1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Doxivex, 100 mg/mL, concentrate for oral solution for chickens and pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Doxycycline 100 mg
(equivalent to 115.3 mg of Doxycycline hyclate)

Excipients:

Qualitative composition of excipients and other constituents
Pyrrolidone
Propylene glycol

Clear yellow to dark brown solution.

3. CLINICAL INFORMATION

3.1 Target species

Chickens (broilers) and pigs.

3.2 Indications for use for each target species

Chickens (broilers): Treatment of colibacillosis, chronic respiratory disease (CRD) and mycoplasmosis caused by microorganisms sensitive to doxycycline.

Pigs: Treatment of respiratory tract diseases caused by *Pasteurella multocida* (atrophic rhinitis), *Bordetella bronchiseptica* and *Mycoplasma hyopneumoniae* (involved in porcine enzootic pneumonia) sensitive 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 in animals with hepatic dysfunction.

3.4 Special warnings

None.

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 birds on farm are highly recommended.
A high resistance rate of *E. coli*, isolated from chickens, against tetracyclines has been documented. Therefore, the product should be used for the treatment of infections caused by *E. coli* only after susceptibility testing has been carried out.
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.
Avoid administration in oxidised troughs.
Inappropriate use of the product, e.g. too low a dosage, may increase the prevalence of bacteria resistant to doxycycline and may decrease the effectiveness of treatment with other tetracyclines due to the potential for cross-resistance.

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

People with known hypersensitivity to tetracyclines should avoid any contact with the veterinary medicinal product.

The product is administered in drinking water by pouring it into the main tank of water. The concentrate product is acid and likely to be irritant. Avoid contact with skin and eyes. Personal protective equipment consisting of gloves, overalls and approved security glasses should be worn when handling the product. In case of contact with skin, rinse immediately with plenty of water. In case of contact with eyes, rinse immediately with copious amounts of water and seek medical advice.
Do not smoke, eat or drink while handling the product.

When handling diluted product, avoid any contact with skin and eyes. In case of contact, wash with abundant clear water. Wash hands after use.
Following handling of the product in either the concentrate or diluted form, if any symptom should appear, such as a cutaneous eruption, seek prompt medical advice. Inflammation of the face, lips or eyes or respiratory difficulties are more serious signs which require urgent medical attention.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Chickens (broilers) and pigs:

Undetermined frequency(1 to 10 animals / 100 animals treated):	Allergic reaction, Photosensitivity, Disorder of gastrointestinal flora[1], Digestive tract disorder[1]
Rare (1 to 10 animals / 10,000 animals treated):	Crystalluria[2]

[1]If treatment is prolonged.
[2] In young birds (seven days old chicks) when the product is administered in water at the doses recommended. This may occur at times when the ambient temperature is higher than normal, when consumption of medicated water is increased.

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

3.7 Use during pregnancy, lactation or lay

Not applicable.

3.8 Interaction with other medicinal products and other forms of interaction

The absorption of doxycycline can be decreased in the presence of high quantities of calcium, iron, magnesium or aluminium in the diet.
Do not administer together with antacids, kaolin and iron preparations.

3.9 Administration routes and dosage

In drinking water use.
Recommended dose is 10 mg doxycycline hyclate /kg body weight / day, corresponding to 0.1 ml of the veterinary medicinal product per kg body weight, for 3 - 5 consecutive days.

Chickens (broilers): Based on the recommended dose, and the number and weight of the birds to be treated, the exact daily amount of the veterinary medicinal product should be calculated according to the following formula:
ml of the veterinary medicinal product per litre drinking water =

$$\frac{\text{0.1 ml veterinary medicinal product/kg body weight/day x Mean body weight (kg) of birds to be treated}}{\text{Mean daily water consumption (litre) per bird}}$$

The product is administered in drinking water by pouring it into the main tank of water.

Pigs: the quantity of veterinary medicinal product to be added to the water (ml product/ L drinking water/day) can be calculated by the following formula:

ml product/ litre drinking water/day =

$$\frac{\text{mg veterinary medicinal product/kg bw/day X Average weight per animal (kg) X number of animals in group}}{\text{total water consumption of the group on the previous day (l) X 100}}$$

To ensure a correct dosage body weight should be determined as accurately as possible.
The uptake of medicated water is dependent on the clinical conditions 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. Medicated drinking water should be freshly prepared every 24 hours. It is recommended to prepare a concentrated pre-solution - approximately 100 grams 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.

Medicated water will be the only drinking water available to the animals during treatment.

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

No data is available.

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

Chickens (broilers) and pigs: Meat and offal: 7 days.
Not permitted for use in laying birds producing eggs for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01AA02

4.2 Pharmacodynamics

Doxycycline is a bacteriostatic agent that acts by interfering with the bacterial protein synthesis of sensitive species.

Doxycycline is a semi-synthetic tetracycline derived from oxytetracycline. It acts on the subunit 30 S of the bacterial ribosome, to which is linked reversibly, blocking the union between aminoacyl-tRNA (transfer RNA) to the mRNA – ribosome complex, preventing the addition of new amino acids into the growing peptide chain and thus interfering with protein synthesis.

Doxycycline is active against Gram positive and Gram negative bacteria. Spectrum of activity:
Escherichia coli
Mycoplasma spp.
Pasteurella multocida
Bordetella bronchiseptica

In vitro sensitivity of doxycycline against *Pasteurella multocida* and *Bordetella bronchiseptica* strains isolated from pigs has been determined, by means of a plate diffusion method, and against *Mycoplasma hyopneumoniae* by a dilution method, with MIC90 values of 0.517 µg/ml, 0.053 µg/ml and 0.200 µg/ml, respectively.

According to the NCCLS standard, strains sensitive to doxycycline have MIC values below or equal to 4 µg/ml and those resistant have MIC values above or equal to 16 µg/ml.

At least two mechanisms of resistance to tetracyclines exist. The most important is due to a decrease in the cellular accumulation of the drug. This is due to the establishment of either a pump elimination path, or an alteration in the transport system that limits the uptake of tetracycline. The alteration in the transport system is produced by inducible proteins codified in plasmids and transposones. The other mechanism is evidenced by decreased ribosome affinity for the Tetracycline-Mg^{2+} complex owing to chromosomal mutations. Frequently, cross resistance occurs between different tetracyclines.

4.3 Pharmacokinetics

Doxycycline is highly bioavailable after oral and intra-muscular administration. When orally administered, it reaches values greater than 70% in most species.

Feeding can slightly modify the oral bioavailability of doxycycline. In fasting conditions bioavailability is around 10-15% greater than when the animal is fed.

Doxycycline is well distributed through the body as it is highly lipid soluble. It accumulates in liver, kidney, bones and intestine; enterohepatic recycling occurs. In lungs it always reaches higher concentrations than in plasma. Therapeutic concentrations have been detected in aqueous humour, myocardium, reproductive tissues, brain and mammary gland. Plasma protein binding is 90-92%.

40% of the drug is metabolised and largely excreted through faeces (biliary and intestinal route), mainly as microbiologically inactive conjugates.

CHICKENS (Broilers)
After oral administration of 20 mg/kg bw, doxycycline is rapidly absorbed, achieving maximum concentrations (C_{max} of 54.4 mg/l) at the mean time of 0.35 h. Bioavailability was 41.3 %. The elimination half – life was 6.03 h.

PIGS
After oral administration of 10 mg/kg bw, doxycycline is rapidly absorbed, achieving maximum concentrations (C_{max} of 1.5 mg/l) at the mean time of 2.3 h. Bioavailability was 21.2 %. The elimination half – life was 3.1 h.

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: 18 months.
Shelf life after dilution according to directions: 24 hours.
Shelf life after first opening the immediate packaging: immediate use.

5.3 Special precautions for storage

Do not store above 25 ºC.

5.4 Nature and composition of immediate packaging

The product is presented in high density white polyethylene containers of 1 L and 5 L volume.
Containers are closed with an induction seal and a green screw seal cap made of the same material.
Presentations: 12 x 1 L containers in cardboard box and 4 x 5 litre containers in cardboard box.
1L
5L
Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products 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

Duggan Veterinary Supplies Limited

7. MARKETING AUTHORISATION NUMBER(S)

VPA10400/002/001

8. DATE OF FIRST AUTHORISATION

03/08/2007

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

17/02/2025

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).