SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Ceftiocyl 50 mg/ml, suspension for injection for cattle and pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Ceftiofur (as hydrochloride) 50.0 mg

Excipients

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection.
Slightly yellow to slightly pink, milky suspension.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle and pigs.

4.2 Indications for use, specifying the target species

Infections associated with bacteria sensitive to ceftiofur:

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

In 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 *Escherichia coli*, *Arcanobacterium pyogenes* and *Fusobacterium necrophorum*, sensitive to ceftiofur. The indication is restricted to cases where treatment with another antimicrobial has failed.

4.3 Contraindications

Do not administer to an animal previously found to be hypersensitive to ceftiofur and other β -lactam antibiotics.
Do not use in case of known resistance to the active substance.

Do not use in poultry (including eggs) due to risk of spread of antimicrobial resistance to human.

4.4 Special warnings for each target species

Accidental injection is dangerous.

4.5 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In case of the occurrence of allergic reaction the treatment should be withdrawn.
Ceftiocyl 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, Ceftiocyl 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, including use of the product deviating from the instructions given in the SPC, may increase the prevalence of such resistance. Whenever possible, Ceftiocyl should only be used based on susceptibility testing.
Ceftiocyl 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.

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.

1.Do not handle this product if you know you are sensitised, or if you have been advised not to work with such preparations.
2. Handle this product with great care to avoid exposure taking all recommended precautions.
3. In case of accidental injection or 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 in breathing are more serious symptoms and require urgent medical attention.

Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Hypersensitivity reactions unrelated to dose can occur. Allergic reactions (e.g. skin reactions, anaphylaxia) may occasionally occur.

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.

4.7 Use during pregnancy, lactation or lay

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.

4.8 Interaction with other medicinal products and other forms of interaction

Erythromycins and tetracyclines may have an antagonistic effect on cephalosporins whereas aminoglycosides may have a potentiating effect.

4.9 Amounts to be administered and administration route

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

Cattle:
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.

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

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

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.

4.11 Withdrawal period(s)

Pigs:
Meat and offal: 6 days.

Cattle:
Meat and offal: 8 days.
Milk: zero hour.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use
ATCvet code: QJ01DD90

5.1 Pharmacodynamic properties

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 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 spp*. (former *Pasteurella haemolytica*), *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*.

The following Minimum Inhibitory Concentrations (MIC) have been determined for ceftiofur in European isolates of target bacteria, isolated from diseased animals:

Pigs

Organism (number of isolates)	**MIC range (µg/mL)**	**MIC_{90} (µg/mL)**
A. pleuropneumoniae (28)	≤ 0.03*	≤ 0.03
Pasteurella multocida (37)	≤ 0.03 - 0.13	≤ 0.03
Streptococcus suis (495)	≤ 0.03 - 0.25	≤ 0.03

Cattle

Organism (number of isolates)	**MIC range (µg/mL)**	**MIC_{90} (µg/mL)**
Mannheimia spp. (87)	≤ 0.03*	≤ 0.03
P.multocida (42)	≤ 0.03 - 0.12	≤ 0.03

H.somnus (24)	≤ 0.03*	≤ 0.03
Arcanobacterium pyogenes (123)	≤ 0.03 - 0.5	0.25
Escherichia coli (188)	0.13 - > 32.0	0.5
Fusobacterium necrophorum (67)(isolates from cases of foot rot)	≤ 0.06 - 0.13	ND
Fusobacterium necrophorum (2)(isolates from cases of acute metritis)	≤ 0.03 - 0.06	ND

*No range; all isolates yielded the same value. ND: not determined.

The following breakpoints are recommended by NCCLS for bovine and porcine respiratory pathogens currently on the label for Ceftiocyl:

Zone Diameter (mm)	MIC (µg/mL)	Interpretation
≥ 21	≤ 2.0	(S) Susceptible
18 - 20	4.0	(I) Intermediate
≤ 17	≥ 8.0	(R) Resistant

No breakpoints have been determined to date for the pathogens associated with foot rot or acute post-partum metritis in cows.

5.2 Pharmacokinetic particulars

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 10.58 ± 2.06 µg/mL were reached after 1 hour (1.6 ± 0.7 h); the terminal elimination half-life (t½) of desfuroylceftiofur was 15.56 ± 4.32 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 7.08 ± 4.32 µg/mL are reached within 2 hours (1.9 ± 0.9 h) 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 11.38± 2.33hours. 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrogenated soya lecithin
Sorbitan monooleate
Cottonseed oil

6.2 Incompatibilities

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

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale.2 years
Shelf life after first opening the immediate packaging: 28 days.

6.4. Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

50,100 and 250 ml dark type I vial closed with a bromobutyl rubber stopper and aluminium cap.

Cardboard box with 1 glass vial of 50 ml with a rubber stopper and aluminium cap.
Cardboard box with 1 glass vial of 100 ml with a rubber stopper and aluminium cap.
Cardboard box with 1 glass vial of 250 ml with a rubber stopper and aluminium cap.
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Vetoquinol UK Limited
Steadings Barn
Pury Hill Business Park
Nr Alderton
Towcester
Northamptonshire
NN12 7LS

8. MARKETING AUTHORISATION NUMBER

Vm 08007/4122

9. DATE OF FIRST AUTHORISATION

06 September 2010

10. DATE OF REVISION OF THE TEXT

September 2018

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (http://www.ema.europa.eu/).

Approved: 11 September 2018