PHENIX

PhoenixPharm
Quality, range and value

KELACEF

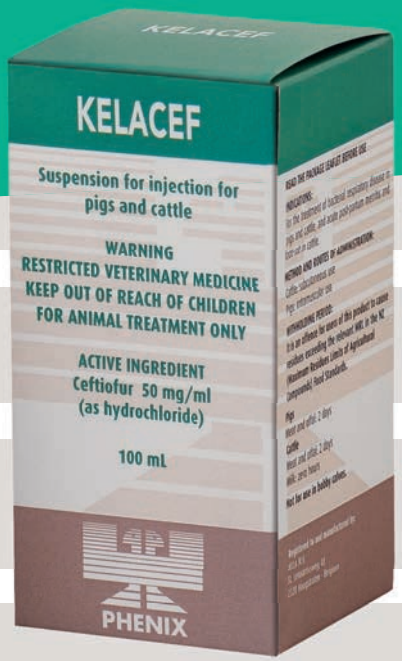
SUSPENSION FOR INJECTION FOR CATTLE AND PIGS

Ceftiofur 50 mg/mL (as hydrochloride)

RTU formulation
with excellent syringeability

Short withdrawal time for meat

No withdrawal for milk



KELACEF

KELACEF is a ready to use suspension for injection for cattle and pigs, containing 50 mg/ml ceftiofur.

Spectrum of activity

Cephalosporins are wide-spectrum antibiotics used to treat a variety of infections in animals. They have been grouped into generations based primarily on their spectrum of antibacterial activity.

Ceftiofur is classified as third-generation cephalosporin. They are the most effective of the cephalosporins against antibiotic-resistant Gram-negative bacteria. Additionally ceftiofur has an important Gram-positive activity, including good activity against Streptococci. It is active against beta-lactamase-producing strains as well as against anaerobes, such as *Fusobacterium necrophorum* and *Bacteroides melaninogenicus*. (ANONYMUS 2007)

Mechanism of action

In actively growing cells, the cephalosporins bind to the Penicillin Binding Proteins within the cell wall, leading to interference in production of cell wall peptidoglycans and subsequent lysis of the cell in an iso-osmotic environment.

Pharmacokinetics

Ceftiofur is rapidly converted in vivo to desfuroylceftiofur, which is structurally similar to and, in most instances, equally active microbiologically to ceftiofur.

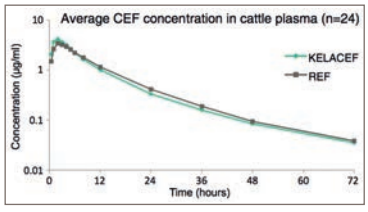
The high level of protein binding by ceftiofur in adult animals causes its distribution to differ from that of other cephalosporins. The active metabolite is also reversibly bound to plasma proteins, and due to transportation with these proteins, the metabolite concentrates at the site of infection, is active and remains active in the presence of necrotic tissue and debris.

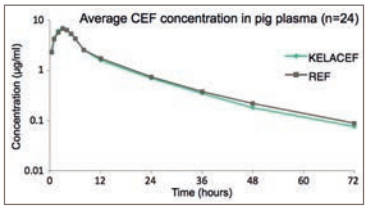
For most cephalosporins, elimination is by renal tubular secretion and/or glomerular filtration.

Following a single 1 mg/kg dose given subcutaneously to cattle, and after a single intramuscular injection of 3 mg ceftiofur per kg bw to pigs, the below mentioned pharmacokinetic parameters were calculated:

Kinetic parameter	CATTLE	PIG
$AUC_{0-\infty}$	42.30 ± 6.33 µg.hr/ml	68.71 ± 8.64 µg.hr/ml
C_{max}	4.288 ± 0.732 µg/ml	7.204 ± 0.522 µg/ml
T_{max}	2.0 ± 0.7 hr	2.0 ± 0.2 hr
T½	15.7 ± 4.2 hr	14.1 ± 2.8 hr

KELACEF proved to be bioequivalent with the reference product in both target species.





Safety

The low toxicity of ceftiofur has been demonstrated in pigs using ceftiofur sodium at doses in excess of 8 times the recommended daily dose intramuscularly administered for 15 consecutive days.
In cattle, no signs of systemic toxicity have been observed following substantial parenteral overdoses.

Mild reactions at the injection site have been observed.

Indications

Infections associated with bacteria sensitive to ceftiofur:

In cattle:

- For the treatment of bacterial respiratory disease associated with *Mannheimia haemolytica* (previously *Pasteurella haemolytica*), *Pasteurella multocida* and *Histophilus somni* (previously *Haemophilus somnus*).
- For the treatment of acute interdigital necrobacillosis (panaritium, foot rot), associated with *Fusobacterium necrophorum* and *Bacteroides melaninogenicus (Porphyromonas asaccharolytica)*.
- Treatment of the bacterial component of acute post-partum metritis within 10 days after calving associated with bacterial organisms sensitive to ceftiofur. The indication is restricted to cases where treatment with another antimicrobial has failed.

In pigs:

- For the treatment of bacterial respiratory disease associated with *Pasteurella multocida*, *Actinobacillus pleuropneumoniae* and *Streptococcus suis*.

Dosage

Cattle:

- Respiratory disease: 1 mg ceftiofur /kg bw/day for 3 days by S.C. injection, i.e. 1 ml/50 kg bw. Additional treatment on day 4 and 5 when no response after 3 days.
- Acute interdigital necrobacillosis: 1 mg/kg bw/day for 3 days by S.C. injection, i.e. 1 ml/50 kg bw.
- Acute post-partum metritis within 10 days after calving: 2.2 mg/kg bw/day for 5 days by S.C. injection, i.e. 4.4 ml/100 kg bw.

Pigs:

- 3 mg ceftiofur /kg bw/day for 3 days I.M., i.e. 1 ml/16 kg bw.

Therapeutic efficacy

Bovine respiratory disease

A clinical study evaluated the efficacy of ceftiofur HCl administered subcutaneously for the treatment of the bacterial component of BRD under natural field conditions.

60 cattle with uniform clinical signs of BRD were treated with ceftiofur HCl at 1mg ceftiofur/kg BW for 3 consecutive days or remained untreated as control.

On Day 15, all surviving animals were euthanized and necropsied and the lung lesions scored.

	Controle	CEFTIOFUR HCl	*p-value*
Mortality rate	65 %	10 %	*< 0.0001*
Rectal t° 24 h after 3rd treatment	40°C	39.5°C	*< 0.05*

Both parameters were significantly improved in the ceftiofur treated group, compared to the control group, indicating that ceftiofur is an effective treatment for the bacterial component of BRD (ANONYMUS 1992).

Acute bovine foot rot

Seven well-controlled studies conducted under multiple management conditions demonstrated the efficacy of ceftiofur for treatment of acute bovine foot rot. Ceftiofur and oxytetracycline were comparable in efficacy, with ceftiofur having excellent injection-site tolerance and short or no milk discard or pre-slaughter withdrawal. (KAUSCHE et al., 2003)

	Ceftiofur HCl 1 mg/kg SC	Oxytetracycline 10 mg/kg SC	Placebo 5 ml SC
No. of animals	14	14	13
Lesion cure rate			
Day 3 Day 7 Day 10	24% 50%* 60%*	12% 38% 60%*	13% 23% 39%
Lameness cure rate			
Day 7 Day 10	42%* 67	15% 46	0% 46

* Significantly different from placebo *(p < 0.05)*.

Acute post-partum metritis

Cows in the first 14 days postpartum with rectal T°≥39.5°C with a fetid vaginal discharge received ceftiofur HCl at a dosage of 2.2 mg/kg, SC or IM, once daily for 5 days. Cows were evaluated on days 6, 10, and 14. Clinical cure was defined as no additional antimicrobial treatment administered, rectal temperature < 39.5°C, and absence of a fetid vaginal discharge.

			Ceftiofur hydrochloride	
	Control		2.2 mg/kg	
Day	**No.**	%	**No.**	%
14	116	62	123	77*
10	121	44	123	41
6	118	23	119	26

* Significantly *(p = 0.01)* different from value for control group.

On day 14, clinical cure rate for the 2.2 mg/kg was significantly different from the control treatment. (CHENAULT et al., 2004)

Bacterial respiratory disease in pigs

In pigs with natural occurrences of bacterial pneumonia, *Pasteurella multocida*, *Actinobacillus pleuropneumoniae*, *Salmonella cholerasuis* and *streptococcus suis* type 2 were isolated. Animals were treated with 3 mg ceftiofur equivalents per kg bw for 3 days. Treatment significantly reduced mortality, lung lesion scores and improved gainers when compared with the pigs that received the placebo.

Dose mg/kg	Number of Pens[1]	Lung Lesion Score[1]	Mortality %	Gainers[3] %
0	30	2.50	7.05	79.36
3	30	1.10	1.92	86.17

1 Each pen had from 18 to 33 pigs.
2 Lesion score expressed on scale 0 = no lesion, 10 = 100%.
3 Gainers = pigs that survived for 14 days and gained > 5 pounds.

Ceftiofur proved to be an effective treatment for bacterial pneumonia of swine. (ANONYMUS 1992)

Withdrawal periods

Meat: 2 days.

Milk: no withdrawal period required when the product is used according to label directions.

Syringeability

KELACEF 50 mg/ml suspension for injection exhibits good syringeability as a result of the low viscosity and particle size of the suspended active substance.

FORMULA	Viscosity	Needling time*
KELACEF 50 mg/ml	10 mPa.sec	5 sec.

* assessed by measuring the time to fill a 10 ml syringe through a 19 Gauge needle.

References

- ANONYMUS, 1992, NADA 140-338 -supplemental approval
- ANONYMUS, 2007, The United States Pharmacopeial Convention, Cephalosporins (Veterinary-Systemic)
- CHENAULT JR et al., JAVMA, Vol 224, No. 10, May 15, 2004
- KAUSCHE FM et al.; Vet Ther. 2003 Spring;4 (1): 83-93

Advantages

- RTU formulation with excellent syringeability
- Short withdrawal time for meat
- No withdrawal time for milk
- Concentrates at site of infection
- Also active against anaerobes and β-lactamase producing bacteria

RESTRICTED VETERINARY MEDICINE
KEEP OUT OF REACH OF CHILDREN
FOR ANIMAL TREATMENT ONLY

KELACEF

Suspension for injection for pigs and cattle
Per ml

Active substance:
50 mg Ceftiofur (as hydrochloride)

White to off-white, beige suspension.

Use during pregnancy and lactation
The reproductive safety of ceftiofur has not been specifically investigated in pregnant sows or cows.
Use only according to a benefit/risk assessment by the responsible veterinarian.

Interactions
None known.

Overdose
The low toxicity of ceftiofur has been demonstrated in pigs using ceftiofur sodium at doses in excess of 8 times the recommended daily dose of ceftiofur intramuscularly administered for 15 consecutive days.
In cattle, no signs of systemic toxicity have been observed following substantial parenteral overdosages.

Incompatibilities
None known.

INDICATIONS

Infections associated with bacteria sensitive to ceftiofur:

Pigs:
For the treatment of bacterial respiratory disease associated with *Pasteurella multocida*, *Actinobacillus pleuropneumoniae* and *Streptococcus suis*.

Cattle:
For the treatment of bacterial respiratory disease associated with *Pasteurella haemolytica* (*Mannheimia spp.*), *Pasteurella multocida* and *Haemophilus somnus*.

For the treatment of acute interdigital necrobacillosis (panaritium, foot rot), associated with *Fusobacterium necrophorum* and *Bacteroides melaninogenicus* (*Porphyromonas asaccharolytica*).

For treatment of the bacterial component of acute post-partum (puerperal) metritis within 10 days after calving associated with bacterial organisms sensitive to ceftiofur.
The indication is restricted to cases where treatment with another antimicrobial has failed.

SPECIAL WARNING(S)

Use of KELACEF 50 mg/ml suspension for injection for pigs and cattle may constitute a risk to public health due to spread of antimicrobial resistance.

KELACEF 50 mg/ml suspension for injection for pigs and cattle should be reserved for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly to first line treatment. Official, national and regional antimicrobial policies should be taken into account when the product is used. Increased use, including use of the product deviating from the instructions given, may increase the prevalence of resistance. Whenever possible, KELACEF 50 mg/ml suspension for injection for pigs and cattle should only be used based on susceptibility testing.

DOSAGE FOR EACH SPECIES, ROUTES AND METHOD OF ADMINISTRATION

Intramuscular injections should be made by directing the needle of suitable gauge and length into the anterior half of the neck. Before injecting the solution, pull back gently on the plunger. If blood appears in the syringe, a blood vessel has been entered; withdraw the needle and select a different site. No more than 10mL solution should be injected per site.

Pigs:
3 mg ceftiofur /kg bw/day for 3 days via intramuscular route, i.e. 1 ml/16 kg bw at each injection. If no improvement is seen within 3-5 days, re-determine the diagnosis.

Cattle:
Respiratory disease: 1 mg ceftiofur /kg bw/day for 3 days by subcutaneous injection, i.e. 2 ml/100 kg bw at each injection. Additional treatments should be given on days 4 and 5 for cattle that do not respond after the first 3 treatments.
Acute interdigital necrobacillosis (foot rot): 1 mg/kg bw/day for 3 days by subcutaneous injection, i.e. 2 ml/100 kg bw at each injection.
Acute post-partum metritis within 10 days after calving: 2.2 mg/kg bw/day at 24 hour intervals for 5 consecutive days by subcutaneous injection, i.e. 4.4 ml/100 kg bw at each injection.

Subsequent injections must be given at different sites.
In case of acute post-partum metritis, additional supportive therapy might be required in some cases.

WITHHOLDING PERIOD

It is an offence for users of this product to cause residues exceeding the relevant MRL in the NZ (Maximum Residues Limits of Agricultural Compounds) Food Standards.

Meat: Cattle and pigs producing meat or offal for human consumption must not be sold for slaughter either during treatment or within 2 days of cessation of the last treatment.

Milk: No milk withholding period is required when the product is used according to label directions. Use of doses in excess of those recommended on the label may result in illegal drug residues in edible tissues.

Not for use in bobby calves.

ADVERSE REACTIONS

Hypersensitivity reactions unrelated to dose can occur. Allergic reactions (e.g. skin reactions, anaphylaxia) may occasionally occur.
Pigs: Mild reactions at the injection site, such as discoloration of the fascia or fat, have been observed in some animals for up to 20 days after injection.
Cattle: Mild inflammatory reactions at the injection site, such as tissue edema and discoloration of the subcutaneous tissue and/or fascial surface of the muscle may be observed. Clinical resolution is reached in most animals by 10 days after injection although slight tissue discoloration may persist for 28 days or more.

CONTRAINDICATIONS

Do not administer to an animal previously found to be hypersensitive to ceftiofur and other ß -lactam antibiotics. Do not inject intravenously.
Do not use in poultry (including eggs) due to risk of spread of antimicrobial resistance to humans.

SPECIAL PRECAUTIONS FOR USE IN ANIMALS

Shake the bottle well before use to bring the product back into suspension.
In case of the occurrence of allergic reaction the treatment should be withdrawn.
Do not use as prophylaxis in case of retained placenta.

SPECIAL PRECAUTIONS TO BE TAKEN BY THE PERSON ADMINISTERING THE PRODUCT

Penicillins and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillins may lead to cross reactions to cephalosporins and vice versa. Allergic reactions to these substances may occasionally be serious. Do not handle this product if you know you are sensitized, or if you have been advised not to work with such preparations. If you develop symptoms following exposure such as a skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.

SPECIAL STORAGE PRECAUTIONS

Keep out of the reach and sight of children.
Do not refrigerate or freeze.
Protect from light.
Store below 25°C.
Do not use after the expiry date stated on the label.
Shelf-life after first opening the container: 28 days.
When the container is broached (opened) for the first time, using the in-use shelf-life which is specified on this package insert, the date on which any product remaining in the container should be discarded should be worked out. This discard date should be written in the space provided on the label.

To be supplied only on veterinary prescription

REGISTRANT/NEW ZEALAND AGENT

Registered to KELA N.V., St. Lenaartseweg 48, 2320 Hoogstraten, Belgium, info@kela.be, + 32 3 340 04 11, manufactured in Belgium
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