ANTIBIOTICS

Cefokel 50 mg/ml

Suspension for injection for pigs and cattle

COMPOSITION:

Ceftiofur (as hydrochloride) 50 mg – excipients up to 1 ml.

PHARMACOLOGICAL PROPERTIES:

Ceftiofur is a third generation of cephalosporin, which is active against many Gram-positive and Gram-negative bacteria, including β-lactamase producing strains (except strains producing some type of extended spectrum betalactamases).
Ceftiofur inhibits the bacterial cell wall synthesis, thereby exerting bactericidal properties. Cell wall synthesis is dependent on enzymes that are called penicillin-binding proteins (PBP's). Bacteria develop resistance to cephalosporins by four basic mechanisms:

1. altering or acquiring penicillin binding proteins insensitive to an otherwise effective β-lactam;
2. altering the permeability of the cell to β-lactams;
3. producing β-lactamases that cleave the β-lactam ring of the molecule, or
4. active efflux.

Some β-lactamases, documented in Gram-negative enteric organisms, may confer elevated MICs to varying degrees to third and fourth generation cephalosporins, as well as penicillins, ampicillins, β -lactam inhibitor combinations, and first and second generation cephalosporins.Ceftiofur is active against the following microorganisms which are involved in respiratory diseases in pigs: *Pasteurella multocida*, *Actinobacillus pleuropneumoniae* and *Streptococcus suis*. *Bordetella bronchiseptica* is intrinsically non-susceptible to ceftiofur.
It is also active against bacteria involved in respiratory disease in cattle: *Pasteurella Multocida*, *Mannheimia haemolytica* (former *Pasteurella haemolytica*), *Histophilus somni* (former *Haemophilus somnus*); bacteria involved in acute bovine foot rot (interdigital necrobacillosis) in cattle: *Fusobacterium necrophorum*, *Bacteroides melaninogenicus* (*Porphyromonas asaccharolytica*); and bacteria associated with acute post-partum (puerperal) metritis in cattle: *Escherichia coli*, *Arcanobacterium pyogenes* and *Fusobacterium necrophorum*.
After administration, ceftiofur is quickly metabolised to desfuroylceftiofur, the principal active metabolite. Desfuroylceftiofur has an equivalent anti-microbial activity to ceftiofur against the bacteria involved in respiratory disease in animals. The active metabolite is reversibly bound to plasma proteins. Due to transportation with these proteins, the metabolite concentrates at a site of infection, is active and remains active in the presence of necrotic tissue and debris.
The elimination occurred mainly via the urine (more than 70 %).
Average recoveries in faeces accounted for approximately 12-15 % of the drug.
Ceftiofur is completely bioavailable following intramuscular and subcutaneous administration.

TARGET SPECIES:
Cattle and pigs.

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*).

For treatment of the bacterial component of acute post-partum (puerperal) metritis within 10 days after calving associated with *Escherichia col*i, *Arcanobacterium pyogenes* and *Fusobacterium necrophorum*, 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*.

CONTRA-INDICATIONS:
Do not administer to an animal previously found to be hypersensitive to ceftiofur and other β-lactam antibiotics.
Do not inject intravenously.
Do not use in cases where resistance to other cephalosporins or beta-lactam antibiotics has occurred.
Do not use in poultry (including eggs) due to risk of spread of antimicrobial resistance to humans.

DOSAGE AND MODE OF ADMINISTRATION:
Cattle:
Respiratory disease: 1 mg ceftiofur /kg b.w./day for 3 to 5 days by subcutaneous injection, i.e. 1 ml/50 kg b.w. at each injection.
Acute interdigital necrobacillosis: 1 mg/kg b.w./day for 3 days by subcutaneous injection, i.e. 1 ml/50 kg b.w. at each injection.
Acute post-partum metritis within 10 days after calving: 1 mg/kg b.w./day for 5 consecutive days by subcutaneous injection, i.e. 1 ml/50 kg b.w. at each injection.

Before use, shake the bottle vigorously for at least 30 seconds until the product appears adequately resuspended. Following shaking the bottle should be visually examined to ensure that the product is brought back into suspension. The absence of settled material can be confirmed by inverting the vial and viewing the contents through the base of the vial.

The recommended maximum volume to be administered at a single injection site is 4 ml in pigs and 6 ml in cattle. Subsequent injections must be given at different sites. The vial cannot be broached more than 66 times.

In case of acute post-partum metritis, additional supportive therapy might be required in some cases.

Pigs:
3 mg ceftiofur /kg b.w./day for 3 days via intramuscular route, i.e. 1 ml/16 kg b.w. at each injection.

UNDESIRABLE EFFECTS:

Hypersensitivity reactions unrelated to dose can occur. Allergic reactions (e.g. skin reactions, anaphylaxia) may occasionally occur. In case of the occurrence of allergic reaction the treatment should be withdrawn.
In 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.
In cattle, mild inflammatory reactions at the injection site, such as tissue oedema 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.

SPECIAL PRECAUTIONS AND WARNINGS:

The product selects for resistant strains such as bacteria carrying extended spectrum betalactamases (ESBL) and may constitute a risk to human health if these strains disseminate to humans e.g. via food. For this reason, the product should be reserved for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly (refers to very acute cases when treatment must be initiated without bacteriological diagnosis) to first line treatment. Official, national and regional anti-microbial policies should be taken into account when the product is used. Increased use, including use of the product deviating from the instructions given in the SPC, may increase the prevalence of such resistance.
Whenever possible, the product should only be used based on susceptibility testing.
The product is intended for treatment of individual animals. Do not use for disease prevention or as a part of herd health programmes. Treatment of groups of animals should be strictly restricted to ongoing disease outbreaks according to the approved conditions of use.

Do not use as prophylaxis in case of retained placenta.
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 sensitised, or if you have been advised not to work with such preparations.
Handle this product with great care to avoid exposure. Wash hands after use.
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.

PACK SIZE:
Glass vials of 100 ml.