CEPTIFUR AP 5% (w/v) SUSPENSION FOR INJECTION

For Animal Use Only

Name and Strength of Active Substance(s):
Ceftiofur – 50mg/ml

Product Description:
Ceptifur AP 5% (w/v) Suspension is a ready to use formulation that contains the hydrochloride salt of ceftiofur, which is a broad spectrum cephalosporinantibiotic. It is pale cream colored to cream colored.

Pharmacodynamics:

- Ceftiofur is a third generation cephalosporin, which is active against Gram-positive and Gram-negative bacteria. Like all beta-lactam antibiotics, ceftiofur inhibits bacterial cell wall synthesis, thereby exerting bactericidal properties.
- Cell wall synthesis is dependent on enzymes that are penicillin-binding proteins (PBPs). Bacteria may develop resistance to cephalosporins by 1) having penicillin binding proteins insensitive to an otherwise effective β-lactam; 2) altering cell membrane permeability to β-lactamses that cleave the β-lactam ring of the antibiotic, or 4) active efflux.
- Some β-lactamses, documented in Gram-negative enteric organisms, may lead to varying degrees of cross resistance between cephalosporins, as well as penicillins, ampicicillins and β-lactam inhibitor combinations.
- Ceftiofur is active against the following microorganisms which are involved in respiratory diseases in pigs: *Pasteurella multocida, Actinobacillus pleuroneumoniae and Streptococcus suis. Bordetella bronchiseptica* is intrinsically non-susceptible to ceftiofur.
- It is also against involved in respiratory disease in cattle: *Pasteurella multocida, Mannheimia haemolytica, Histophilus somni*; bacteria involved in acute bovine foot rot (interdigital necrobacillosis): Fusobacterium necrophorum, Bacteroides melaninogenicus (Porphyromonas asacharolytica); and bacteria associated with acute post-partum (puerperal) metritis in cattle: Escherichia coli, Arcanobacterium pyogenes and Fusobacterium necrophorum.

Pharmacokinetics:

- 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. It is reversibly bound to plasma proteins and as a result, the metabolite concentrates at sites of infection. It remains active in the presence of necrotic tissue and debris.
- Elimination occurs mainly via the urine (more than 70%); 12-15 % is eliminated via faeces.
- Ceftiofur is completely bioavailable following subcutaneous administration or intramuscular administration.

Indications:
<u>In pigs:</u>
For the treatment of bacterial respiratory disease associated with *Pasteurella multocida*, *Actinobacillus pleuropneumoniae* and *Streptococcus suis*.

<u>In cattle:</u>

- For the treatment of bacterial respiratory disease associated with *Pasteurella haemolytica*, *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 metritis within 10 days after calving associated with *Escherichia coli*, *Arcanobacterium pyogenes* and *Fusobacterium necrophorum*, sensitive to ceftiofur, were treatment with another antimicrobial has failed.

Recommended Dosage:
<u>Pigs:</u>
3 mg ceftiofur /kg bw/day for 3 days via intramuscular route, i.e. 1 ml/16 kg bw at each injection. Not more than 4ml should be administered per injection site.

Cattle:
Not more than 13 ml should be administered per injection site.
+*Respiratory disease*: 1 mg ceftiofur /kg bw/day for 3 to 5 days by subcutaneous injection, i.e. 1 ml/50 kg bw at each injection.
+*Acute interdigital necrobacillosis:* 1 mg/kg bw/day for 3 days by subcutaneous injection, i.e. 1 ml/50 kg bw at each injection.
+*Acute post-partum metritis within 10 days after calving*: 1 mg/kg bw/day for 5 consecutive days by subcutaneous injection, i.e. 1 ml/50 kg bw at each injection.

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

Mode of Administration:
Shake well before injection. For intramuscular use in swine and subcutaneous use in cattle. Once daily.

Contraindication:
- 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 β–lactam antibiotics has occurred.
- Do not use in poultry (including eggs) due to risk of spread of antimicrobial resistance to humans.

Warning and Precautions:
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.
- Ceftiofur 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, ceftiofur 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 antimicrobial policies should be taken into account when the product is used. Increased use may increase the prevalence of such resistance. Whenever possible, ceftiofur should only be based on susceptibility testing.
- Ceftiofur is intended for treatment of individual animals. Do not use for disease prevention or as a part of heard 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.
- TO BE PRESCRIBED AND TREATED WITH BY REGISTERED VETERINARY SURGEONS ONLY

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
- 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.
- 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.
- Wash hands after use.

Interaction with Other Medicinal Product:
The bactericidal properties of β–lactams are neutralised by simultaneous use of bacteriostatic antibiotics (macrolides, sulphonamides and tetracyclines).

Pregnancy and Lactation:
Studies in laboratory species have not produced any evidence of teratogenic, foetus toxic or maternal toxic effects. The safety of the veterinary medicinal product has not been established during pregnancy. Use only according to the benefit/risk assessment by the responsible veterinarian.

Adverse Effects and Toxicity:

- In pigs, mild reactions at the injection site, such as discoloration of the fascia or fat, have been observed in very rare cases for up to 20 days after injection.
- In cattle, firmness and swelling were observed at the injection site after SC injection of the test article. Mild to moderate local chronic inflammation was observed in most animals until 42 days post injection. Injection site reactions have been reported from the field in very rare cases.

Overdose and Treatment:
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 over dosages.

Withdrawal Period:
Pigs: meat and offal: 2 days.
Cattle: meat and offal: 6 days; milk: 0 hours.

Incompatibilities:
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

Storage Condition:
Store in a dry cool place at temperature below 25°C (air conditioning), keep away from direct sunlight. Keep out of reach of children.

Proposed shelf life (first opening of container):
28 days

Dosage Form:
Suspension

Packaging Available:
100ml

Date of Revision of Package Insert: 28th August 2017

Name & Address of Manufacturer:
Anova Pharma Joint Stock Company
Anova Corporation Industrial Zone, Long Cang Commune, Can Duoc District, Long An Province, VietNam

Marketing Authorisation Holder:
Sunzen Corporation Sdn Bhd (470468-W)
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