SUMMARY OF THE PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cefenil 50mg/ml Powder and Solvent for Solution for Injection for Cattle and Pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Powder vial contains:

Active Substance
Ceftiofur (as ceftiofur sodium) 1g
Or
Ceftiofur (as ceftiofur sodium) 4g

Solvent contains: Water for Injection

One ml of reconstituted solution contains:

Active Substance
Ceftiofur (as ceftiofur sodium) 50mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection

Powder: off white to brown coloured powder
Solvent: clear, colourless, solution
Reconstituted solution: clear solution, free of particulates

4. CLINCIAL PARTICULARS

4.1 Target species

Cattle and pigs.

4.2 Indications for use, specifying the target species

Cattle

Treatment of cattle with acute bacterial respiratory disease in which *Mannheimia haemolytica, Pasteurella multocida or Histophilus somni* sensitive to ceftiofur are involved.

Treatment of cattle with acute interdigital necrobacillosis (foul in the foot) in which *Fusobacterium necrophorum* and *Bacteroides melaninogenicus* are involved.

Pigs

Treatment of pigs with bacterial respiratory disease in which *Actinobacillus (Haemophilus) pleuropneumoniae, Pasteurella multocida* and/or *Streptococcus suis* sensitive to ceftiofur are involved.

4.3 Contraindications

Do not use in animals previously found to be hypersensitive to ceftiofur and other b-lactam antibiotics.
Do not use in case of known resistance to the active substance.
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.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

(i) Special precautions for use in animals

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 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, 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.

Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to ceftiofur and may decrease the effectiveness of treatment with other cephalosporins, due to the potential for cross resistance.

In the pig, particular care must be taken to avoid injection into the fat tissue. See section 4.9.

Avoid repeated injection at the same site.

(ii) 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 are sensitised or if you have been advised not to work with such preparations.

Handle this product with great care to avoid exposure, taking all recommended precautions.

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.

4.6 Adverse reactions (frequency and seriousness)

Adverse reactions are very rare. Use of this product may cause transient local discomfort at the site of the injection.
Hypersensitivity reactions can occasionally occur. In the case of an allergic reaction, treatment should be stopped.
In pigs, local irritation at the injection site may occur and can persist for 5 days or more.

4.7 Use during pregnancy, lactation or lay

Laboratory studies in the rat have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects.
The safety of the veterinary medicinal product has not been assessed during pregnancy and lactation in cattle or pigs. Use only according to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

The bactericidal properties of β-lactams are neutralised by simultaneous use of bacteriostatic antibiotics (macrolides, sulphonamides and tetracyclines).

4.9 Amounts to be administered and administration route

This product is for intramuscular use only. See section 4.5(i). Normal aseptic injection technique should be practiced.

Reconstitution

1 g vial: reconstitute by adding 20 ml of water for injection.
4 g vial: reconstitute by adding 80 ml of water for injection.

Directions for Reconstitution:
1. Remove stopper overseal from diluent and sterile powder vials.
2. Remove exactly 20ml (80ml) Water for Injections using a sterile 18G needle and syringe.
3. Inject the exact volume of diluent into sterile powder vial.
4. Shake solution until complete reconstitution of powder occurs.
Rapid addition of diluent maintained at room temperature will give best results. Normally accepted aseptic technique should be followed during reconstitution to avoid microbial contamination.

The resulting solution contains 50 mg of ceftiofur per ml.

Dosage in cattle and pigs.

Target Species	Dosage	Dosage of reconstituted product	Indication	Frequency of administration
Cattle	1 mg/kg	1ml/50kg	Respiratory disease	Once daily at 24 hour intervals for 3-5 days in total
			Foul in the foot	Once daily at 24 hour intervals for 3 days in total
Pigs	3 mg/kg	1ml/16kg	Respiratory disease	Once daily at 24 hour intervals for 3 days in total

In pigs, an appropriately-graduated syringe must be used to allow accurate administration of the required dose volume. This is particularly important when injecting piglets weighing less than 16 kg.

Do not administer more than 10 ml per injection site.

Do not exceed 20 broachings per vial. If more than 20 broachings are required, the use of a draw-off needle is recommended.

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

In cattle, no evidence of systemic toxicity was observed following administration of an overdose.
In pigs, no evidence of systemic toxicity was observed following the administration of doses of up to 8 times the recommended dose, administered daily by intramuscular injection for 15 days.

4.11 Withdrawal periods

Cattle Meat and offal: 2 days.

Milk: zero hours.
Pigs Meat and offal: 2 days.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, third-generation cephalosporins.
ATCvet code: QJ01DD90

5.1 Pharmacodynamic properties

The active ingredient, ceftiofur sodium, is a third-generation cephalosporin (beta-lactam antibiotic) which acts against both gram-positive and gram-negative bacteria, including betalactam-producing bacteria. Also its main metabolite, desfuroylceftiofur, shows some antibacterial activity.

Ceftiofur is a bactericidal antibiotic *in vitro* which acts by interfering with bacterial cell-wall synthesis.

In cattle, ceftiofur is active against the following microorganisms found in respiratory-tract infections: *Mannheimia haemolytica, Pasteurella multocida, Histophilus somni* as well as the following bacteria responsible for acute interdigital necrobacillosis: *Fusobacterium necrophorum* and *Bacteroides melaninogenicus*.

In pigs, ceftiofur is active against the following microorganisms: *Actinobacillus (Haemophilus) pleuropneumoniae, Pasteurella multocida* and/or *Streptococcus suis*.

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 b-lactam; 2) altering the permeability of the cell to b-lactams; 3) producing b-lactamases that cleave the b-lactam ring of the molecule, or 4) active efflux.
The following ceftiofur breakpoints are used: ≤ 2 µg/mL (Susceptible), 4 µg/mL (Intermediate) and ≥ 8 µg/mL (Resistant).

The following Minimum Inhibitory Concentrations (MIC) have been determined for ceftiofur in European isolates (France, United Kingdom, Netherlands, Denmark, Germany, Belgium, Italy, Czech Republic, Ireland, Poland and Spain) collected from diseased animals between 2000 to 2007:

Bacteria species	Origin	Year	No. of strains	MIC of ceftiofur (µg/mL)		
				Range	MIC_{50}	MIC_{90}
Pasteurella multocida	Cattle	2004 to 2006	82	0.0019 – 0.0625	≤0.003	≤0.005
	Pigs	2004 to 2006	66	0.0019 – 0.0156	≤0.003	≤0.006

Mannheimia haemolytica	Cattle	2004 to 2006	72	0.0019 – 0.0156	≤0.005	≤0.008
Histophilus somni	Cattle	2005 to 2007	62	0.0019 – 0.125	≤0.004	≤0.02
Actinobacillus pleuropneumoniae	Pigs	2003 / 2004	58	0.0039 – 0.0312	≤0.006	≤0.02
Streptococcus suis	Pigs	2004 to 2006	44	0.0312 – 0.5	≤0.2	≤0.3
Fusobacterium necrophorum	Cattle	2000 to 2006	27	0.015 – 16	0.1	0.2

The following ceftiofur breakpoints are used: ≤2 µg/mL (Susceptible), 4 µg/mL (Intermediate) and ≥8 µg/mL (Resistant).

5.2 Pharmacokinetic particulars

After intramuscular administration ceftiofur is quickly metabolised to desfuroylceftiofur which reaches maximum plasma concentration within 1 hour. The plasma half-life for desfuroylceftiofur is on average over 9 hours in cattle and 13 hours in pigs. No accumulation has been shown after several administrations.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder:
Potassium dihydrogen phosphate
Sodium hydroxide (pH adjustment)

Solvent:
Water for injections

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 (powder): 3 years.
Shelf-life of the veterinary medicinal product after reconstitution: 24 hours.
Shelf-life of diluent: 3 years.

6.4 Special precautions for storage

Store unreconstituted product (powder and diluent) in a refrigerator (2°C to 8°C).
Keep the container in the outer carton in order to protect from light.
After reconstitution, store in a refrigerator (2°C to 8°C).
Any reconstituted product remaining after the stated periods should be discarded.

6.5 Nature and composition of immediate packaging

Powder: Type II clear glass vials sealed by bromobutyl stoppers and an aluminium seal with a cool green (1g) or yellow (4g) flip-off plastic disc.

Diluent: Type I clear glass vials sealed with bromobutyl stoppers and aluminium caps.

One vial with 1 g Cefenil Sterile Powder with one vial with 20 ml Water for Injections per carton in packs of 1, 6 and 12 presentations.

One vial with 4 g Cefenil Sterile Powder with one vial with 80 ml Water for Injections per carton in packs of 1, 6 and 12 presentations.

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

Norbrook Laboratories Limited
Station Works
Camlough Road
Newry
Co Down, BT35 6JP
Northern Ireland

8. MARKETING AUTHORISATION NUMBER

Vm 02000/4278

9. DATE OF FIRST AUTHORISATION

Date: 02 September 2009

10. DATE OF REVISION OF THE TEXT

Date: September 2014

25 September 2014