Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Marbodex Aural Ear Drops, Suspension for Dogs

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains:

Active substances:

Marbofloxacin	3.0 mg
Clotrimazole	10.0 mg
Dexamethasone	0.9 mg
(equivalent to dexamethasone acetate	1.0 mg)

Excipients

Propyl gallate (E310)	1.0 mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Ear drops, suspension.
Homogenous beige to yellow oily suspension.

4 CLINICAL PARTICULARS

4.1 Target Species

Dogs

4.2 Indications for use, specifying the target species

Treatment of otitis externa of both bacterial and fungal origin respectively due to bacteria susceptible to marbofloxacin, and fungi especially *Malassezia pachydermatis* susceptible to clotrimazole.

4.3 Contraindications

Do not use in dogs suffering from perforation of the tympanic membrane.
Do not use in known cases of hypersensitivity to the active substances or to any of the excipients.
See section 4.7.

4.4 Special warnings for each target species

The external ear canal should be meticulously cleaned and dried before treatment.

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
For external use only.
Avoid contact with the eyes in animals. In case of accidental contact, rinse thoroughly with water.

Heavy reliance on a single class of antibiotic may result in the induction of resistance in a bacterial population. It is prudent to reserve the fluoroquinolones for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly, to other classes of antibiotics.
Before treating with the product, the integrity of the tympanic membrane must be verified.
Official and local antimicrobial policies should be taken into account when the product is used.
See section 4.4

Quinolone class drugs have been associated with cartilage erosions in weight-bearing joints and other forms of arthropathy in immature animals of various species. The use of the product in young animals is not recommended.

The product should be used based on susceptibility testing of isolated bacteria.

Special precautions to be taken by the person administering the medicinal products to animals
Wash hands carefully after applying the product.
Avoid contact with eyes. If splashed in the eye, rinse with large amounts of clean water.
If skin or eye symptoms persist, or the product is accidentally swallowed, seek medical attention and show the package insert to the physician.
People with known hypersensitivity (allergy) to (fluoro)quinolones, (cortico)steroids or antifungals and to other ingredients in the product should take care to avoid contact with the product during administration.

4.6 Adverse reactions (frequency and seriousness)

Usual adverse reactions associated with corticosteroid drugs may be observed (changes in biochemical and haematological parameters, such as increase of alkaline phosphatase, and of aminotransferase, some limited neutrophilia).
Prolonged and intensive use of topical corticosteroid preparations is known to trigger local and systemic effects, including suppression of adrenal function, thinning of the epidermis and delayed wound healing.
On rare occasions, the use of this product may be associated with deafness, mainly in elderly dogs and mostly of a transient nature.
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)

4.7 Use during pregnancy, lactation or lay

Do not administer to pregnant or lactating bitches.

4.8 Interaction with other medicinal products and other forms of interactions

None known.

4.9 Amounts to be administered and administration route

Auricular use.
One drop of the preparation contains 71 µg marbofloxacin, 237 µg clotrimazole and 23.7 µg dexamethasone acetate.
Shake well for 1 minute before use.
Apply ten drops into the ear once daily for 7 to 14 days.
After application, the base of the ear may be massaged briefly and gently to allow the preparation to penetrate to the lower part of the ear canal.
After 7 days of treatment, the veterinary surgeon should evaluate the necessity to extend the treatment another week.
When the product is intended for use in several dogs, use one cannula per dog.

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

Changes in biochemical and haematological parameters (such as increase of alkaline phosphatase, aminotransferase, some limited neutrophilia, eosinopenia, lymphopenia) are observed with three fold the recommended dosage; such changes are not serious and will reverse once the treatment has stopped.

4.11 Withdrawal period(s)

Not applicable.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: corticosteroids and antiinfectives in combination
ATCvet code: QS02CA06

5.1 Pharmacodynamic properties

The preparation combines three active ingredients:

Marbofloxacin is a synthetic bactericidal agent belonging to the fluoroquinolone family that acts by inhibiting DNA gyrase. It exhibits a broad spectrum of activity against Gram-positive bacteria (e.g. *Staphylococcus intermedius*) and against Gram-negative organisms (*Pseudomonasaeruginosa, Escherichia coli* and *Proteus mirabilis*).

For Marbofloxacin:
European literature published up to 2018 reports susceptibility of target pathogens to the active.
Reports of microbiological susceptibility data (collected from 1994 – 2012) involving hundreds of canine and feline pathogens susceptible to marbofloxacin are outlined below:

Microorganism	MIC (µg/ml)
Staphylococcus pseudintermedius	0.125-1
Pseudomonas aeruginosa	0.12-1

Susceptibility breakpoints have been determined as ≤ 1 µg/ml for susceptible, 2 µg/ml for intermediate and ≥ 4 µg/ml for resistant bacterial strains.

Marbofloxacin is not active against anaerobes, yeast or fungi. 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 molecule binding.

Clotrimazole is an anti-fungal agent that belongs to the imidazole family and which acts by causing changes in membrane permeability, allowing intracellular compounds to leak from the cell and thus inhibiting cellular molecular synthesis. It exhibits a wide spectrum of activity and is aimed, in particular, at *Malassezia pachydermatis*.

For Clotrimazole:
Susceptibility breakpoints have been determined as ≤ 25 µg/ml for susceptible fungal strains.

Dexamethasone acetate is a synthetic glucocorticoid exhibiting anti-inflammatory and anti-pruritic activity.

5.2 Pharmacokinetic particulars

Pharmacokinetics studies in dogs at the therapeutic dosage have shown that: Marbofloxacin plasma concentrations peak at 0.06 µg/ml on the 14th day of treatment. Marbofloxacin bonds weakly to plasma proteins (< 10% in dogs) and is eliminated slowly, mainly in the active form, over 2/3 in urine and over 1/3 in faeces. Clotrimazole absorption is extremely poor (plasma concentration < 0.04 µg/ml). Dexamethasone acetate plasma concentration reaches 1.25 ng/ml on the 14^{th} day of treatment. Dexamethasone resorption is not increased by the inflammatory process induced by otitis.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propyl gallate (E310)
Sorbitan oleate
Silica, hydrophobic colloidal
Triglycerides, medium-chain

6.2 Major incompatibilities

Not applicable.

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

Do not store above 30°C.

6.5 Nature and composition of immediate packaging

Details of the primary packaging:
Low-density polyethylene bottle.
Low-density polyethylene nozzle.
Threaded high-density polyethylene cap.
PVC cannula.

Presentation:
- Box containing 1 x 10 ml bottle and 2 cannulae
- Box containing 1 x 20 ml bottle and 2 cannulae
- Box containing 1 x 30 ml bottle and 2 cannulae

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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

Norbrook Laboratories (Ireland) Limited
Rossmore Industrial Estate
Monaghan
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

VPA22664/124/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21 August 2015
Date of last renewal: 20 August 2020

10 DATE OF REVISION OF THE TEXT

August 2020