ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

BOX FOR 50/100/250 ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Advocin 180, 180 mg/ml, Solution for Injection.

2. STATEMENT OF ACTIVE SUBSTANCES

Danofloxacin 180 mg/ml
(Equivalent to 228.4 mg/ml Danofloxacin mesylate)

3. PACKAGE SIZE

50ml
100 ml
250 ml

4. TARGET SPECIES

Cattle

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

For subcutaneous or intravenous use.

7. WITHDRAWAL PERIODS

Withdrawal period:
Meat and offal: 8 days
Milk: 4 days

8. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use within 28 days.

9. SPECIAL STORAGE PRECAUTIONS

Keep the vial in the outer carton.
Store in the original package in order to protect from light.
Do not freeze.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Zoetis UK Limited
1st Floor, Birchwood Building
Springfield Drive
Leatherhead
Surrey
KT22 7LP

14. MARKETING AUTHORISATION NUMBER

Vm 42058/3008

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

VIAL LABEL (100/250 ml)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Advocin 180, 180 mg/ml, Solution for Injection.

2. STATEMENT OF ACTIVE SUBSTANCES

Danofloxacin 180 mg/ml
(Equivalent to 228.4 mg/ml Danofloxacin mesylate).

3. TARGET SPECIES

Cattle

4. ROUTES OF ADMINISTRATION

SC/IV.
Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal period:
Meat and offal: 8 days
Milk: 4 days

6. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use by…

7. SPECIAL STORAGE PRECAUTIONS

Keep the vial in the outer carton.
Store in the original package in order to protect from light.
Do not freeze.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Zoetis UK Limited
1st Floor, Birchwood Building
Springfield Drive
Leatherhead
Surrey
KT22 7LP

9. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL (50 ml)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Advocin 180, 180 mg/ml, Solution for Injection for Cattle

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Danofloxacin 180 mg/ml
(Equivalent to 228.4 mg/ml Danofloxacin mesylate).

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}
Once broached use by:

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Advocin 180, 180 mg/ml, Solution for Injection for Cattle.

2. Composition

Each ml contains:

Active substance:
Danofloxacin 180 mg
(Equivalent to 228.4 mg Danofloxacin mesylate)
Excipients:
Phenol 2.5 mg
Monothioglycerol 5 mg

Medium yellow to amber solution.

3. Target species

Cattle.

4. Indications for use

In cattle:
Treatment of bovine respiratory disease caused by *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni* sensitive to danofloxacin.
For the treatment of acute bovine mastitis caused by *Escherichia coli* sensitive to danofloxacin.

In neo-natal calves:
Treatment of enteric infections caused by *Escherichia coli* sensitive to danofloxacin.

5. Contraindications

Do not use in cases of hypersensitivity to the active substance, to other (fluoro)quinolones or to any of the excipients.

6. Special warnings

Special warnings:
Do not use in cases where the pathogen involved is resistant to other fluoroquinolones (due to the potential for cross resistance).

Special precautions for safe use in the target species:

Use of fluoroquinolones should be based on susceptibility testing and take into account official and local antimicrobial use policies. It is prudent to reserve fluoroquinolones for

the treatment of clinical conditions which have responded poorly, or are expected to respond poorly, to other classes of antimicrobials. Efficacy against gram positive strains has not been established.

For fluoroquinolones as a class, over-dosage at multiples of the recommended dose has been shown to induce erosion of articular cartilage. Care should be taken to dose accurately and the veterinary medicinal product should be used with caution in animals with joint disease or cartilage growth disorders.

Use of the veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to fluoroquinolones and may decrease the effectiveness of treatment with other quinolones due to the potential for cross resistance.
The safety of the veterinary medicinal product has not been assessed in breeding bulls.

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

People with known hypersensitivity to (fluoro)quinolones should avoid contact with the veterinary medicinal product.
Care should be taken to avoid accidental self-injection, it can induce a slight irritation.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
In case of contact with skin or eyes, rinse with plenty of water.

Wash hands after use.
Do not eat, drink or smoke during application.

Pregnancy:

The safety of the veterinary medicinal product has not been established during pregnancy in cows nor assessed in breeding bulls.
The use of the veterinary medicinal product is not recommended during pregnancy.
Studies in laboratory animals have shown adverse effects on reproduction. At high doses in rats (100 to 200 mg/kg/day), increase in foetal delayed ossification and in dilatation of the cerebral ventricles were observed. Dams given high doses produced fewer live pups per litter and pup weight and survival were adversely affected.

Interaction with other medicinal products and other forms of interaction:

When fluoroquinolones have been combined with bacteriostatic antimicrobials, such as tetracyclines and macrolides or phenicols, an antagonism was demonstrated *in vitro*.

Overdose:

A subcutaneous injection of the veterinary medicinal product at two times the recommended dose induced a moderate inflammatory response in the tissue around the injection site. The resultant lesions may persist for up to 30 days.

At doses of three times the therapeutic dose (18 mg/kg bw), erythema of the nasal and ocular mucosae was induced and food intake was reduced. At even higher doses and prolonged exposure, there was damage to the cartilage in the joints and some animals displayed paresis, ataxia or nystagmus.

Major incompatibilities:

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

7. Adverse events

Cattle:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):
Anaphylactic shock[1]

[1] In sensitive animals, immediate or delayed.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder< or the local representative of the marketing authorisation holder> using the contact details at the end of this leaflet, or via your national reporting system: *{national system details}*.

8. Dosage for each species, routes and method of administration

Intravenous or subcutaneous routes.
6 mg/kg body weight (1 ml/30 kg body weight) as a single injection.

If clinical signs of respiratory or enteric disease persist 48 hours after the first injection, an additional dose at 6 mg/kg body weight may be administered.

It is recommended to treat animals in the early stages of disease and to evaluate the response to treatment within 48 hours.

For the treatment of acute bovine mastitis, the veterinary medicinal product should be administered at 6 mg/kg body weight (1 ml/30 kg body weight) as a single injection by the subcutaneous or intravenous route. The clinical signs should be monitored carefully and supportive therapy should be given as appropriate. If clinical signs of acute bovine mastitis persist 36-48 hours after the first injection, the antibiotic treatment strategy should be reviewed. It is recommended to treat animals in the early stages of disease and to evaluate the response to treatment within 36-48 hours. To ensure a correct dosage body weight should be determined as accurately as possible.

9. Advice on correct administration

For treatment of cattle weighing more than 450 kg, divide the subcutaneous dose so that no more than 15 ml are injected at one site.

When dosing a large number of animals from a single vial, the use of an automatic syringe is recommended to avoid excessive broaching of the rubber stopper.

10. Withdrawal periods

Meat and offal: 8 days
Milk: 4 days

11. Special storage precautions

Keep out of the sight and reach of children.
Store in the original packaging in order to protect from light.
Do not freeze.

Do not use this veterinary medicinal product after the expiry date which is stated on the label after Exp. The expiry date refers to the last day of that month.

Shelf life after first opening the immediate packaging: 28 days.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.
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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Vm 42058/3008

Supplied in boxes containing one vial of 50 ml, 100 ml or 250 ml. Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder <and contact details to report suspected adverse reactions>:

Zoetis UK Limited
1st Floor, Birchwood Building
Springfield Drive
Leatherhead
Surrey
KT22 7LP

Manufacturer responsible for batch release:

Zoetis Manufacturing & Research Spain S.L.
Carretera. De Camprodon S/n
La Vall De Bianya
17813 Girona
Spain

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