SEFTIONEL 50MG/ML INJECTION

Description and Composition

SEFTIONEL 50MG/ML INJECTION is an off-white to yellow oily suspension. Each ml contains 50mg of Ceftiofur (as hydrochloride) as its active ingredient and 1mg Chlorocresol as preservative.

Pharmacodynamics

Ceftiofur is a late generation cephalosporin, which is active against many Gram-positive and Gram-negative bacteria. Ceftiofur inhibits the bacterial cell wall synthesis, thereby exerting bactericidal properties. Beta-lactams act by interfering with synthesis of the bacterial cell wall. 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 b -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 micro-organisms 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.*

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. 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.

In pigs given a single intramuscular dose of 3 mg/kg body weight (bw), maximum plasma concentrations of 11.8 ± 1.67 µg/mL were reached after 1 hour; the terminal elimination half-life (t½) of desfuroylceftiofur was 16.7 ± 2.3 hours. No accumulation of desfuroylceftiofur has been observed after a dose of 3 mg ceftiofur/kg bw/day administered daily over 3 days. 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 administration.

After a single 1 mg/kg dose given subcutaneously to cattle, maximum plasma levels of 2.85 ± 1.11 µg/mL are reached within 2 hours after administration. In healthy cows, a Cmax of 2.25 ± 0.79 µg/mL was reached in the endometrium 5 ± 2 hours after a single administration. Maximum concentrations reached in caruncles and lochiae of healthy cows were 1.11 ± 0.24 µg/mL and 0.98 ± 0.25 µg/mL, respectively.

The terminal elimination half-life (t½) of desfuroylceftiofur in cattle is 11.5 ± 2.57 hours. No accumulation was observed after a daily treatment over 5 days. The elimination occurred mainly via the urine (more than 55 %); 31 % of the dose was recovered in the faeces. Ceftiofur is completely bioavailable following subcutaneous administration.

Indication

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 *Mannheimia haemolytica* (former *Pasteurella haemolytica*), *Pasteurella multocida* and *Histophilus somni* (former *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 coli*, *Arcanobacterium pyogenes* and *Fusobacterium necrophorum*, sensitive to ceftiofur, where treatment with another antimicrobial has failed.

Recommended Dose
Pigs:
3mg ceftiofur per kg body weight per day for 3 days via intramuscular route, i.e. 1ml per 16kg body weight at each injection. Not more than 4ml should be administered per injection site.
Cattle:
Respiratory disease:
1mg ceftiofur per kg body weight per day for 3 to 5 days by subcutaneous injection, i.e. 1ml per 50kg body weight at each injection.
Acute interdigital necrobacillosis:
1mg per kg body weight per day for 3 days by subcutaneous injection, i.e. 1ml per 50kg body weight at each injection.
Acute post-partum metritis within 10 days after calving:
1mg per kg body weight per day for 5 consecutive days by subcutaneous injection, i.e. 1ml per 50kg body weight at each injection. Not more than 13ml should be administered per injection site.

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

Route of Administration
To be given by intramuscular injection to pigs and subcutaneous injection to cattle.

Contraindications
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.

Warning and Precautions
Special warnings for each target species:
None known.
Special precautions for use:
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.
The active ingredient Ceftiofur hydrochloride selects for resistant strains such as bacteria carrying extended spectrum betalactamases (ESBL) which may constitute a risk to human health if these strains disseminate to humans e.g. via food. For this reason, it 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 more narrow spectrum antimicrobials 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 such resistance bacteria resistant to Ceftiofur hydrochloride. Whenever possible, it should only be used based on susceptibility testing. Do not use as prophylaxis in case of retained placenta. Ceftiofur hydrochloride 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 limited to ongoing disease outbreaks according to the approved conditions of use.

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 beta-lactams are neutralised by simultaneous use of bacteriostatic antibiotics (macrolides, sulphonamides and tetracyclines). Aminoglycosides may have a potentiating effect on cephalosporins.

Pregnancy and Lactation
Even though studies in laboratory animals show no evidence of teratogenesis, abortion or influence on reproduction, 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.

Side Effects
Hypersensitivity reactions unrelated to dose can occur. Allergic reactions (e.g. skin reactions, anaphylaxia) have been reported in very rare cases (less than 1 animal in 10,000 animals, including isolated reports).
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.

Symptoms and Treatment of 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.

Storage Condition
Store below 30ºC.

Shelf life
3 years. Following withdrawal of the first dose, use the product within 24 hours. Any unused material should be discarded.

Withdrawal Periods
Pigs: Meat and offal: 2 days
Cattle: Meat and offal: 6 days Milk: Zero hours

Packing
20ml, 50ml, 100ml.

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	Manufacturer & Product Registration Holder
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