ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Posatex ear drops suspension for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substances:

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

Excipients:

Paraffin liquid

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Ear drops suspension
White to off-white viscous suspension

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the 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.*

4.3 Contraindications

Do not use if the eardrum is perforated.
Do not use in case of hypersensitivity to the active substances, 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).

4.4 Special warnings for each target species

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

4.5 Special precautions for use

Special precautions for use in animals

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 product should be based on susceptibility testing of isolated bacteria, and/or other appropriate diagnostic tests.

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. See section 4.10..

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.

4.6 Adverse reactions (frequency and seriousness)

Mild erythematous lesions have been observed.
The use of auricular preparations may be associated with hearing impairment, usually temporary, and primarily in geriatric dogs.

4.7 Use during pregnancy, lactation or lay

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

Pregnancy:
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.

4.8 Interaction with other medicinal products and other forms of interaction

No data available..

4.9 Amounts to be administered and administration route

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

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

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.

4.11 Withdrawal period

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Otologic - Corticosteroids and anti-infectives in combination.
ATC vet code: QS02CA91

5.1 Pharmacodynamic properties

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

5.2 Pharmacokinetic particulars

Systemic absorption of the active ingredients 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 topical medications is determined by many factors including the integrity of the epidermal barrier. Inflammation can increase the percutaneous absorption of veterinary medicinal products.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lauric acid
Paraffin, Liquid
Plasticised hydrocarbon gel (5% polyethylene in 95% mineral oil)

6.2 Incompatibilities

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

6.3 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

6.4. Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.
Store in the original bottle and carton.

6.5 Nature and composition of immediate packaging

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

packl sizes: 8.8 mL (7.5 g), 17.5 mL (15 g) and 35.1 mL (30 g)

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

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

7. MARKETING AUTHORISATION HOLDER

Intervet International BV
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

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

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23/06/2008
Date of last renewal: 23/06/2013

10 DATE OF REVISION OF THE TEXT

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. STATEMENT OF THE MRLs

D. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

A. MANUFACTURING AUTHORISATION HOLDER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Vet Pharma Friesoythe
Sedelsberger Straße 2
26169 Friesoythe
Germany

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

Not applicable.

D. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

None.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Box 17.5 mL and 35.1 mL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Posatex ear drops suspension for dogs

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

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

3. PHARMACEUTICAL FORM

Ear drops suspension

4. PACKAGE SIZE

17.5 mL
35.1 mL

5. TARGET SPECIES

Dogs

6. INDICATIONS

7. METHOD AND ROUTE OF ADMINISTRATION

For auricular use only.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Not applicable.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month /year}
Once opened use within 28 days.

11. SPECIAL STORAGE CONDITIONS

Store in the original carton.

12. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Dispose of waste material in accordance with local requirements.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only - to be supplied only on veterinary prescription.

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

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Intervet International BV
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

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

17. MANUFACTURER'S BATCH NUMBER

Batch {number}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Box 8.8 mL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Posatex ear drops suspension for dogs

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

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

3. PHARMACEUTICAL FORM

Ear drops suspension

4. PACKAGE SIZE

8.8 mL

5. TARGET SPECIES

Dogs

6. INDICATIONS

7. METHOD AND ROUTES OF ADMINISTRATION

For auricular use only.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Not applicable.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {2 digits /year}
Once opened use within 7 days.

11. SPECIAL STORAGE CONDITIONS

Store in the original bottle and carton.

12. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read the package leaflet

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only - to be supplied only on veterinary prescription.

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

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Intervet International BV
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/08/081/001

17. MANUFACTURER'S BATCH NUMBER

Batch {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Bottle 17.5 mL and 35.1 mL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Posatex ear drops suspension for dogs

2. QUANTITY OF THE ACTIVE SUBSTANCES

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

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

17.5 mL
35.1 mL

6. BATCH NUMBER

Batch {number}

7. EXPIRY DATE

EXP {2 month/year}
Once opened use within 28 days.

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Bottle 8.8 mL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Posatex ear drops for dogs

2. QUANTITY OF THE ACTIVE SUBSTANCES

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

6. BATCH NUMBER

Batch {number}

7. EXPIRY DATE

EXP {2 digits /year}
Once opened use within 7 days.

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:
Posatex ear drops suspension dogs

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:

Intervet International BV
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

Manufacturer for the batch release:

Vet Pharma Friesoythe
Sedelsberger Straße 2
26169 Friesoythe
Germany

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Posatex, ear drops suspension for dogs

3. STATEMENT OF THE ACTIVE SUBSTANCES AND OTHER INGREDIENTS

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

4. INDICATIONS

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 any of the ingredients of the veterinary medicinal product, to corticosteroids, to other azole antifungal agents or to other fluoroquinolones.

6. ADVERSE REACTIONS

Mild erythematous lesions have been observed.
The use of auricular preparations may be associated with hearing impairment, usually temporary, and primarily in geriatric dogs.

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs

8. DOSAGE FOR EACH SPECIES, ROUTES AND METHOD OF ADMINISTRATION

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

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 PERIOD

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special storage conditions.

Do not use after the expiry date, which is stated on the label.

Shelf-life after first opening the bottle:
8.8 mL: Once opened use within 7 days.
17.5 and 35.1 mL: Once opened use within 28 days.

12. SPECIAL WARNINGS

Special warnings for each target species:

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

Special precautions for use in animals:

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 product should be based on susceptibility testing of isolated bacteria, and/or other appropriate diagnostic tests.

Quinolone class drugs 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 data available.

Overdose (symptoms, emergency procedures, 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.

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

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

Detailed information on this product is available on the website of the European Medicines Agency http://www.ema.europa.eu/.

15. OTHER INFORMATION

Not all pack sizes may be marketed.