SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Advocin Injectable Solution 2.5% Veterinary

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance: Danofloxacine (as mesylate) equivalent to danofloxacine 25.0 mg/ml
For the full list of all other excipients see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, light yellow solution

4. CLINICAL PARTICULARS

4.1. Target species

Cattle.

4.2. Indications for use, specifying the target species

For the treatment of cattle (calves, beef cattle and non-lactating dairy cattle) with respiratory infections caused by *Pasteurella haemolytica* and *Pasteurella multocida*, enteric infections caused by *E.coli* and *Salmonela* spp. Only after sensitivity to danofloxacin has been confirmed by laboratory tests and after no alternative treatment was found effective (proved resistance to other treatments).

4.3. Contraindications

None

4.4. Special warnings for each target species

Not applicable

4.5. Special precautions for use

Special precautions for use in animals

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, fluoroquinolones 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 veterinary medicinal product to animals

Wash hands after use.

4.6. Adverse reactions (frequency and seriousness)

None
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form (http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType =Adv ersEffectMedic@moh.health.gov.il).

4.7. Use during pregnancy, lactation or lay

The effects of danofloxacin on pregnancy or milking 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

Administer by the intramuscular or subcutaneous 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.
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

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.

No antidote is recommended.

4.11. Withdrawal periods

Meat and offal: 3 days

5. PHARMACOLOGICAL PROPERTIES

ATCVet code: QJ01MA92

Danofloxacin is a new synthetic fluoroquinolone antimicrobial agent which possesses potent *in vitro* activity against *Mannheimia 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, and for *Mycoplasma bovis* 0.5 µg/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 Observed Effect Level of 2.4 mg/kg/day has been established in repeat administration studies in young dogs, the most sensitive test species.

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.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Lactic Acid
Sodium Hydroxide
Monothioglycerol
Liquified phenol
Water for injections

6.2. Incompatibilities

None known.

6.3. Shelf life

The expiry date of the product is indicated on the packaging materials.
Shelf-life of the veterinary medicinal product after first opening the immediate packaging: 28 days, when stored at 2-8°C.

6.4. Special precautions for storage

Do not store above 30°C.
Keep out of the reach of children
Protect from light.
After first opening of the immediate packaging store in a refrigerator (2°C–8°C).

6.5. Nature and composition of immediate packaging

Advocin Injectable Solution 2.5% Veterinary 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 bromobutyl 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 product or waste materials derived from the use of such products, if appropriate

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

7. MARKETING AUTHORISATION HOLDER

Zoetis Israel Holding B.V., 5 Atir Yeda Street, Kfar Saba, Israel

8. MARKETING AUTHORISATION NUMBER

083-84-92073-00

9. MANUFACTURER
Fareva Amboise, France

10. DATE OF REVISION OF THE TEXT
20.01.2020

The leaflet format has been determined by the Ministry of Health and the content was updated according to the guidelines of the Ministry of Health in 02.2020.