SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Otoxolan Ear Drops, Suspension for Dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of suspension contains:

Active substances:

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

Excipients:

Propyl gallate (E310)	1.0 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Ear drops, suspension.
Off yellow, opalescent, viscous 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 sensitive to marbofloxacin, and fungi especially *Malassezia pachydermatis* sensitive to clotrimazole.

4.3 Contraindications

Do not use in dogs suffering from perforation of the tympanic membrane.
Do not use in cases of hypersensitivity to the active substances, to other azole antifungal agents or to any other fluoroquinolones or to any of the excipients.
Do not use in animals, where resistance of causative agents to marbofloxacin and/or clotrimazole is known.
See section 4.7.

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

Before treating with the product, the integrity of the tympanic membrane must be verified.
Use of the product should be based on susceptibility testing of the bacteria and/or fungi isolated from the animal. If this is not possible, therapy should be based on local (regional) epidemiological information about susceptibility of the target pathogens.
Official and local antimicrobial policies should be taken in to account when the veterinary medicinal product is used.
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.
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.
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.
Avoid contact with eyes in animals. In case of accidental contact, rinse thoroughly with water.

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

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.
Avoid contact of the skin and eyes with the product. In case of accidental spillage onto skin or eyes, rinse the affected area with large amounts of water.
Take care to avoid accidental ingestion. In case of accidental ingestion, seek medical advice immediately and show the leaflet or the label to the physician.
Wash hands after use.

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).

On rare occasions, the use of this combination 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 use during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

For auricular use.

Apply ten drops into the ear once daily for 7 to 14 days.
After 7 days of treatment, the veterinary surgeon should evaluate the necessity to extend the treatment another week.

One drop of the preparation contains 71 µg marbofloxacin, 237 µg clotrimazole and 23.7 µg dexamethasone acetate.

The external ear canal should be meticulously cleaned and dried before treatment.
Shake well for 30 seconds before use and squeeze gently to fill the dropper with the product.
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.
When the product is intended for use in several dogs, use one dropper 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, eosinopaenia, lymphopaenia) 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 PROPERTIES

Pharmacotherapeutic group: Otologicals, corticosteroids and antiinfectives in combination, dexamethasone and antiinfectives
ATCvet code: QS02CA06

5.1 Pharmacodynamic properties

The preparation combines three active ingredients, marbofloxacin, clotrimazole and dexamethasone.

Marbofloxacin, 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 *(Pseudomonas aeruginosa, Escherichia coli* and *Proteus mirabilis*). In the European literature susceptibility data (MIC_{50} values) for canine and feline otitis pathogens are presented:

Microorganism	MIC_{50} (µg/ml)
Ps. aeruginosa	0.50
S. (pseudo)intermedius	0.25
S. aureus	0.50

Susceptibility breakpoints have been determined as ≤ 1 µg/ml for sensitive, 2 µg/ml for intermediate and ≥ 4 µg/ml for resistant bacterial strains.
Marbofloxacin is not active against anaerobes. 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, 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*;

Dexamethasone acetate, 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, predominantly in urine (2/3) and in faeces (1/3).
Clotrimazole absorption is extremely poor (plasma concentration < 0.04 µg/ml).
Dexamethasone acetate plasma concentration reaches 1.25 ng/ml on the 14th day of treatment. Dexamethasone resorption is not increased by the inflammatory process induced by otitis.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Triglycerides medium-chain
Propyl gallate (E310)
Sorbitan oleate

Silica,hydrophobic colloidal

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.
Keep the bottles in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

Box containing 1 x 10 ml LDPE bottle with an LDPE dropper and HDPE screw cap, and a thermoplastic elastomer dropper with cap.
Box containing 1 x 20 ml LDPE bottle with an LDPE dropper and HDPE screw cap, and 2 thermoplastic elastomer droppers with caps.
Box containing 1 x 30 ml LDPE bottle with an LDPE dropper and HDPE screw cap, and 3 thermoplastic elastomer droppers with caps.
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

KRKA d.d., Novo mesto
Šmarješka cesta 6
8501 Novo mesto
Slovenia

8. MARKETING AUTHORISATION NUMBER

Vm 01656/4117

9. DATE OF FIRST AUTHORISATION

23 December 2016

10. DATE OF REVISION OF THE TEXT

March 2022

Approved 02 March 2022