

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT
DOXYGAL VETERINARY

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Doxycycline (AS HYDROCHLORIDE) 100 %

3. PHARMACEUTICAL FORM

Powder for solution. For use in drinking water.
Yellowish powder.

4. CLINICAL PARTICULARS

4.1 Target species

Turkeys.

4.2 Indications for use, specifying the target species

For the treatment of diseases caused by *Mycoplasma gallisepticum* in turkeys.

4.3 Contraindications

Do not use in cases of hypersensitivity to the active substance.
Do not use in animals with hepatic dysfunction.

4.4 Special warnings for each target species

The uptake of medication by animals can be altered as a consequence of illness. In case of insufficient uptake of drinking water, animals should be treated parenterally.

Under-dosing and/or treating for an insufficient length of time are considered to promote the development of resistance in bacteria and should be avoided.

4.5 Special precautions for use

Special precautions for use in animals

Inappropriate use of the product may increase the prevalence of bacteria resistant to tetracycline due to the potential for cross resistance.

Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.

Avoid administration in oxidised drinking equipment.

Do not use when tetracycline resistance has been detected in the flock due to the potential for cross resistance.

Due to the likely variability (time, geographical) in the occurrence of resistance of bacteria for doxycycline, bacteriological sampling and susceptibility testing are highly recommended.

As eradication of the target pathogens may not be achieved, medication should therefore be combined with good management practices, e.g. good hygiene, proper ventilation, no overstocking.

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

During preparation and administration direct contact of the product with the skin, eyes and mucous membranes and inhalation of dust particles should be avoided. People with known hypersensitivity to tetracyclines should avoid contact with the veterinary medicinal product.

Personal protective equipment consisting of protective gloves (e.g. rubber or latex), goggles and an appropriate dust mask should be worn when handling the veterinary medicinal product. Wash exposed skin after preparation. In case of accidental projection into the eyes, rinse abundantly with water. Do not smoke, eat or drink when handling the product.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician. Inflammation of the face, lips or eyes or respiratory difficulties are the most serious signs which require urgent medical attention.

4.6 Adverse reactions (frequency and seriousness)

On rare occasions allergic reactions and photosensitivity may occur. If suspected adverse re-actions occur, treatment should be discontinued.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form

<https://sideeffects.health.gov.il>

4.7 Use during pregnancy, lactation or lay

Laboratory studies in rats and rabbits have not produced any evidence of a teratogenic, foetotoxic, maternotoxic effects.

Do not use in birds in lay and within 4 weeks before the onset of the laying period.

4.8 Interaction with other medicinal products and other forms of interaction

Do not administer concurrently with feed overloaded with polyvalent cations such as Ca^{2+} , Mg^{2+} , Zn^{2+} and Fe^{3+} because the formation of doxycycline complexes with these cations is possible. It is advised that the interval between

administration of other products containing polyvalent cations should be 1-2 hours because they limit the absorption of tetracycline.
 Do not administer together with antacids, kaolin or iron preparations.
 Do not administer in conjunction with bactericidal antibiotics such as beta-lactams as tetracyclines are bacteriostatic antimicrobials.
 Doxycycline increases the action of anticoagulants.

4.9 Amounts to be administered and administration route

In drinking water use.

In turkeys, 25 mg per kg body weight daily, administered in the drinking water for 5-7 consecutive days.

Based on the recommended dose, and the number and weight of the animals to be treated, the exact daily amount of the veterinary product should be calculated according to the following formula:

mg product / kg body weight / day	x	Mean body weight (kg) of animals to be treated	= mg product per l drinking water
Mean daily water consumption (l) per animal			

To ensure a correct dosage body weight should be determined as accurately as possible. The uptake of medicated water is dependent on the clinical condition of the animals. In order to obtain the correct dosage, the concentration in drinking water may have to be adjusted.

The use of suitably calibrated weighing equipment is recommended if part packs are used. The daily amount is to be added to the drinking water such that all medication will be consumed in 24 hours. It is recommended to prepare a concentrated pre-solution and to dilute this further to therapeutic concentrations if required.

Medicated water should be refreshed every 24 hours. The medicated water should be the only source of drinking water, throughout the treatment period. The medicated water must not be prepared or stored in a metal container.

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

During the target animal tolerance study, no adverse effect was observed even at the fivefold therapeutic dose administered for two times the recommended duration in the target animal species.

If suspected toxic reactions do occur due to extreme overdose, the medication should be discontinued and appropriate symptomatic treatment should be initiated if necessary.

4.11 Withdrawal period(s)

Turkeys: Meat and offal: 12 days

Not for use in birds producing or intended to produce eggs for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterial for systemic use, tetracyclines.
ATCvet code: QJ01AA02

5.1 Pharmacodynamic properties

Doxycycline is a semisynthetic tetracycline derivative. It acts by inhibiting protein synthesis at the ribosomal level, predominantly by binding to the 30S ribosomal subunits of bacteria. Doxycycline is a broad-spectrum antibiotic. It exhibits a wide range of activity against gram-positive and gram-negative, aerobic and anaerobic pathogens, especially against *Mycoplasma gallisepticum* associated with clinical respiratory infections in turkeys.

Resistance is mostly due to interference with the active transport of the tetracyclines into, and increased efflux from the cells, or ribosomal protection in which protein synthesis becomes resistant to inhibition. Basically there is a complete cross-resistance within the class of tetracyclines. Doxycycline may be effective against certain strains resistant to conventional tetracyclines due to ribosomal protection or efflux pump mechanisms.

5.2 Pharmacokinetic particulars

Pharmacokinetics of doxycycline after single oral administration to **turkeys** characterised by a quite rapid and substantial absorption from the gastrointestinal tract providing peak plasma concentrations between 1.5 to 7.5 hours depending on age and the presence of food. The drug is widely distributed in the organism with Vd values close to or greater than 1 L/kg, and exhibits an elimination half-life of 7.9 to 10.8 hours. The protein binding ratio at therapeutic plasma concentrations is in the range of 70-85%. The bioavailability may vary between 25 and 64% also depending on the age and feeding. The presence of food in the gastrointestinal tract results in a lower bioavailability compared to that obtained in the fasted state.

The average plasma concentrations over the whole treatment period were reported 2.24 ± 1.02 µg/ml.

In avian species the PK/PD analysis of $fAUC/MIC_{90}$ data resulted in >24 h values that meet the requirements for tetracyclines.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Not applicable.

6.2 Major incompatibilities

Doxycycline may form insoluble complexes with divalent ions, especially iron or calcium, zinc and magnesium.

Do not mix with any other veterinary medicinal product.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and composition of immediate packaging

Pack sizes:

Bag of 500 g

Jar of 100 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 products should be disposed of in accordance with local requirements.

7. Manufacturer:

BIOVAC LTD., HAILAN STR. 6, POB 300, NORTH INDUSTRIAL ZONE, OR-AKIVA 30600, ISRAEL

Registration number: 081-21-92207

PROHIBITION OF SALE, SUPPLY AND/OR USE

To be supplied only on veterinary prescription

This leaflet format has been determined by the Ministry of Health and the content has been checked and approved in 5.2020