SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

EXCENEL Flow 50 mg/ml suspension for injection for pigs and cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Ceftiofur (as hydrochloride) 50 mg.

Excipients:

Qualitative composition of excipients and other constituents
Polysorbate 80
Triglycerides, Medium-chain
Water for injections

Opaque suspension, white to off-white.

3. CLINICAL INFORMATION

3.1 Target species

Pigs and cattle.

3.2 Indications for use for each target species

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 *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni*.
For the treatment of acute interdigital necrobacillosis (panaritium, foot rot), associated with *Fusobacterium necrophorum* and *Prevotella melaninogenica*.
For treatment of the bacterial component of acute post-partum (puerperal) metritis within 10 days after calving associated with *Escherichia coli*, *Trueperella pyogenes* and *Fusobacterium necrophorum*, sensitive to ceftiofur, where treatment with another antimicrobial has failed.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance and other β-lactam antibiotics or to any of the excipients.

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.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

In case of the occurrence of allergic reaction the treatment should be withdrawn.

The veterinary medicinal product 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, the veterinary medicinal 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 more narrow spectrum antimicrobials first line treatment. Official, national and regional antimicrobial policies should be taken into account when the veterinary medicinal product is used. Increased use, including use of the veterinary medicinal product deviating from the instructions given in the SPC, may increase the prevalence of such resistance bacteria resistant to the veterinary medicinal product. Whenever possible, the veterinary medicinal product should only be used based on susceptibility testing.

Do not use as prophylaxis in case of retained placenta.

The veterinary medicinal 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 limited to ongoing disease outbreaks according to the approved conditions of use.

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.

People with known hypersensitivity to cephalosporins and penicillins should avoid contact with the veterinary medicinal product.

If you develop symptoms following exposure such as a skin rash, seek medical advice immediately and show the package leaflet or the label to the physician.

Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.

Wash hands after use.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Pigs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypersensitivity reaction (e.g. allergic skin reaction, anaphylaxis), Injection site reaction (e.g. discolouration of fascia or fat)[1]

[1]Mild, observed for up to 20 days.

Cattle:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypersensitivity reaction (e.g. allergic skin reaction, anaphylaxis), Injection site induration, Injection site swelling, Injection site inflammation[1]

[1]Mild to moderate, observed until 42 days post injection.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

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

3.8 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, sulfonamides and tetracyclines).

Aminoglycosides may have a potentiating effect on cephalosporins.

3.9 Administration routes and dosage

Before use, shake the bottle vigorously for a maximum of 60 seconds or until the veterinary medicinal product appears adequately resuspended.

To ensure a correct dosage, body weight should be determined as accurately as possible.
Pigs:
3 mg ceftiofur/kg bw/day for 3 days via intramuscular route, i.e. 1 ml/16 kg bw/day.
Not more than 4 ml should be administered per injection site.

Cattle:
Respiratory disease: 1 mg ceftiofur/kg bw/day for 3 to 5 days by subcutaneous injection, i.e. 1 ml/50 kg bw/day.
Acute interdigital necrobacillosis: 1 mg ceftiofur/kg bw/day for 3 days by subcutaneous injection, i.e. 1 ml/50 kg bw/day.
Acute post-partum metritis within 10 days after calving: 1 mg ceftiofur/kg bw/day for 5 consecutive days by subcutaneous injection, i.e. 1 ml/50 kg bw/day.
Not more than 13 ml 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.
50 ml and 100 ml vials can be broached a maximum of 50 times. 250 ml vials can be broached a maximum of 33 times. Otherwise, the use of a multiple-dose syringe is recommended.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

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.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Pigs:
Meat and offal: 2 days.

Cattle:
Meat and offal: 6 days; milk: zero hours.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01DD90

4.2 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.

β-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 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*.

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 (mcg/ml)**	**MIC_{90} (mcg/ml)**
Actinobacillus pleuropneumoniae (157)	0.008 - 2	0.03
Pasteurella multocida (152)	≤ 0.002 - 0.06	0.004
Streptococcus suis (151)	0.06 - ≥16	0.5
Cattle		
Organism (number of isolates)	**MIC range (mcg/ml)**	**MIC_{90} (mcg/ml)**

Mannheimia haemolytica (149)	≤ 0.002 - 0.12	0.015
Pasteurella.multocida (134)	≤ 0.002 - 0.015	0.004
Histophilus somni (66)	≤ 0.002 - 0.008	0.004
Truperella pyogenes (35)	0.25 - 4	2
Escherichia coli (209)	0.13 - 2	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

ND: not determined.

The following breakpoints are recommended by CLSI for bovine and porcine respiratory pathogens currently on the label for the veterinary medicinal product:

Zone Diameter (mm)	**MIC (mcg/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.

4.3 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 mcg/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 mcg/ml are reached within 2 hours after administration. In healthy cows, a Cmax of 2.25 ± 0.79 mcg/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 mcg/ml and 0.98 ± 0.25 mcg/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.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 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.

5.3 Special precautions for storage

Do not store above 25 °C.

5.4 Nature and composition of immediate packaging

Type I glass vial with either a chlorobutyl stopper and an aluminium overseal with plastic flip-off cap (50 and 100 ml vials) or a bromobutyl stopper and an aluminium overseal with a pull-off cap (250 ml vial).

Pack sizes:

Cardboard box containing 1 vial of 50 ml.
Cardboard box containing 1 vial of 100 ml.
Cardboard box containing 1 vial of 250 ml.
Cardboard box containing 10 vials of 50 ml.
Cardboard box containing 10 vials of 100 ml.

Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Zoetis UK Limited

7. MARKETING AUTHORISATION NUMBERS

Vm 42058/5151 (GB)
Vm 42058/3044 (NI)

8. DATE OF FIRST AUTHORISATION

21 July 1997

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

October 2024

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCT

Veterinary medicinal product subject to prescription.

Find more product information by searching for the 'Product Information Database' on www.gov.uk.

Gavin Hall
Approved: 14 March 2025