Ceftiofur sodium for Injection 1 g pack – Vial label

DIN 02412284

Pr

Ceftiofur sodium for Injection
Ceftiofur for Injection (as Ceftiofur Sodium Trihydrate)/Ceftiofur pour Injection (sous forme de trihydrate de ceftiofur sodique)

Veterinary Use Only/ Usage vétérinaire seulement

Sterile/Stérile

Broad-spectrum antibiotic/ Antibiotique à large spectre

For cattle, lactating dairy cattle, horses, swine, lambs and dogs.

Pour bovins, vaches laitières en lactation, chevaux, porcs, agneaux et chiens.

Active Ingredient: Ceftiofur (as ceftiofur sodium), 50 mg per mL of reconstituted solution.

Warnings: See package insert for complete warnings.

Storage: Store unreconstituted product at a temperature between 15° and 25°C. Protect from light.

See package insert for complete product information.

Ingrédient actif : 50 mg de ceftiofur (sous forme de ceftiofur sodique) par mL de solution reconstituée.
Mises en garde: Voir le dépliant pour les mises en garde complètes.

Entreposage : Entreposer le produit non-reconstitué entre 15 et 25°C. Protéger de la lumière.

Voir le dépliant pour les informations complètes du produit.

Net : 1g

Bio Agri Mix LP

P.O. Box 399, Mitchell, ON. N0K 1N0

Lot No. :

Exp. :

Version: BAM Nov-03-17

Ceftiofur sodium for Injection 4 g pack – Vial label

DIN 02412284

Pr

Ceftiofur sodium for Injection

Ceftiofur sodium trihydrate sterile powder for injection/ poudre stérile de trihydrate de ceftiofur sodique pour injection

Veterinary Use Only/ Usage vétérinaire seulement

Sterile/Stérile

Broad-spectrum antibiotic/ Antibiotique à large spectre

For cattle, lactating dairy cattle, horses, swine, lambs and dogs.

Pour bovins, vaches laitières en lactation, chevaux, porcs, agneaux et chiens.

Active Ingredient: Ceftiofur (as ceftiofur sodium), 50 mg per mL of reconstituted solution.

Warnings: See package insert for complete warnings.

Storage: Store unreconstituted product at a temperature between 15° and 25°C. Protect from light.

See package insert for complete product information.

Ingrédient actif : 50 mg de ceftiofur (sous forme de ceftiofur sodique) par mL de solution reconstituée.

Mises en garde: Voir le dépliant pour les mises en garde complètes.

Entreposage : Entreposer le produit non-reconstitué entre 15 et 25°C. Protéger de la lumière.

Voir le dépliant pour les informations complètes du produit.

Net : 4g

Bio Agri Mix LP

P.O. Box 399, Mitchell, ON. N0K 1N0

Lot No. :

Exp. :

Version: Nov-03-17

Ceftiofur sodium for Injection 1 g pack – Carton-Lid

Ceftiofur sodium for Injection

Ceftiofur for Injection (as Ceftiofur Sodium Trihydrate)/ Ceftiofur pour Injection (sous forme de trihydrate de ceftiofur sodique)

Lot.:

Exp.:

Ceftiofur sodium for Injection 4 g pack – Carton-Lid

Ceftiofur sodium for Injection

Ceftiofur for Injection (as Ceftiofur Sodium Trihydrate)/ Ceftiofur pour Injection (sous forme trihydrate de ceftiofur sodique)

Lot.:

Exp.:

Ceftiofur sodium for Injection 1 g pack – Carton-Front Panel-English

DIN 02412284

Pr

Ceftiofur sodium for Injection

Ceftiofur for Injection (as Ceftiofur Sodium Trihydrate)

Veterinary Use Only

Sterile

Broad-spectrum antibiotic

For cattle, lactating dairy cattle, horses, swine, lambs and dogs.

WARNINGS

Treated swine and lambs must not be slaughtered for use in food for at least 24 hours after the latest treatment with this drug.

No meat withdrawal period or milk withholding time is required for cattle when the drug is used according to the label directions and dosage.

Do not use in calves to be processed for veal

This drug is not to be administered to horses that are to be slaughtered for use in food.

Antimicrobial drugs, including penicillins and cephalosporins can cause allergic reactions in sensitized individuals. (To minimize the possibility of such a reaction, users of such antimicrobial products, including ceftiofur, are advised to avoid direct contact of the product with the skin and mucous membranes).

To limit the development of antimicrobial resistance:

- **Ceftiofur sodium for Injection** should not be used as a mass medication for cattle, swine or any other species **Ceftiofur sodium for Injection** should only be used to treat individual animals as per the indications.
- The choice of **Ceftiofur sodium for Injection** as the most appropriate treatment should be confirmed by clinical experience supported where possible by pathogen culture and drug susceptibility testing.
- The extra-label drug use of **Ceftiofur sodium for Injection** is not recommended.

KEEP OUT OF REACH OF CHILDREN

Net 1 g

Ceftiofur sodium for Injection 1 g pack – Carton-Side Panel-English

This package contains:

1 g Ceftiofur sodium for Injection.

Active Ingredient: Ceftiofur (as ceftiofur sodium trihydrate), 50 mg per mL of reconstituted solution.

Storage: Store unreconstituted product at a temperature between 15° and 25°C.

Reconstituted product - store reconstituted product at a temperature between 2° and 8°C for up 7 days, between 15° and 30° C for up to 12 hours, or frozen for up to 8 weeks. Protect from light.

See package insert for complete product information.

Bio Agri Mix LP

P.O. Box 399, Mitchell, ON. N0K 1N0

Ceftiofur sodium for Injection 4 g pack – Carton-Front Panel-English

DIN 02412284

Pr

Ceftiofur sodium for Injection

Ceftiofur for Injection (as Ceftiofur Sodium Trihydrate)

Veterinary Use Only

Sterile

Broad-spectrum antibiotic

For cattle, lactating dairy cattle, horses, swine, lambs and dogs.

WARNINGS
Treated swine and lambs must not be slaughtered for use in food for at least 24 hours after the latest treatment with this drug.
No meat withdrawal period or milk withholding time is required for cattle when the drug is used according to the label directions and dosage.
Do not use in calves to be processed for veal.
This drug is not to be administered to horses that are to be slaughtered for use in food.
Antimicrobial drugs, including penicillins and cephalosporins can cause allergic reactions in sensitized individuals. (To minimize the possibility of such a reaction, users of such antimicrobial products, including ceftiofur, are advised to avoid direct contact of the product with the skin and mucous membranes).
To limit the development of antimicrobial resistance:
- **Ceftiofur sodium for Injection** should not be used as a mass medication for cattle, swine or any other species. **Ceftiofur sodium for Injection** should only be used to treat individual animals as per the indications.
- The choice of **Ceftiofur sodium for Injection** as the most appropriate treatment should be confirmed by clinical experience supported where possible by pathogen culture and drug susceptibility testing.
- The extra-label drug use of **Ceftiofur sodium for Injection** is not recommended.

KEEP OUT OF REACH OF CHILDREN

Net 4 g

Ceftiofur sodium for Injection 4 g pack – Carton-Side Panel-English

This package contains:

4 g Ceftiofur sodium trihydrate for Injection.

Active Ingredient: Ceftiofur (as ceftiofur sodium), 50 mg per mL of reconstituted solution.

Storage: Store unreconstituted product at a temperature between 15° and 25°C.

Reconstituted product - store reconstituted product at a temperature between 2° and 8°C for up 7 days, between 15° and 30° C for up to 12 hours, or frozen for up to 8 weeks. Protect from light.

See package insert for complete product information.

Bio Agri Mix LP

P.O. Box 399, Mitchell, ON. N0K 1N0

Ceftiofur sodium for Injection

Ceftiofur for Injection (as Ceftiofur Sodium Trihydrate)

℞

Veterinary Use Only

Sterile

DESCRIPTION

Ceftiofur sodium for Injection contains the sodium salt of ceftiofur which is a broad spectrum cephalosporin antibiotic active against Gram-positive and Gram-negative bacteria including ß-lactamase-producing strains. Like other cephalosporins, ceftiofur is bactericidal *in vitro* as a result of inhibition of cell wall synthesis.

Active ingredient: Each mL of reconstituted solution contains 50 mg ceftiofur (as ceftiofur sodium).

ACTION

Ceftiofur sodium has demonstrated excellent *in vitro* and *in vivo* activity against *Mannheimia haemolytica* and *Pasteurella multocida*, two of the major pathogenic organisms associated with bovine respiratory disease (pneumonia, shipping fever). This drug has also demonstrated excellent *in vitro* and *in vivo* activity against *Histophilus somni (Haemophilus somnus)* and *in vitro* activity against *Corynebacterium pyogenes*, two other bacterial pathogens associated with bovine respiratory disease (BRD). Ceftiofur has demonstrated *in vivo* and *in vitro* activity against *Fusobacterium necrophorum* and *Bacteroides melaninogenicus*, two of the major pathogenic anaerobic bacterial associated with acute bovine interdigital necrobacillosis (foot rot, pododermatitis). Ceftiofur has excellent *in vitro* activity against Gram-negative pathogens such as *Actinobacillus pleuropneumoniae*, *Salmonella choleraesuis*, *Pasteurella multocida* and the Gram-positive pathogen *Streptococcus suis*, all of which singly or in combination can be associated with swine bacterial respiratory disease (swine bacterial pneumonia). Ceftiofur has also demonstrated excellent *in vitro* and *in vivo* activity against respiratory pathogens of horses. The drug was very active *in vitro* against *Streptococcus zooepidemicus*, *S.equi*, *Streptococcus spp. and Pasteurella spp.* isolated from patients with infections. Ceftiofur has demonstrated *in vitro* and *in vivo* activity against *Mannheimia haemolytica*, the major pathogenic bacterium associated with ovine respiratory disease (pneumonia). Ceftiofur has also demonstrated *in vivo* and *in vitro* activity against bacterial pathogens from dogs with urinary tract infections. Ceftiofur was more potent (*in vitro*) than other beta-lactam antibiotics against strains of *Escherichia coli* and *Proteus mirabilis*

In addition, ceftiofur has excellent *in vitro* activity against other Gram-negative pathogens, such as *Proteus vulgaris*, *Klebsiella pneumoniae*, *Salmonella typhimurium* and some *in vitro* action against certain strains of Gram-positive pathogens such as *Staphylococcus aureus*, *Staphylococcal xylosus*, *Staphylococcus simulans*, *Staphylococcus epidermis*, *Streptococcus uberis* and *Streptococcus bovis*. The clinical significance of these findings is not known. Clinical efficacy for the treatment of bovine respiratory disease has been demonstrated on the basis of well controlled multi-location clinical trials involving large numbers of cattle.

INDICATIONS

Cattle and lactating dairy cattle:
For treatment of bovine respiratory disease (shipping fever, pneumonia) associated with *Mannheimia haemolytica*, *Pasteurella multocida* and *Haemophilus somnus*. For the treatment of acute bovine interdigital necrobacillosis (foot rot, pododermatitis) associated with *Fusobacterium necrophorum* and *Bacteroides melaninogenicus*..

Horses: For treatment of respiratory infections in horses associated with *Streptococcus zooepidemicus*.

Swine: For treatment of swine bacterial respiratory disease (swine bacterial pneumonia) associated with *Actinobacillus pleuropneumoniae* and *Pasteurella multocida*.

Lambs; For treatment of respiratory disease (pneumonia) in lambs associated with *Mannheimia haemolytica*.

Dogs: For the treatment of canine urinary tract infections associated with *Escherichia coli* and *Proteus mirabilis*.

DOSAGE AND ADMINISTRATION

1 g

Ceftiofur Sodium for Injection should be reconstituted by adding 20 mL of bacteriostatic water for injection (containing benzyl alcohol) to each 1 g vial. For ease in reconstitution use an 18 gauge needle or larger.

4 g

Ceftiofur Sodium for Injection should be reconstituted by adding 80 mL of bacteriostatic water for injection (containing benzyl alcohol) to each 4 g vial.

Directions for Reconstitution:

1. Remove stopper overseal from bacteriostatic water for injection (containing benzyl alcohol) and sterile powder vials.
2. Manually transfer bacteriostatic water for injection (containing benzyl alcohol) to the sterile powder vial using an appropriate needle and syringe prior to use of the product.
3. Shake solution until complete reconstitution of powder occurs.

Rapid addition of bacteriostatic water for injection (containing benzyl alcohol) maintained at room temperature will give best results. Normally accepted aseptic technique should be followed during reconstitution to avoid microbial contamination.

A sterile needle and syringe should be used for each injection. Before withdrawing the solution from the bottle, disinfect the rubber cap on the bottle with suitable disinfectant, such as 70 percent alcohol. The injection site should be similarly cleaned with the disinfectant. Needles of 18 gauge and 1 to 1.5 inches long are adequate for intramuscular injections.

Administer intramuscular injections by directing the needle of suitable gauge and length into the neck of cattle, horses and swine. Avoid blood vessels and major nerves. 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 10 mL should be injected per site.

Cattle and Lactating Dairy Cattle: Reconstituted **Ceftiofur sodium for Injection** should be administered by intramuscular injection to cattle at the dosage of 1.0 mg ceftiofur per kg of body weight (1.0 mL per 50 kg body weight). Treatment should be repeated every 24 hours for a total of three treatments. Additional treatments may be given on days four and five for animals which do not show a satisfactory response (not recovered) after the initial three treatments.

Horses: Reconstituted **Ceftiofur sodium for Injection** should be administered by intramuscular injection to horses at a dosage of 2.0 mg ceftiofur per kg of bodyweight (2.0 mL per 50 kg body weight) and repeated every 24 hours. Treatments should be continued for 48 hours after symptoms have disappeared. If no response is observed within 4 - 5 days, the diagnosis should be re-evaluated.

Swine: Reconstituted **Ceftiofur sodium for Injection** should be administered by intramuscular injection to swine at the dosage of 3.0 mg ceftiofur per kg of body weight (1 mL per 17 kg body weight). Treatment should be repeated every 24 hours for a total of three treatments.

Lambs: Reconstituted **Ceftiofur sodium for Injection** is to be administered by intramuscular injection at the dosage of 2.0 mg/kg body weight. Treatment should be repeated at 24 hour intervals for a total of three treatments. Additional treatments may be given on days four and five for animals which do not show a satisfactory response (not recovered) after the initial three treatments.

Dogs: Reconstituted **Ceftiofur sodium for Injection** should be administered by subcutaneous injection at a dosage of 2.0 mg ceftiofur per kg of body weight (0.2 mL per 5 kg body weight). Treatment should be repeated at 24-hour intervals for 5 - 14 days.

Contraindications
As with all drugs, the use of **Ceftiofur sodium for Injection** is contraindicated in animals previously found to be hypersensitive to the drug. In the event of a hypersensitivity reaction following the administration of this drug, immediate appropriate therapy should be instituted.

CAUTIONS

1. The use of ceftiofur sodium in cattle may result in some signs of immediate and, transient local pain at the injection site. If no improvement is seen within 3 - 5 days, redetermine the diagnosis.
2. The administration of antibiotics to horses under conditions of stress may be associated with acute diarrhea that could be fatal. If acute diarrhea is observed, discontinue use of this drug and initiate appropriate therapy.
3. Since safety in breeding swine has not been determined, use in animals intended for breeding is not recommended.
4. For horses, safety in breeding animals and suckling foals (under 6 months of age) has not been established.
5. Reversible thrombocytopenia and anemia have occasionally been observed in dogs treated with ceftiofur for prolonged periods. Thus, the use of this drug is contraindicated in animals with pre-existing signs of these conditions. Prolonged therapy (greater than 14 days) should be undertaken only with appropriate evaluation and monitoring of hematologic values
6. In dogs, safety in breeding, pregnant, lactating and neonatal animals has not been established.

WARNINGS

Treated swine and lambs must not be slaughtered for use in food for at least 24 hours after the latest treatment with this drug. No meat withdrawal period or milk withholding time is required for cattle when the drug is used according to the label directions and dosage. Do not use in calves to be processed for veal. This drug is not to be administered to horses that are to be slaughtered for use in food. Antimicrobial drugs, including penicillins and cephalosporins can cause allergic reactions in sensitized individuals. (To minimize the possibility of such a reaction, users of such antimicrobial products, including ceftiofur, are advised to avoid direct contact of the product with the skin and mucous membranes). To limit the potential development of antimicrobial resistance:

- **Ceftiofur sodium for Injection** should not be used as a mass medication for cattle, swine or any other species
- **Ceftiofur sodium for Injection** should only be used to treat individual animals as per the indications.
- **The choice of Ceftiofur sodium for Injection** as the most appropriate treatment should be confirmed by clinical experience supported where possible by pathogen culture and drug susceptibility testing.
- The extra-label drug use of **Ceftiofur sodium for Injection** is not recommended.

KEEP OUT OF REACH OF CHILDREN

NOTE

Cattle: Neither a pre-slaughter drug withdrawal interval nor a milk discard time is required in cattle when this product is used according to label directions and dosage. Use of dosages in excess of those indicated may result in illegal residues in tissues and/or in milk. Residual drug concentrations in milk at all time intervals after last treatment (e.g., 3, 6, 9,12, 24, etc, to 120 hours) are well below the published Safe Concentration of 1.0 ppm which has been established on the basis of extensive metabolism and toxicity data. Drug residues were not detectable by any of several screening assay procedures commonly used by the dairy industry. Assay procedures used were Delvotest P*, *Bacillus stearothermophilus* disk assay (BSDA) and the cylinder/plate (*M. luteus*) assay. Lower limits of detection for microbiologically active residues for these assays, respectively, were 0.05 ppm, 0.08 ppm and 0.015 ppm.

ANIMAL SAFETY

Cattle:
Results from a 5-day tolerance study in normal feeder calves indicated that formulated ceftiofur sodium was well tolerated at over 55 times (55.0 mg/kg/day) the recommended dose of 1.0 mg/kg/day for 5 consecutive days. Ceftiofur sodium administered intramuscularly had no adverse systemic effects. Local effects of muscle irritation were detected after the last dose (5 consecutive daily doses) as evidenced by significantly elevated aspartate transaminase and creatine phosphokinase values. However, these transient elevated values returned to baseline values 9 days post-treatment.

In a 15-day safety/toxicity study; 5 steer and 5 heifer calves per group were intramuscularly administered formulated ceftiofur sodium,at just over 0 (vehicle control), 2, 6, 10 and 20 times the maximum recommended dose of 1.0 mg/kg/day to determine the safety factor and to measure the muscle irritancy potential in the target species. There were no adverse systemic effects indicating that formulated ceftiofur sodium has a wide margin of safety when injected intramuscularly into feeder calves at over 22 times (22.0 mg/kg/day) the recommended dose for 3 times (15 days) the recommended 3 to 5 days of therapy. The formulation was shown to be a slight muscle irritant based on results of histopathological evaluation of the injection sites at post-treatment days 1, 3, 7 and 14.

Horses:
In a safety study, horses received a daily intramuscular injection of either 0 mg/kg/day (saline control), 2.2 mg/kg/day (50 mg/mL), 6.6 mg/kg/day (100 mg/mL), or 11.0 mg/kg/day (200 mg/mL) of an aqueous solution of ceftiofur sodium for 30 or 31 days. Ceftiofur sodium was well tolerated when administered intramuscularly to male and female horses at doses up to 11.0 mg/kg/day for 30 or 31 days. No clinical evidence of irritation was noted at any dose. The drug-related changes detected in this study were limited to a transient decrease in food consumption in horses receiving 6.6 or 11.0 mg/kg/day ceftiofur, and a general mild skeletal muscle irritation at the injection sites of ceftiofur treated horses evident only on gross and histopathological examination.

In a tolerance study, horses received a single daily intravenous infusion of either 0 (saline), 22.0 or 55.0 mg/kg/day of an aqueous solution (50 mg/mL) of ceftiofur for 10 days. The results indicated that ceftiofur administered intravenously at a dose of 22.0 or 55.0 mg/kg/day apparently can change the bacterial flora of the large intestine leading to inflammation of the large intestine with subsequent diarrhea and other clinical signs (loose feces, eating bedding straw, dehydration, rolling or colic and a dull, inactive demeanor). Decreased food consumption, a loss of body weight, hematologic changes related to acute inflammation and stress, and serum chemistry changes related to decreased food consumption and diarrhea were also associated with treatment at these doses. The adverse effects were most severe a few days after dosing was initiated and tended to become less severe towards the end of the 10-day dosing period.

Swine:
Results from a 5-day tolerance study in normal feeder pigs indicated that formulated ceftiofur was well tolerated when administered at 125.0 mg/kg (more than 40 times the recommended daily dosage of 3.0 mg/kg of body weight) for 5 consecutive days. Ceftiofur sodium administered intramuscularly to pigs produced no overt adverse signs of toxicity.

To determine the safety factors and to measure the muscle irritancy potential in swine, a safety/toxicity study was conducted. Five barrows and 5 gilts per group were intramuscularly administered formulated ceftiofur sodium at 0, 5.0, 15.0 and 25.0 mg/kg of body weight for 15 days which is 0, 1.66, 5 and 8.33 times the recommended dose of 3.0 mg/kg of body weight/day and 5-times the recommended treatment length of 3 days. There were no adverse systemic effects indicating that formulated ceftiofur has a wide margin of safety when injected intramuscularly into feeder pigs at the recommended dose of 3.0 mg/kg/day for 3 days or at levels up to 8.33 times the recommended dose for 5 times the recommended length of treatment. The formulation was shown to be a slight muscle irritant based on results of histopathological evaluation of the injection sites at post treatment days 1,2, 3 and 4. By day 10 post injection, the muscle reaction was subsiding and at day 15 post injection there was little evidence of muscle damage in any of the pigs in any of the treatment groups.

Lambs:
In a 15-day safety/toxicity study in sheep, 3 wether and 3 ewe lambs per group were given formulated ceftiofur sodium by the intramuscular route 0 (sterile water vehicle), 1, 3 or 5 times the recommended dose of 2.0 mg/kg/day for 3 times the recommended maximum duration of 5 days of treatment. There were no adverse systemic effects indicating that formulated ceftiofur is well tolerated and has a wide margin of safety in lambs. Based on examination of injection sites from study days 9, 11, 13 and 15, a low incidence of visual changes and histopathologic findings of a mild, reversible inflammation from all groups including the controls indicated that the formulation is .a slight muscle irritant.

Dogs:
Ceftiofur sodium was well tolerated at the therapeutic dose and is safe for the treatment of urinary tract infections in dogs. In clinical studies, ceftiofur was well tolerated by dogs at the recommended level (2.0 mg/kg) for 5 - 14 days. In the acute study, minimal inflammation at the injection site was noted when administered subcutaneously for 42 consecutive days. One of four females also developed thrombocytopenia (15 days) and anemia (36 days). Thrombocytopenia and anemia also occurred at the 3X and 5X dose levels. In the reversibility phase of the study (5X dose), the thrombocytopenia reversed within 8 days, and of the two anemic animals, the male recovered within 6 weeks and the female was sacrificed due to the severity of the anemia.

In the 15-day tolerance study in dogs, exaggerated high subcutaneous doses of 25 and 125 times the recommended therapeutic dose produced a progressive and dose-related thrombocytopenia, with some dogs also exhibiting anemia and bone marrow changes. The hematopoietic changes noted in dogs treated with ceftiofur were similar to those associated with long-term cephalosporin administration in dogs and humans. The hematopoietic effects are not expected to occur as a result of recommended therapy.

STORAGE

1. Store unreconstituted product at a temperature between15° and 25°C.
2. Reconstituted product - store reconstituted product at a temperature between 2° and 8°C for up 7 days, between 15° and 30°C for up to 12 hours, or frozen for up to 8 weeks. Although some breakage may occur with the frozen product, thaw by immersing the vial in hot, running tap water until a clear, ice-free solution is obtained and then use according to label. Do not freeze and thaw reconstituted product more than once.
3. Colour of cake may vary from off-white to tan and does not affect potency.
4. Protect from light.

PRESENTATION

Ceftiofur Sodium for Injection is available in 1 g (20 mL) and 4 g (100 mL) vials.

Bio Agri Mix LP, P.O. Box 399, Mitchell, ON. N0K 1N0

DIN 02412284