SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Doxylin, 433 mg/g, Powder for Use in Drinking Water for Chickens and Turkeys

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One gram contains:

Active substance:
Doxycycline: 433.3 mg
(as doxycycline hyclate 500.0 mg)

Excipients:

Qualitative composition of excipients and other constituents
Citric acid, anhydrous
Lactose monohydrate

Yellow, crystalline powder.

3. CLINICAL INFORMATION

3.1 Target species

Chickens (broilers, broiler breeders) and turkeys (broilers, breeders).

3.2 Indications for use for each target species

Treatment of clinical respiratory infections associated with *Mycoplasma gallisepticum* susceptible to doxycycline.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use when tetracycline resistance has been detected in the herd/flock due to the potential for cross resistance.
Do not use in animals with hepatic dysfunction.

3.4 Special warnings

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

3.5 Special precautions for use

Special precautions for safe use in the target species:
Due to variability (time, geographical) in susceptibility of bacteria for doxycycline, bacteriological sampling and susceptibility testing of micro-organisms from diseased animals on farm are highly recommended.
Use of the veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to doxycycline and may decrease effectiveness of treatment with tetracyclines due to the potential for cross resistance.
Use of the veterinary medicinal product should take into account official and local antimicrobial policies.
Avoid administration in oxidized drinking equipment.
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 veterinary medicinal 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), glasses and an appropriate dust mask (e.g. disposable half-mask respirator conforming to European Standard EN149 or a non-disposable respirator to European Standard EN140 with a filter to EN143) should be worn when handling the veterinary medicinal product.
Wash exposed skin after preparation of medicated drinking water.
In case of accidental eye contact, rinse with plenty of fresh water. Do not smoke, eat or drink when handling the veterinary medicinal 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.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Chickens (broilers, broiler breeders) and turkeys (broilers, breeders):

Rare (1 to 10 animals / 10,000 animals treated):	Allergic reaction Photosensitivity

If suspected adverse reactions occur, treatment should be discontinued.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

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

3.8 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. Do not administer together with antacids, kaolin and iron preparations as tetracyclines are bacteriostatic antimicrobials, do not administer in conjunction with bactericidal antibiotics like beta-lactams. It is advised that the interval between administration of other veterinary medicinal products containing polyvalent cations should be 1-2 hours because they limit the absorption of tetracycline.
Doxycycline increases the action of anticoagulants.

3.9 Administration routes and dosage

To be administered in drinking water.

To ensure a correct dosage, body weight should be determined as accurately as possible. The intake of medicated water depends on the clinical conditions of the animals. In order to obtain the correct dosage, the concentration of doxycycline may need to be adjusted accordingly.
The use of suitably calibrated measuring equipment is recommended if part packs are used

Dosage:

In chickens
20 mg doxycycline per kg of body weight daily (equivalent to 46 mg veterinary medicinal product per kg of body weight), administered in the drinking water for 5 consecutive days.

In turkeys
25 mg doxycycline per kg of body weight daily (equivalent to 58 mg veterinary medicinal product per kg of body weight), administered in the drinking water for 5 consecutive days.

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

$$\frac{\text{..... mg veterinary medicinal product per kg body weight per day} \times \text{mean body weight (kg) of animals to be treated}}{\text{mean daily water consumption (litre per animal)}} = \text{.... mg veterinary medicinal product per litre of drinking water}$$

The daily amount is to be added to the drinking water such that all medication will be consumed in 24 hours. Medicated drinking water should be freshly prepared every 24 hours. It is recommended to prepare a concentrated pre-solution - not exceeding 100 grams veterinary medicinal product per litre drinking water - and to dilute this further to

therapeutic concentrations, if required. Alternatively; the concentrated solution can be used in a proportional water medicator.
It should be ensured that all animals intended for treatment should have free access to the drinking facilities. At the end of treatment, the watering equipment should be cleaned adequately to avoid the intake of remaining quantities in sub-therapeutic doses. The medicated water should be the only source of drinking water, throughout the treatment period. The medicated water must not be made or stored in a metal container. Solubility of the veterinary medicinal product is pH dependent and it will precipitate if it is mixed in an alkaline solution. In order to ensure a complete and permanent dissolution of the veterinary medicinal product in each water quality, a minimum concentration is required. The minimum concentration in drinking water is 200 mg veterinary medicinal product per litre. Animals requiring a lower concentration should not be treated with the veterinary medicinal product.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

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 either 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.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Meat and offal:
Chickens: 5 days.
Turkeys: 12 days.
Not for use in birds producing eggs for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QJ01AA02

4.2 Pharmacodynamics

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 chickens and turkeys. The MIC_{90} of doxycycline against *M. gallisepticum* strains isolated in France, Germany and Hungary (2003-2009) was reported 0.5 µg/ml.
The resistance rate of *M. gallisepticum* isolates against doxycycline is low (0-6%).

Four resistance mechanisms acquired by micro-organisms against tetracyclines in general have been reported: decreased accumulation of tetracyclines (decreased permeability of the bacterial cell wall and active efflux), protein protection of the bacterial ribosome, enzymatic inactivation of the antibiotic and rRNA mutations (preventing the tetracycline binding to ribosome). Tetracycline resistance is usually acquired by means of plasmids or other mobile elements (e.g. conjugative transposones). Cross resistance between tetracyclines has also been described. Due to the greater liposolubility and greater facility to pass through cell membranes (in comparison to tetracycline), doxycycline retains a certain degree of efficacy against microorganisms with acquired resistance to tetracyclines.
According to the CLSI regulation, organisms other than streptococci with MIC values ≤ 4µg/ml are considered sensitive, at 8 µg/ml intermediate and with MIC values ≥16µg/ml resistant to doxycycline.

4.3 Pharmacokinetics

In general, doxycycline is quite rapidly and extensively absorbed from the gastrointestinal tract, widely distributed in the organism, not metabolised to any significant extent and excreted mostly via the faeces.
Pharmacokinetics of doxycycline after single oral administration to chickens and turkeys is characterised by a quite rapid and substantial absorption from the gastrointestinal tract providing peak plasma concentrations between 0.4 and 3.3 hours in chickens and 1.5 to 7.5 hours in turkeys depending on age and the presence of food. The drug is widely distributed in the organism with V_d values close to or greater than 1, and exhibits shorter elimination half-life in chickens (4.8 to 9.4 hours) than in turkeys (7.9 to 10.8 hours). The protein binding ratio at therapeutic plasma concentrations is in the range of 70-85%. The bioavailability in chickens and turkeys may vary between 41 and 73%, and 25 and 64%, respectively also depending on the age and feeding. The presence of food in the gastrointestinal tract determines a lower bioavailability compared to that obtained in the fasted state.
After continuous in-water administration of the veterinary medicinal product at dosages of 20 mg doxycycline/kg (chickens) and 25 mg doxycycline/kg (turkeys) for 5 days the average plasma concentrations over the whole treatment period were reported 1.86±0.71 µg/ml in chickens and 2.24±1.02 µg/ml in turkeys. In both avian species the PK/PD analysis of $fAUC/MIC_{90}$ data resulted in >24 h values that meet the requirements for tetracyclines.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale:
- Securitainer: 3 years;
- Bucket: 2 years.

Shelf life after first opening of the immediate packaging: 3 months.
Shelf life after dissolution according to directions: 24 hours.

5.3 Special precautions for storage

Store below 25 °C
Keep the container tightly closed in order to protect from light.
Medicated drinking water should be protected from light.

5.4 Nature and composition of immediate packaging

- Securitainer: white polypropylene container, covered with a low-density polyethylene cap.
The securitainer contains 1 kg of veterinary medicinal product.
- Bucket: white polypropylene container provided with a polypropylene cap.
The bucket contains 1, 2.5 or 5 kg of veterinary medicinal product.

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Dopharma Research B.V.

7. MARKETING AUTHORISATION NUMBER

Vm 28365/4006

8. DATE OF FIRST AUTHORISATION

29 March 2015

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

February 2025

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCT

Veterinary medicinal product subject to prescription.

Find more product information by searching for the ‘Product Information Database’ on www.gov.uk.

Gavin Hall
Approved: 25 March 2025