in the United States and Canada, 2011 to 2015. J Swine Health Prod. 2017;25(3):106-120.
- <sup>4</sup> Schionning S, et al. Determination of tissue concentrations of desfuroylceftiofur in pigs after intramuscular injection of Excenel Sterile Powder. 6th EAVPT Congress. August 1994.
- <sup>5</sup> Sweeney M, et al. Antimicrobial susceptibility of *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Streptococcus suis*, and *Bordetella bronchiseptica* isolated from pigs in the United States and Canada, 2011 to 2015.
- <sup>6</sup> Leman AMR Roundtable Proceedings, Mapping a course for responsible, effective antimicrobial use in swine. 2019, pages 5, 7.
- <sup>7</sup> Blondeau J, et al. Mutant prevention and minimum inhibitory concentration drug values for enrofloxacin, ceftiofur, florfenicol, tilimicosin and tulathromycin tested against swine pathogens *Actinobacillus pleuropneumoniae*, *Pasteurella multocida* and *Streptococcus suis*. PLOS ONE. Volume 14(1); 2019.
- <sup>8</sup> Ibid.
- <sup>9</sup> Data on file, Study Report No. ORPORK 2030, Zoetis LLC.
- <sup>10</sup> Data on file, Study Report No. 1123C-60-08-315, Zoetis LLC.
- <sup>11</sup> Ibid.

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## discoveries

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