ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

OUTER CARTON

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Neptra ear drops solution for dogs
terbinafine hydrochloride/florfenicol/mometasone furoate

2. STATEMENT OF ACTIVE SUBSTANCES

1 dose (1 ml): 16.7 mg terbinafine hydrochloride, 16.7 mg florfenicol, 2.2 mg mometasone furoate

3. PHARMACEUTICAL FORM

Ear drops solution

4. PACKAGE SIZE

1 tube
2 tubes
10 tubes
20 tubes

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

11. SPECIAL STORAGE CONDITIONS

Do not store above 25°C.

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

Elanco Animal Health GmbH
Alfred-Nobel-Str. 50
40789 Monheim
Germany

16. MARKETING AUTHORISATION NUMBER

Vm 04895/5007

17. MANUFACTURER'S BATCH NUMBER

Lot

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Neptra ear drops for dogs

terbinafine hydrochloride, florfenicol, mometasone furoate (EN or Latin)

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

16.7 mg terbinafine hydrochloride, 16.7 mg florfenicol, 2.2 mg mometasone furoate

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

1 ml

4. ROUTE(S) OF ADMINISTRATION

Auricular use

5. WITHDRAWAL PERIOD

6. BATCH NUMBER

Lot

7. EXPIRY DATE

EXP

8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Single-dose container

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Neptra ear drops for dogs

terbinafine hydrochloride, florfenicol, mometasone furoate (EN or Latin)

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

16.7 mg terbinafine hydrochloride, 16.7 mg florfenicol, 2.2 mg mometasone furoate

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

1 ml

4. ROUTE(S) OF ADMINISTRATION

Auricular use

5. WITHDRAWAL PERIOD

6. BATCH NUMBER

Lot

7. EXPIRY DATE

EXP

8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.
(Reference is made to the pictogram of a dog in section 1).

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Neptra ear drops solution 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:
Elanco Animal Health GmbH
Alfred-Nobel-Str. 50
40789 Monheim
Germany

Manufacturer responsible for batch release:
KVP Pharma + Veterinär Produkte GmbH
Projensdorfer Str. 324,
24106 Kiel
Germany

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Neptra ear drops solution for dogs
florfenicol/terbinafine hydrochloride/mometasone furoate

3. STATEMENT OF THE ACTIVE SUBSTANCES AND OTHER INGREDIENTS

One dose (1 ml) contains 16.7 mg florfenicol, 16.7 mg terbinafine hydrochloride (equivalent to 14.9 mg terbinafine base) and 2.2 mg mometasone furoate.

Clear, colourless to yellow, slightly viscous liquid.

4. INDICATION(S)

For the treatment of acute canine otitis externa or acute exacerbations of recurrent otitis caused by mixed infections of susceptible strains of bacteria sensitive to florfenicol (*Staphylococcus pseudintermedius*) and fungi sensitive to terbinafine (*Malassezia pachydermatis*).

5. CONTRAINDICATIONS

Do not use in case of hypersensitivity to the active substances, to other corticosteroids or to any of the excipients.
Do not use if the ear drum is perforated.
Do not use in dogs with generalised demodicosis. Do not use in pregnant or breeding animals.

6. ADVERSE REACTIONS

Deafness or impaired hearing have been reported in very rare cases in dogs, mainly in elderly animals, in post authorisation experience. Vocalisation, head shaking and application site pain shortly after product application have been reported in very rare cases in post authorisation experience. Ataxia, internal ear disorder, nystagmus, emesis, application site erythema, hyperactivity, anorexia and application site inflammation and eye disorders (such as eye irritation, blepharospasm, conjunctivitis, corneal ulcer, keratoconjunctivitis sicca) have been reported in very rare cases in post authorisation experience.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

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.

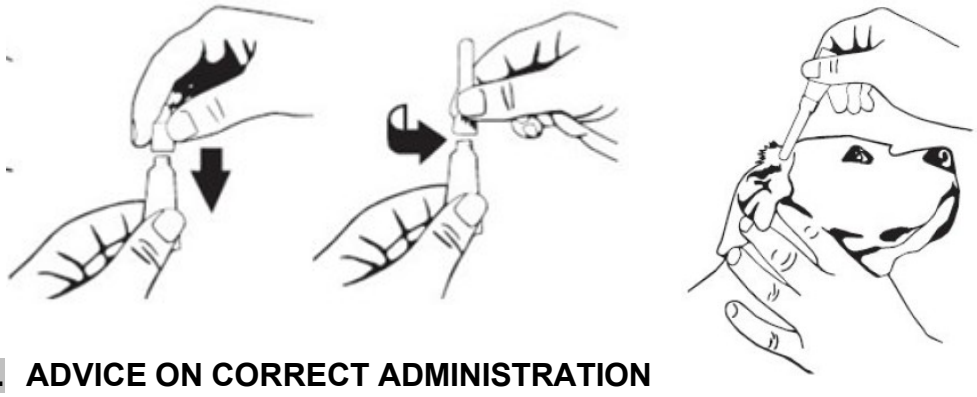
7. TARGET SPECIES

Dogs

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

Auricular use.
Single treatment.

The recommended dosage is 1 single-dose container (i.e. 1 ml of solution) per infected ear.
The maximum clinical response may not be seen until 28 days after administration.
Shake well before use for 5 seconds.
While holding the single-use container in an upright position, remove the cap.
Use the upper end of the cap to completely break the seal and then remove cap from the single-use container.
Screw the applicator nozzle onto the single-use container.
Insert the applicator nozzle into the affected external ear canal and squeeze the entire contents into the ear.



9. ADVICE ON CORRECT ADMINISTRATION

Clean with saline solution and dry the external ear canal before administering the product.
After application, gently massage the base of the ear for 30 seconds to allow distribution of the solution. Restrain the dog's head to prevent shaking, for 2 minutes.

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Do not store above 25°C.

Do not use this veterinary medicinal product after the expiry date which is stated on the outer carton and container label after EXP.

12. SPECIAL WARNING(S)

Special warnings for each target species:
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 to avoid ineffective treatment with a veterinary medicinal product.
In cases of parasitic otitis, an appropriate acaricidal treatment should be implemented.
Ears must be cleaned before administration of the product. It is recommended not to repeat ear cleaning until 28 days after administration of the product. In clinical trials, only saline was used for ear cleaning before treatment initiation with the veterinary medicinal product.
This combination is intended for the treatment of acute otitis when mixed infections caused by *Staphylococcus pseudintermedius* susceptible to florfenicol and *Malassezia pachydermatis* susceptible to terbinafine have been demonstrated.

Special precautions for use in animals:
The safety of the veterinary medicinal product has not been established in dogs less than 3 months of age. Target animal safety was not studied in dogs under 4 kg bodyweight. However, no safety issues were identified in field studies in dogs weighing less than 4kg.
Before the veterinary medicinal product is applied, the external auditory canal must be examined thoroughly to ensure that the ear drum is not perforated.
Re-evaluate the dog if hearing loss or signs of vestibular dysfunction are observed during treatment.
After the administration, wet ears or clear discharge can be observed which is not related to the disease pathology.
Whenever possible, the use of the veterinary medicinal product should be based on identification of infecting organisms and susceptibility testing.
Use of the veterinary medicinal product deviating from the instructions given in the package leaflet may increase the prevalence of bacteria resistant to florfenicol and fungi resistant to terbinafine and may decrease the effectiveness of treatment with other antibiotics and antifungal agents.
Decreased cortisol levels were observed after product instillation in tolerance studies (before and after ACTH stimulation), indicating that mometasone furoate is absorbed and enters the systemic circulation. The main findings observed at the 1X dose were decreases in cortical response to ACTH stimulation, decreased absolute lymphocyte and eosinophil counts, and decreased adrenal weight. Prolonged and intensive use of topical corticosteroid preparations is known to trigger systemic effects, including suppression of adrenal function.
If hypersensitivity to any of the components occurs, the ear should be thoroughly washed. Additional corticosteroid treatments should be avoided.
Use with caution in dogs with a suspected or confirmed endocrine disorder (i.e., diabetes mellitus; hypo- or hyperthyroidism, etc.).
Caution should be taken to prevent the veterinary medicinal product from getting into the eyes of the dog being treated e.g. by restraining the dog's head to prevent shaking (see section "advice on correct administration"). In case of exposure to the eye, rinse with plenty of water.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
The veterinary medicinal product has serious eye irritation potential. Accidental eye exposure may occur when the dog shakes its head during or just after administration. To avoid this risk for the owners, it is recommended that this veterinary product is administered only by veterinarians or under their close supervision. Appropriate measures (e.g. wearing safety glasses during administration, massaging the ear canal well after administration to ensure even distribution of product, restraining the dog after administration) are needed to avoid exposure to the eyes. In case of accidental ocular exposure, flush the eyes thoroughly with water for 10 to 15 minutes. If symptoms develop, seek medical advice and show the package leaflet or the label to the 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 exposed skin thoroughly with water.
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.
Compatibility with ear cleaners, other than saline solution, has not been demonstrated.

Overdose (symptoms, emergency procedures, antidotes):
Auricular administration of up to five times the recommended dose at biweekly intervals for a total of three treatments was generally well tolerated. The most prominent effects were consistent with glucocorticoid administration; specific observations included suppression of the adrenal cortical response to ACTH-stimulation, decreased adrenal weight and atrophy of the adrenal cortex, decreased absolute lymphocyte and eosinophil counts, increased absolute neutrophil count, increased liver weight with hepatocellular enlargement/cytoplasmic change, and decreased thymus weight. Other potentially treatment-related effects included mild changes to aspartate aminotransferase (AST), total protein, cholesterol, inorganic phosphorus, creatinine and calcium. After 3 weekly administrations of up to 5x the recommended posology, the test product induced slight erythema in one or both ears that returned to normal within 48 hours.

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

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

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon 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

August 2023

15. OTHER INFORMATION

Pack sizes: 1, 2, 10 or 20 tubes. Not all pack sizes may be marketed.

Approved: 15 August 2023