Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Advocin Injectable Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:	**Quantity:**	
Danofloxacin (as danofloxacin mesylate)	25	mg
Excipients:		
Phenol (as liquified phenol)	2.5	mg

For a full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
A clear, light yellow solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle, pigs.

4.2 Indications for use, specifying the target species

Cattle
The treatment of respiratory disease caused by *Pasteurella haemolytica* and *P. multocida* and the treatment of enteric infections caused by *Escherichia coli* and *Salmonella* spp in cattle.

Pigs
The treatment of respiratory disease caused by *P. multocida* and *A. pleuropneumoniae*, and the treatment of enteric infection caused by *E.coli* in pigs.

4.3 Contraindications

None.

4.4 Special warnings for each target species

See 4.9 Pigs, regarding use in animals less than 2 kg.

4.5 Special precautions for use

Special precautions for use in animals

Official and local antimicrobial policies should be taken into account when the product is used.
Fluoroquinolones should be reserved for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly, to other classes of antimicrobials.
Whenever possible, fluoroquinoones should only be used based on susceptibility testing.
Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to the fluoroquinolones and may decrease the effectiveness of treatment with other quinolones due to the potential for cross resistance.

Special precautions to be taken by the person administering the medical veterinary product to animals

Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

None have been observed.

4.7 Use during pregnancy, lactation or lay

May be used in pregnant cows and in lactating dairy cows.

The effects of danofloxacin on reproductive performance and on pregnancy in pigs have not been assessed.

4.8 Interaction with other medicinal products and other forms of interaction

No interactions with other products have been noted.

4.9 Amounts to be administered and administration route

Cattle: Administer by the intramuscular or intravenous routes at a dosage rate of 1.25 mg/kg body weight (1 ml/20 kg body weight). Three treatments should be given at 24 hour intervals. Treatment may be extended by up to 2 additional days for animals not fully recovered after the initial 3 treatments. For the treatment of cattle weighing more than 400 kg, the dose should be divided so that not more than 20 ml are injected at one site.

Pigs: Administer by intramuscular injection at a dosage rate of 1.25 mg/kg body weight (1 ml/20 kg body weight). Three treatments should be given at 24 hour intervals. For the treatment of pigs weighing more than 100 kg, the dose should be divided so that no more than 5 ml are injected at one site.
Seek veterinary advice regarding use of appropriately sized needles and syringes when dosing animals of low bodyweight.
An appropriately graduated syringe must be used to allow accurate administration of the required dose volume. This is particularly important when injecting small volumes, e.g. piglets less than 2 kg body weight.
When dosing a large number of animals from a single bottle, the use of an aspirating needle is recommended to avoid excessive broaching of the stopper.

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

Cattle: Overdosage by up to 25 times the recommended dose produces only mild signs of intolerance, including head tremors, ataxia and mild depression. No treatment related effects have been seen on gestation, parturition or calf viability.

Pigs: Overdosing of pigs by ten times the recommended dose showed only minor adverse clinical reactions including transient reduction in mobility. Three times the recommended dose given on three consecutive days to neonatal pigs produced no adverse clinical effects.

No antidote is recommended.

4.11 Withdrawal Period(s)

Animals may not be slaughtered for human consumption during treatment.

Cattle may be slaughtered for human consumption only after 5 days following the last injection.
Milk for human consumption must not be taken during treatment. The with-holding time for milk is 48 hours after the last dose. With cows milked twice daily, milk may only be taken for human consumption from 48 hours (i.e. at the 4^{th} milking) from the last treatment.

Pigs may be slaughtered for human consumption only after 3 days following the last injection.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Danofloxacin is a new synthetic fluoroquinolone antimicrobial agent which possesses potent *in vitro* activity against *Pasteurella haemolytica, Pasteurella multocida, Escherichia coli* and *Salmonella* spp, the bacterial pathogens most commonly associated with bovine respiratory and enteric disease. Danofloxacin also possesses potent antibacterial activity against *P.multocida* and *Actinobacillus pleuropneumoniae,* the causative agents of porcine respiratory disease, and *E.coli*, a causative agent of enteric disease in swine. Danofloxacin is active against pathogens showing resistance to other classes of antimicrobial agents. The *in vitro* MIC_{90} for *Mycoplasma hyopneumoniae* is reported to be 0.06µg/ml.

The antimicrobial activity of danofloxacin is based upon the inhibition of microbial DNA gyrase. The inhibitory effect is on the second step of the enzymatic process, uncoupling the breakage and reunion functions. Danofloxacin, in common with other quinolones, produces a stable complex between the enzyme and DNA. This results in the cessation of DNA replication and transcription, an effect which is the basis of the antimicrobial effect. Pharmacological studies showed that danofloxacin has little effect on the cardiovascular, renal or neurological systems, and, in common with other quinolones, has only mild effects on the gastric system at high
dose levels.

In general pharmacological terms, danofloxacin is well tolerated in laboratory animals. Acute toxicity values are high and a limiting No Observable Effect Level of 2.4 mg/kg/day has been established in repeat administration studies in young dogs, the most sensitive test species.

5.2 Pharmacokinetic properties

The pharmacokinetic properties of danofloxacin, which give high and rapidly achievable levels of danofloxacin in target tissues, show the product to be well suited to the therapy of respiratory and enteric diseases.

Cattle: Peak plasma levels after intramuscular and subcutaneous injection (where authorised) are seen one hour after treatment. High tissue to plasma ratios of up to 4:1 are seen in lung and gastrointestinal tissues.

Pigs: Peak plasma levels after intramuscular injection to pigs are seen one hour after treatment. High tissue to plasma ratios of up to 3:1 for lung and up to 8:1 for gastrointestinal tissues were recorded.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactic Acid
Sodium Hydroxide
Monothioglycerol
Phenol (as liquified phenol)
Water for Injection

6.2 Incompatibilities

None.

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 24 months.
Following withdrawal of the first dose, the product should be used within 4 weeks.

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and composition of immediate packaging

Advocin injectable solution is a clear sterile aqueous solution of danofloxacin mesylate, packaged in 50 ml, 100 ml and 250 ml Type II amber glass round vials with butyl rubber stopper and lacquered one-piece aluminium shell.
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

Unused product or waste material should be disposed of in accordance with any guidance from an appropriate waste regulation authority.

7 MARKETING AUTHORISATION HOLDER

Zoetis Ireland Limited
25/28 North Wall Quay
Dublin 1
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10438/001/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21st December 2005

10 DATE OF REVISION OF THE TEXT

August 2013