ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Mometamax Ultra ear drops, suspension for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substances:

Each dose (0.8 ml) contains:

Gentamicin sulfate equivalent to	6880 IU gentamicin
Posaconazole	2.08 mg
Mometasone furoate monohydrate equivalent to	1.68 mg mometasone furoate

Excipients:

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 or acute exacerbation of recurrent otitis externa caused by mixed bacterial and fungal infections with *Staphylococcus pseudintermedius* susceptible to gentamicin and *Malassezia pachydermatis* susceptible to posaconazole.

4.3 Contraindications

Do not use in cases of hypersensitivity to the active substances or to any of the excipients, to corticosteroids, to other azole antifungal agents and to other aminoglycosides.
Do not use if the eardrum is perforated.
Do not use in pregnant or breeding animals.
Do not use concurrently with substances known to cause ototoxicity.
Do not use in dogs with generalised demodicosis.

4.4 Special warnings for each target species

Antimicrobial activity can be reduced by low pH and the presence of purulent and/or inflammatory debris. Ears must be cleaned before administration of the veterinary medicinal product. Compatibility with ear cleaners has not been demonstrated.

Bacterial and fungal otitis is often secondary to other conditions. In animals with a history of recurrent otitis externa, the underlying causes of the condition such as allergy or anatomical conformation of the ear must be addressed in order to avoid ineffective treatment with a veterinary medicinal product.

Efficacy of this veterinary medicinal product was not assessed in dogs with atopic or allergic skin conditions.

Cross-resistance between gentamicin and other members of the aminoglycoside class has been shown in *Staphylococcus pseudintermedius*. Use of the product should be carefully considered when susceptibility testing has shown resistance to aminoglycosides because its effectiveness may be reduced. Co-selection for other classes of antimicrobials is common (see section 5.1. for further details).

4.5 Special precautions for use

Special precautions for use in animals

The safety of the product has not been established in dogs less than 3 months of age or weighing less than 3 kg.

Before the veterinary medicinal product is applied, the external auditory canal must be examined thoroughly to ensure that the eardrum 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.

Re-evaluate the dog immediately if worsening of clinical signs, hearing loss or signs of vestibular dysfunction are observed during treatment or if the dog is not showing signs of improvement by day 14.

Cytology of ear canal is recommended prior to the use of the product to identify a mixed infection.

This antimicrobial combination should only be used where diagnostic testing has indicated the need for simultaneous administration of each of the active substances.

Use of the product should be based on identification and susceptibility testing of the target pathogens. Ideally, 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.

If hypersensitivity to any of the components occurs, treatment should be discontinued and appropriate therapy instituted.

In case of parasitic otitis, an appropriate acaricidal treatment should be implemented.

Prolonged and intensive use of topical corticosteroids preparation is known to trigger systemic effects, including suppression of adrenal function (see section 4.10).

Use with precaution in dogs with suspected or confirmed endocrine disorder (i.e. diabetes mellitus; hypo-thyroid disease, etc).

Ototoxicity may be associated with gentamicin treatment. Experience shows that geriatric dogs are more at risk of hearing impairment after topical ear product administration.

Objective hearing assessments were not performed in the pivotal field trial. Dogs with signs of impaired balance or loss of hearing after administration should be re-examined.

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

The veterinary medicinal product may be slightly irritating to eyes. Accidental eye exposure may occur when the dog shakes its head during or just after administration. In case of accidental eye

contact, flush the eyes thoroughly with water for 15 minutes. If symptoms develop, seek medical advice and show the package leaflet or the label to a physician.

Although no potential for skin irritation was indicated by experimental studies, contact of the product with the skin should be avoided. In case of accidental skin contact, wash the exposed skin with water.

Close contact between the dog and children should be limited in the days following the treatment due to unknown amount of the product possibly leaking from treated ear/s.

The product may be harmful after ingestion. Avoid ingestion of the product including hand-to-mouth exposure. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

No adverse reactions related to treatment were observed in clinical trials.

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation. Do not use during pregnancy and lactation.
Studies to determine the effect 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

None known.

4.9 Amounts to be administered and administration route

Auricular use.
Single treatment.
The recommended dosage is a single dose of 0.8 ml per infected ear.

The maximum clinical response may not be seen until 28 to 42 days after administration.

Instructions for use:

The product should be administered only by veterinarians or by trained personnel under close veterinary supervision.

Clean and dry the external ear canal before administering the product.

The product is preservative-free and should be handled using clean technique.

Before first use, shake the bottle vigorously for 15 seconds. Unwrap the syringe with the adapter attached. Remove the cap from the bottle and insert the adapter by pressing it firmly into the top of the bottle using the attached syringe. Follow steps 1. to 5. of the dosing instructions.

1. Invert the bottle and draw up 0.8 ml per ear.
2. Return the bottle to an upright position and remove the syringe from the adapter.
3. Leave the adapter in place and replace the cap on the bottle.

4. Place the tip of the syringe at the entrance of external ear and administer the 0.8 ml dose. The applied dose will flow into the ear canal.
5. After application, the ear can be massaged gently to ensure distribution of the product throughout the ear canal. Following dosing, the head should be restrained for approx. 2 minutes to prevent shaking and dislodging of product.

Use a new syringe for each infected ear. Shake the bottle vigorously for 15 seconds before each use. Remove the cap. Insert the syringe tip into the adapter. Follow steps 1 to 5 of the dosing instructions.

It is recommended not to repeat ear cleaning for at least 28 days after administration unless clinically indicated. Care should also be taken to avoid water entering the ear canal during this period. For this reason, dogs should not be bathed nor allowed to swim until confirmation of clinical cure 28-42 days after treatment.

Dogs should be re-examined 28-42 days after product administration to assess response to treatment. After confirmation of clinical resolution, the ears should be cleaned to remove any remaining debris or residual product.

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

Auricular administration to puppies at up to 5 times the recommended dose to both ears on 3 occasions at 2-week intervals was well-tolerated.

All findings were consistent with glucocorticoid administration. Findings in the 3X and 5X overdose groups included mild eosinopenia, lower baseline and ACTH-induced cortisol levels, lower mean adrenal weights with correlating minimal to mild atrophy of the adrenal cortex. Minimal to mild atrophy of the epidermis of the external auditory canal and the epithelium of the external surface of the tympanic membrane, consistent with the pharmacological effects of glucocorticoids, was observable in the 1X, 3X and 5X group, and shown to be reversible after cessation of treatment. ACTH administration at the end of the study elicited an increase in cortisol levels in all study groups, indicative of sufficient adrenal function.

All findings were of low severity and are considered reversible after cessation of treatment.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

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

5.1 Pharmacodynamic properties

The veterinary medicinal product is a fixed combination of three active substances (antibiotic, antifungal and corticosteroid).

Gentamicin is an aminoglycoside bactericidal, concentration-dependent antibiotic. Its mechanism of action involves inhibition of bacterial protein synthesis by binding to 30S ribosomes. In *S. pseudintermedius*, the most common mechanism of antimicrobial resistance is the production of aminoglycoside modifying enzymes encoded by the transposon-borne resistance genes, aac(6')-aph(2"), conferring cross-resistance to all aminoglycosides with the exception of streptomycin. In addition, co-resistance against other classes of antibiotics is commonly seen (including tetracyclines,

oxacillin (MRSP), macrolides etc) in various bacterial species including *S. pseudintermedius* (e.g. MRSP).

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, nystatin and terbinafine.

The most common mechanisms of resistance to azoles in clinical isolates are alterations in lanosterol 14α-demethylase biosynthesis (e.g. by mutations), increased production of this enzyme or increased efflux (e.g. by ABC transporters or major facilitators). Posaconazole is not an MDR1 major facilitator substrate.

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

Table 1: Minimum Inhibitory Concentration (MIC) range, MIC_{50} and MIC_{90} of gentamicin determined for *Staphylococcus pseudintermedius* isolates (n=50).

Species	**MIC range µg/ml**	**MIC_{50} µg/ml**	**MIC_{90} µg/ml**
Staphylococcus pseudintermedius	≤ 0.063 - 16	0.125	0.25

Table 2: MIC range, MIC_{50} and MIC_{90} of posaconazole determined for *Malassezia pachydermatis* isolates (n=50).

Species	**MIC range µg/ml**	**MIC_{50} µg/ml**	**MIC_{90} µg/ml**
Malassezia pachydermatis	≤ 0.016	≤ 0.016	≤ 0.016

All isolates were collected from dogs between 2017 and 2020 in different European countries and were epidemiologically unrelated.

5.2 Pharmacokinetic particulars

Systemic absorption and depletion from the ear wax of the three active substances was determined after a single administration of the recommended dose into both ear canals of healthy beagle dogs. Plasma and ear wax concentrations were measured at 1, 7, 14, 21, 30, and 45 days post-administration.

Systemic exposure was only detected at 1-day post-administration with low plasma concentrations (≤ 7.9 ng/ml) of gentamicin and posaconazole. At 14 days and 45 days post-administration, only one dog out of eight was found to have a detectable amount of gentamicin and posaconazole in the plasma, respectively. Plasma concentrations for all other time points for gentamicin and posaconazole were below the limit of quantification. Plasma concentrations of mometasone furoate were below the limit of quantification at every time point.

Gentamicin, posaconazole, and mometasone furoate were detected in ear wax throughout the 45 day study with depletion occurring progressively. From days 1 to 14, concentrations of all three active substances were detectable in all animals. The number of animals with concentrations of active ingredients below the limit of quantification gradually increased (depending on the active ingredient) from one or two animals on day 21 to most of the animals on day 45 days post-administration. Gentamicin concentrations were above ten times the MIC_{90} of *S. pseudintermedius* in the majority of samples for 30 days post treatment.

The extent of transcutaneous absorption of topical medications is determined by many factors including the integrity of the epidermal barrier. The influence on the absorption of the veterinary medicinal product by factors such as inflammation and skin atrophy associated with prolonged treatment with glucocorticoids has not been established.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Paraffin liquid
Plasticized hydrocarbon gel (polyethylene, mineral oil)

6.2 Major incompatibilities

None known.

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: 3 months.

6.4. Special precautions for storage

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

6.5 Nature and composition of immediate packaging

White high-density polyethylene (HDPE) bottle with a white low-density polyethylene (LDPE) screw cap. One bottle contains sufficient product to withdraw 20 doses of 0.8 ml.

Polypropylene syringes of 1.0 ml capacity
Carton box containing 1 bottle, an LDPE adapter and 20 syringes.

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 B. V.
Wim de Körverstraat 35
5831 AN Boxmeer
Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/22/289/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22 November 2022

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. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Vet Pharma Friesoythe GmbH
Sedelsberger Straße 2-4
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

· **CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

For use by veterinary surgeons only.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Mometamax Ultra ear drops, suspension for dogs
gentamicin, posaconazole, mometasone furoate

2. STATEMENT OF ACTIVE SUBSTANCES

1 dose (0.8 ml): 6880 IU gentamicin, 2.08 mg posaconazole, 1.68 mg mometasone furoate

3. PHARMACEUTICAL FORM

Ear drops, suspension

4. PACKAGE SIZE

20 doses
20 syringes

5. TARGET SPECIES

Dogs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Auricular use.
Single treatment.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP

Once opened use within 3 months.

11. SPECIAL STORAGE CONDITIONS

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

Disposal: read 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. Administration by a veterinarian surgeon or under their close supervision.

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
Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/22/289/001

17. MANUFACTURER'S BATCH NUMBER

Lot

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Multidose bottle/HDPE

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Mometamax Ultra ear drops, suspension for dogs

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

1 dose (0.8 ml): 6880 IU gentamicin, 2.08 mg posaconazole, 1.68 mg mometasone furoate

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

20 doses

4. ROUTE(S) OF ADMINISTRATION

Auricular use.

5. WITHDRAWAL PERIOD(S)

6. BATCH NUMBER

Lot

7. EXPIRY DATE

EXP
Once opened use within 3 months.

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Mometamax Ultra ear drops, suspension for 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 B. V.
Wim de Körverstraat 35
5831 AN Boxmeer
Netherlands

Manufacturer responsible for batch release:
Vet Pharma Friesoythe GmbH
Sedelsberger Straße 2 - 4
26169 Friesoythe
Germany

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Mometamax Ultra ear drops, suspension for dogs
gentamicin, posaconazole, mometasone furoate

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each dose (0.8 ml) contains:

Gentamicin sulfate equivalent to	6880 IU gentamicin
Posaconazole	2.08 mg
Mometasone furoate monohydrate equivalent to	1.68 mg mometasone furoate

Ear drops, suspension.
White to off-white, viscous suspension.

4. INDICATION(S)

Treatment of acute otitis externa or acute exacerbation of recurrent otitis externa caused by mixed bacterial and fungal infections with *Staphylococcus pseudintermedius* susceptible to gentamicin and *Malassezia pachydermatis* susceptible to posaconazole.

5. CONTRAINDICATIONS

Do not use in cases of hypersensitivity to the active substances or to any of the excipients, to corticosteroids, to other azole antifungal agents and to other aminoglycosides.
Do not use if the eardrum is perforated.
Do not use in pregnant or breeding animals.
Do not use concurrently with substances known to cause ototoxicity.
Do not use in dogs with generalised demodicosis.

6. ADVERSE REACTIONS

No adverse reactions related to treatment were observed in clinical trials.

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 inform your veterinary surgeon.

7. TARGET SPECIES

Dogs

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Auricular use.
Single treatment.
The recommended dosage is a single dose of 0.8 ml per infected ear.

The maximum clinical response may not be seen until 28 to 42 days after administration.

9. ADVICE ON CORRECT ADMINISTRATION

The product should be administered only by veterinarians or by trained personnel under close veterinary supervision.

Clean and dry the external ear canal before administering the product.

The product is preservative-free and should be handled using clean technique.

Before first use, shake the bottle vigorously for 15 seconds. Unwrap the syringe with the adapter attached. Remove the cap from the bottle and insert the adapter by pressing it firmly into the top of the bottle using the attached syringe. Follow steps 1. to 5. of the dosing instructions.

1. Invert the bottle and draw up 0.8 ml per ear.
2. Return the bottle to an upright position and remove the syringe from the adapter.
3. Leave the syringe adapter in place and replace the cap on the bottle.

4. Place the tip of the syringe at the entrance of external ear and administer the 0.8 ml dose. The applied dose will flow into the ear canal.
5. After application, the ear can be massaged gently to ensure distribution of the product throughout the ear canal. Following dosing, the head should be restrained for approx. 2 minutes to prevent shaking and dislodging of product.

Use a new syringe for each infected ear. Shake the bottle vigorously for 15 seconds before each use. Remove the cap. Insert the syringe tip into the adapter. Follow steps 1 to 5 of the dosing instructions.

It is recommended not to repeat ear cleaning for at least 28 days after administration unless clinically indicated. Care should also be taken to avoid water entering the ear canal during this period. For this reason, dogs should not be bathed nor allowed to swim until confirmation of clinical cure 28-42 days after treatment.

Dogs should be re-examined 28-42 days after product administration to assess response to treatment. After confirmation of clinical resolution, the ears should be cleaned to remove any remaining debris or residual product.

10. WITHDRAWAL PERIOD(S)

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 this veterinary medicinal product after the expiry date which is stated on the outer carton and bottle after EXP.

Shelf life after first opening the container: 3 months.

12. SPECIAL WARNING(S)

Special warnings for each target species:
Antimicrobial activity can be reduced by low pH and the presence of purulent and/or inflammatory debris. Ears must be cleaned before administration of the veterinary medicinal product. Compatibility with ear cleaners has not been demonstrated.

Bacterial and fungal otitis is often secondary to other conditions. In animals with a history of recurrent otitis externa, the underlying causes of the condition such as allergy or anatomical conformation of the ear must be addressed in order to avoid ineffective treatment with a veterinary medicinal product. Efficacy of this veterinary medicinal product was not assessed in dogs with atopic or allergic skin conditions.

Cross-resistance between gentamicin and other members of the aminoglycoside class has been shown in *Staphylococcus pseudintermedius.* Use of the product should be carefully considered when susceptibility testing has shown resistance to aminoglycosides because its effectiveness may be reduced. Co-selection for other classes of antimicrobials is common.

Special precautions for use in animals:
The safety of the product has not been established in dogs less than 3 months of age or weighing less than 3 kg.

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.

Re-evaluate the dog immediately if worsening of clinical signs, hearing loss or signs of vestibular dysfunction are observed during treatment or if the dog is not showing signs of improvement by day 14.

Cytology of ear canal is recommended prior to the use of the product to identify a mixed infection.

This antimicrobial combination should only be used where diagnostic testing has indicated the need for simultaneous administration of each of the active substances.

Use of the product should be based on identification and susceptibility testing of the target pathogens. Ideally, 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.

If hypersensitivity to any of the components occurs, treatment should be discontinued and appropriate therapy instituted.

In case of parasitic otitis, an appropriate acaricidal treatment should be implemented.

Prolonged and intensive use of topical corticosteroids preparation is known to trigger systemic effects, including suppression of adrenal function.

Use with precaution in dogs with suspected or confirmed endocrine disorder (i.e. diabetes mellitus; hypo- thyroid disease, etc).

Ototoxicity may be associated with gentamicin treatment. Experience shows that geriatric dogs are more at risk of hearing impairment after topical ear product administration.

Objective hearing assessments were not performed in the pivotal field trial. Dogs with signs of impaired balance or loss of hearing after administration should be re-examined.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
The veterinary medicinal product may be slightly irritating to eyes. Accidental eye exposure may occur when the dog shakes its head during or just after administration.
In case of accidental eye contact, flush the eyes thoroughly with water for 15 minutes. If symptoms develop, seek medical advice and show the package leaflet or the label to a physician.

Although no potential for skin irritation was indicated by experimental studies, contact of the product with the skin should be avoided. In case of accidental skin contact, wash the exposed skin with water.

Close contact between the dog and children should be limited in the days following the treatment due to unknown amount of the product possibly leaking from treated ear/s.
The product may be harmful after ingestion. Avoid ingestion of the product including hand-to-mouth exposure. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

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

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

Interaction with other medicinal products and other forms of interaction:
None known.

Overdose (symptoms, emergency procedures, antidotes):
Auricular administration to puppies at up to 5 times the recommended dose to both ears on 3 occasions at 2-week intervals was well-tolerated.

All findings were consistent with glucocorticoid administration. Findings in the 3X and 5X overdose groups included mild eosinopenia, lower baseline and ACTH-induced cortisol levels, lower mean adrenal weights with correlating minimal to mild atrophy of the adrenal cortex. Minimal to mild

atrophy of the epidermis of the external auditory canal and the epithelium of the external surface of the tympanic membrane, consistent with the pharmacological effects of glucocorticoids, was observable in the 1X, 3X and 5X group, and shown to be reversible after cessation of treatment. ACTH administration at the end of the study elicited an increase in cortisol levels in all study groups, indicative of sufficient adrenal function.

All findings were of low severity and are considered reversible after cessation of treatment.

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

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

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

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

15. OTHER INFORMATION

Pack size: Carton box containing 1 bottle, an LDPE adapter and 20 syringes.