ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Posatex ear drops suspension for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of the ear drops suspension contains:

Active substances:

Orbifloxacin	8.5 mg
Mometasone furoate (as monohydrate)	0.9 mg
Posaconazole	0.9 mg

Excipients:

Qualitative composition of excipients and other constituents
Lauric acid
Paraffin, liquid
Plasticised hydrocarbon gel (5% polyethylene in 95% mineral oil)

White to off-white viscous suspension.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

Treatment of acute otitis externa and acute exacerbations of recurrent otitis externa, associated with bacteria susceptible to orbifloxacin and fungi susceptible to posaconazole, in particular *Malassezia pachydermatis.*

3.3 Contraindications

Do not use if the eardrum is perforated.
Do not use in cases of hypersensitivity to the active substances, to any of the excipients, to corticosteroids, to other azole antifungal agents or to other fluoroquinolones.
Do not use during the whole or part of the pregnancy.

3.4 Special warnings

Bacterial and fungal otitis is often secondary in nature. The underlying cause should be identified and treated.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Heavy reliance on a single class of antibiotic may result in the induction of resistance in a bacterial population. 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 antibiotics.

Use of the veterinary medicinal product should be based on identification and susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at local/regional level.

Use of the product should be in accordance with official, national and regional antimicrobial policies.

An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

Narrow spectrum antibiotic therapy with a lower risk of antimicrobial resistance selection should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

Quinolone class veterinary medicinal products have been associated with cartilage erosions in weightbearing joints and other forms of arthropathy in immature animals of various species. Therefore, do not use in animals less than 4 months of age.

Prolonged and intensive use of topical corticosteroids preparation is known to trigger local and systemic effects, including suppression of adrenal function, thinning of the epidermis and delayed healing. See section 3.10.

Before the veterinary medicinal product is applied, the **external auditory canal** must be examined thoroughly to ensure that the ear drum is not perforated in order to avoid the risk of transmission of the infection to the middle ear and to prevent damage to the cochlear and vestibular apparatus.

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

Wash hands carefully after applying the veterinary medicinal product. Avoid skin contact. In case of accidental exposure, rinse the affected area with copious quantities of water.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs:

Common (1 to 10 animals / 100 animals treated):	Pinnal erythema[1]
Uncommon (1 to 10 animals / 1,000 animals treated):	Impaired hearing[2]

[1] Mild
[2] Usually temporary and primarily in geriatric dogs.

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

The safety of the veterinary medicinal product has not been established during pregnancy or lactation.

Pregnancy and lactation:
Do not use during the whole or part of the pregnancy.
The use is not recommended during lactation.

Laboratory studies in puppies have shown evidence of arthropathy after systemic administration of orbifloxacin. Fluoroquinolones are known to cross the placenta and to be distributed into milk.

Fertility:
Studies to determine the effect of orbifloxacin on fertility of dogs have not been conducted.
Do not use in breeding animals.

3.8 Interaction with other medicinal products and other forms of interaction

No data available.

3.9 Administration routes and dosage

Auricular use.

One drop contains 267 mcg orbifloxacin, 27 mcg mometasone furoate and 27 mcg posaconazole.

The external ear canal should be meticulously cleaned and dried before treatment. Excess hair around the treatment area should be cut.

Shake well before use.

Dogs weighing less than 2 kg, apply 2 drops to the ear once a day.
Dogs weighing 2 - 15 kg, apply 4 drops to the ear once a day.
Dogs weighing 15 kg or more, apply 8 drops to the ear once a day.

Treatment should continue for 7 consecutive days.

After application, the base of the ear may be massaged briefly and gently to allow the veterinary medicinal product to penetrate the lower part of the ear canal.

Posatex is a viscous suspension. The inherent viscosity will result in a reduced delivery volume compared to the fill volume (see section 5.4).

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

Administration of the recommended dose (4 drops per ear) 5 times daily for 21 consecutive days to dogs weighing 7.6 to 11.4 kg bodyweight caused a slight decrease in serum cortisol response after adrenocorticotropic hormone (ACTH) administration in an ACTH stimulation test. Discontinuation of treatment will result in a complete return to normal adrenal response.

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

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QS02CA91

4.2 Pharmacodynamics

Orbifloxacin is a synthetic broad-spectrum bactericidal agent classified as a quinolone carboxylic acid derivative, or more specifically, a fluoroquinolone. The bactericidal action of orbifloxacin results from interference with the enzymes DNA topoisomerase II (DNA-gyrase) and DNA topoisomerase IV which are needed for the synthesis and maintenance of bacterial DNA. Such impairment disrupts replication of the bacterial cell, leading to rapid cell death. The rapidity and extent of killing are directly proportional to the drug concentration. Orbifloxacin has *in vitro* activity against a wide range of Gram-positive and Gram-negative organisms.

Mometasone furoate is a corticosteroid with high topical potency but little systemic effect. Like other topical corticosteroids, it has anti-inflammatory and anti-pruritic properties.

Posaconazole is a broad-spectrum triazole antifungal agent. The mechanism by which Posaconazole exerts fungicidal action involves the selective inhibition of the enzyme lanosterol 14-demethylase (CYP51) involved in ergosterol biosynthesis in yeasts and filamentous fungi. In *in vitro* tests, posaconazole has shown fungicidal activity against most of the approximately 7,000 strains of yeast and filamentous fungi tested. Posaconazole is 40 – 100 times more potent *in vitro* against *Malassezia pachydermatis* than clotrimazole, miconazole and nystatin.

Resistance to fluoroquinolones occurs by chromosomal mutation with three mechanisms: Decrease of the bacterial wall permeability, expression of efflux pump, or mutation of enzymes responsible for the molecule's binding site. Cross-resistance across the fluoroquinolone class of antibiotics is common. *Malassezia pachydermatis* resistance to azoles, including posaconazole, has not been reported.

The *in vitro* activity of orbifloxacin against pathogens isolated from clinical cases of canine otitis externa in an EU field trial conducted in 2000 - 2001 was:

Minimum Inhibitory Concentrations vs. Orbifloxacin – Summary

Pathogen	**N**	**Min**	**Max**	**MIC_{50}**	**MIC_{90}**
E coli	10	0.06	0.5	0.125	0.5
Enterococci	19	0.250	16	4	8
Proteus mirabilis	9	0.5	8	1	8
Pseudomonas aeruginosa	18	1	> 16	4	8
Staphylococcus intermedius	96	0.25	2	0.5	1
Streptococcus ß-*haemolyticus* G	19	2	4	2	4

4.3 Pharmacokinetics

Systemic absorption of the active substances was determined in single-dose studies with [^{14}C]-orbifloxacin, [^{3}H]-mometasone furoate and [^{14}C]-posaconazole contained within the Posatex formulation and placed into the ear canals of normal Beagle dogs. Most of the absorption occurred in the first few days after administration. The extent of percutaneous absorption of topically administered veterinary medicinal products is determined by many factors including the integrity of the epidermal barrier. Inflammation can increase the percutaneous absorption of veterinary medicinal products.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

None known.
Studies with a range of proprietary ear cleaners have shown no chemical incompatibilities.

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:
8.8 mL: 7 days
17.5 mL and 35.1 mL: 28 days

5.3 Special precautions for storage

Keep the bottle in the outer carton.

5.4 Nature and composition of immediate packaging

White HDPE bottle with a white LDPE cap, a natural or white LDPE applicator and a sheath.

Pack sizes: 8.8 mL (corresponding to 5.0 mL delivery volume), 17.5 mL (corresponding to 12.6 mL delivery volume), and 35.1 mL (corresponding to 28.6 mL delivery volume).

Not all pack sizes may be marketed.

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

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 national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/08/081/001
EU/2/08/081/002
EU/2/08/081/003

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 23 June 2008.

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

{DD month YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

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

ANNEX II

OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

None

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carboard box, 17.5 mL / 35.1 mL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Posatex ear drops suspension

2. STATEMENT OF ACTIVE SUBSTANCES

Orbifloxacin	8.5 mg/ml
Mometasone furoate	0.9 mg/ml
Posaconazole	0.9 mg/ml

3. PACKAGE SIZE

17.5 mL
35.1 mL

4. TARGET SPECIES

Dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Auricular use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

Once opened use within 28 days.

9. SPECIAL STORAGE PRECAUTIONS

Keep the bottle in the outer carton.

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

Intervet International B.V.

14. MARKETING AUTHORISATION NUMBERS

EU/2/08/081/002 17.5 mL bottle
EU/2/08/081/003 35.1 mL bottle

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carboard box, 8.8 mL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Posatex ear drops suspension

2. STATEMENT OF ACTIVE SUBSTANCES

Orbifloxacin	8.5 mg/ml
Mometasone furoate	0.9 mg/ml
Posaconazole	0.9 mg/ml

3. PACKAGE SIZE

8.8 mL

4. TARGET SPECIES

Dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Auricular use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

Once opened use within 7 days.

9. SPECIAL STORAGE PRECAUTIONS

Keep the bottle in the outer carton.

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

Intervet International B.V.

14. MARKETING AUTHORISATION NUMBERS

EU/2/08/081/001 8.8 mL bottle

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Bottle 17.5 mL and 35.1 mL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Posatex ear drops suspension

2. STATEMENT OF ACTIVE SUBSTANCES

Orbifloxacin	8.5 mg/ml
Mometasone furoate	0.9 mg/ml
Posaconazole	0.9 mg/ml

3. TARGET SPECIES

Dogs.

4. ROUTES OF ADMINISTRATION

Auricular use.
Read the package leaflet before use.

5. WITHDRAWAL PERIODS

6. EXPIRY DATE

Exp. {mm/yyyy}

Once opened use within 28 days.

7. SPECIAL STORAGE PRECAUTIONS

Keep the bottle in the outer carton.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.

9. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Bottle 8.8 mL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Posatex

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Orbifloxacin	8.5 mg/ml
Mometasone furoate	0.9 mg/ml
Posaconazole	0.9 mg/ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

Once opened use within 7 days.

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Posatex ear drops suspension for dogs

2. Composition

Orbifloxacin	8.5 mg/ml
Mometasone furoate (as monohydrate)	0.9 mg/ml
Posaconazole	0.9 mg/ml

White to off-white viscous suspension.

3. Target species

Dogs.

4. Indications for use

Treatment of acute otitis externa and acute exacerbations of recurrent otitis externa, associated with bacteria susceptible to orbifloxacin and fungi susceptible to posaconazole, in particular *Malassezia pachydermatis.*

5. Contraindications

Do not use if the eardrum is perforated.
Do not use in case of hypersensitivity to the active substance, to any of the ingredients, to corticosteroids, to other azole antifungal agents or to other fluoroquinolones.
Do not use during the whole or part of the pregnancy.

6. Special warnings

Special warnings:
Bacterial and fungal otitis is often secondary in nature. The underlying cause should be identified and treated.

Special precautions for safe use in the target species:
Heavy reliance on a single class of antibiotic may result in the induction of resistance in a bacterial population. 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 antibiotics.

Use of the veterinary medicinal product should be based on identification and susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at local/regional level.

Use of the product should be in accordance with official, national and regional antimicrobial policies.

An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

Narrow spectrum antibiotic therapy with a lower risk of antimicrobial resistance selection should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

Quinolone class veterinary medicinal products have been associated with cartilage erosions in weight-bearing joints and other forms of arthropathy in immature animals of various species. Therefore, do not use in animals less than 4 months of age.

Prolonged and intensive use of topical corticosteroids preparation is known to trigger local and systemic effects, including suppression of adrenal function, thinning of the epidermis and delayed healing.

Before the veterinary medicinal product is applied, the **external auditory canal** must be examined thoroughly to ensure that the ear drum is not perforated in order to avoid the risk of transmission of the infection to the middle ear and to prevent damage to the cochlear and vestibular apparatus.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Wash hands carefully after applying the veterinary medicinal product. Avoid skin contact. In case of accidental exposure, rinse the affected area with copious quantities of water.

Pregnancy:
The safety of the veterinary medicinal product has not been established during pregnancy or lactation.
Do not use during the whole or part of the pregnancy.

Lactation:
The use of the veterinary medicinal product is not recommended during lactation.
Laboratory studies in puppies have shown evidence of arthropathy after systemic administration of orbifloxacin. Fluoroquinolones are known to cross the placenta and to be distributed into milk.

Fertility:
Studies to determine the effect of orbifloxacin on fertility in dogs have not been conducted.
Do not use in breeding animals.

Interaction with other medicinal products and other forms of interaction:
No clinical data available.

Overdose:
Administration of the recommended dose (4 drops per ear) 5 times daily for 21 consecutive days to dogs weighing 7.6 to 11.4 kg bodyweight caused a slight decrease in serum cortisol response after adrenocorticotropic hormone (ACTH) administration in an ACTH stimulation test. Discontinuation of treatment will result in a complete return to normal adrenal response.

Major incompatibilities:
None known.
Studies with a range of proprietary ear cleaners have shown no chemical incompatibilities.

7. Adverse events

Dogs:

Common (1 to 10 animals / 100 animals treated):	Pinnal erythema[1]

Uncommon (1 to 10 animals / 1,000 animals treated):	Impaired hearing[2]

[1] Mild
[2] Usually temporary and primarily in geriatric dogs.

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 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

Auricular use.
One drop contains 267 mcg orbifloxacin, 27 mcg mometasone furoate and 27 mcg posaconazole.

Shake well before use.

With dogs weighing less than 2 kg, apply 2 drops to the ear once a day.
With dogs weighing 2-15 kg, apply 4 drops to the ear once a day.
With dogs weighing 15 kg or more, apply 8 drops to the ear once a day.

Treatment should continue for 7 consecutive days.

Posatex is a viscous suspension. The inherent viscosity will result in a reduced delivery volume compared to the fill volume (see section “Marketing authorisation numbers and pack sizes”).

9. Advice on correct administration

The external ear canal should be meticulously cleaned and dried before treatment. Excess hair around the treatment area should be cut.

After application, the base of the ear may be massaged briefly and gently to allow the preparation to penetrate the lower part of the ear canal.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

Keep the bottle in the outer carton.
Do not use this veterinary medicinal product after the expiry date which is stated on the carton and bottle after Exp. The expiry date refers to the last day of that month.

Shelf life after first opening the immediate packaging:
8.8 mL: Once opened use within 7 days.
17.5 mL and 35.1 mL: Once opened use within 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 or pharmacist 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

EU/2/08/081/001 (8.8 mL bottle)
EU/2/08/081/002 (17.5 mL bottle)
EU/2/08/081/003 (35.1 mL bottle)

Pack sizes: 8.8 mL (corresponding to 5.0 mL delivery volume), 17.5 mL (corresponding to 12.6 mL delivery volume) and 35.1 mL (corresponding to 28.6 mL delivery volume).

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{DD month YYYY}

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:

Intervet International B.V., Wim de Körverstraat 35, 5831 AN Boxmeer, The Netherlands

België/Belgique/Belgien
Tél/Tel: + 32 (0)2 370 94 01

Република България
Тел: + 359 28193749

Česká republika
Tel: + 420 233 010 242

Danmark
Tlf: + 45 44 82 42 00

Lietuva
Tel: + 37052196111

Luxembourg/Luxemburg
Tél/Tel: + 32 (0)2 370 94 01

Magyarország
Tel.: + 36 1 439 4597

Malta
Tel: + 39 02 516861

Deutschland
Tel: + 49 (0)8945614100

Eesti
Tel: + 37052196111

Ελλάδα
Τηλ: + 30 210 989 7452

España
Tel: + 34 923 19 03 45

France
Tél: + 33 (0)241228383

Hrvatska
Tel: + 385 1 6611339

Ireland
Tel: + 353 (0) 1 2970220

Ísland
Sími: + 354 535 7000

Italia
Tel: + 39 02 516861

Κύπρος
Τηλ: + 30 210 989 7452

Latvija
Tel: + 37052196111

Nederland
Tel: + 32 (0)2 370 94 01

Norge
Tlf: + 47 55 54 37 35

Österreich
Tel: + 43 (1) 256 87 87

Polska
Tel.: + 48 22 18 32 200

Portugal
Tel: + 351 214 465 700

România
Tel: + 40 21 311 83 11

Slovenija
Tel: + 385 1 6611339

Slovenská republika
Tel: + 420 233 010 242

Suomi/Finland
Puh/Tel: + 358 10 2310 750

Sverige
Tel: + 46 (0)8 522 216 60

United Kingdom (Northern Ireland)
Tel: + 353 (0) 1 2970220

Manufacturer responsible for batch release:

Vet Pharma Friesoythe GmbH
Sedelsberger Strasse 2
26169 Friesoythe
Germany