1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Soludox 500 mg/g powder for use in drinking water for pigs and chickens

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:

Active substance:
Doxycycline 433 mg (equivalent to 500 mg of doxycycline hyclate)

Excipients:

Qualitative composition of excipients and other constituents
Tartaric acid

Yellow crystalline powder.

3. CLINICAL INFORMATION

3.1 Target species

Pigs and chickens (broilers, pullets, breeders).

3.2 Indications for use for each target species

Pigs: For the treatment of the clinical signs associated with porcine respiratory disease caused by *Actinobacillus pleuropneumoniae, Pasteurella multocida*, and *Mycoplasma hyopneumoniae* susceptible to doxycycline.
Chickens: Where clinical disease is present in the flock, to reduce mortality, morbidity, clinical signs and to reduce lesions due to Pasteurellosis caused by *Pasteurella multocida,* or to reduce morbidity and lesions due to respiratory infections caused by *Ornithobacterium rhinotracheale (ORT)*.

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 an impaired liver function.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Due to the likely variability (time, geographical) in susceptibility of bacteria to doxycycline, especially in susceptibility of *A. pleuropneumoniae* and *O. rhinotracheale* which may differ from country to country and even farm to farm, bacteriological sampling and susceptibility testing are recommended. Use of the veterinary medicinal product should be based on the culture and sensitivity of micro-organisms from diseased cases on the farm. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.
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:

People with known hypersensitivity to the tetracycline class of antibiotics should handle this veterinary medicinal product or the medicated solution with caution.
During preparation and administration of the medicated drinking water, skin contact with the veterinary medicinal product and inhalation of dust particles should be avoided. Personal protective equipment consisting of impermeable gloves (e.g. rubber or latex) and an appropriate dust mask (e.g. disposable half-mask respirator conforming to European Standard EN149) should be worn when applying the veterinary medicinal product.
In case of accidental eye or skin contact, rinse the affected area with large amounts of clean water and if irritation occurs, seek medical attention. Wash hands and contaminated skin immediately after handling the veterinary medicinal product.
If you develop symptoms following exposure such as skin rash, you should seek medical advice and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes, or difficulty with breathing are more serious symptoms and require urgent medical attention.
Do not smoke, eat or drink while handling the veterinary medicinal product.
Take measures to avoid producing dust when incorporating the veterinary medicinal product into water. Avoid direct contact with skin and eyes when handling the veterinary medicinal product to prevent sensitisation and contact dermatitis.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Pigs and chickens (broilers, pullets, breeders):

Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Allergic reaction* Photosensitivity*

*If these adverse events 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 its local representative or the national competent authority via the national reporting system. See the package leaflet or immediate packaging for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
The use is not recommended during pregnancy or lactation.
Doxycycline has a low affinity for forming complexes with calcium and studies have demonstrated that doxycycline scarcely affects skeleton formation. No negative effects were observed in poultry after the administration of therapeutic doses of doxycycline.

3.8 Interaction with other medicinal products and other forms of interaction

Do not combine with antibiotics that are bactericidal, e.g. penicillins or cephalosporins.
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.
It is advised that the interval between the administration of other products containing polyvalent cations should be 1-2 hours because they limit the absorption of tetracyclines.

Doxycycline increases the action of anticoagulants.
The solubility of the veterinary medicinal product is pH dependent and it will precipitate if mixed in alkaline solution.
Do not store the drinking water in metallic containers.

3.9 Administration routes and dosage

In drinking water use.

The recommended dose in pigs is:
12.5 mg doxycycline hyclate (25 mg veterinary medicinal product) per kg body weight per day for 4 consecutive days. If no improvement in clinical signs is seen within this time, the diagnosis should be reviewed and treatment changed. In case of severe infections the medication period may be prolonged for a maximum of 8 consecutive days as determined by the attending veterinary surgeon.

The recommended dose in chickens is:
10 mg doxycycline hyclate (20 mg veterinary medicinal product) per kg body weight per day for 3-4 consecutive days in case of infections caused by *P. multocida* and 20 mg doxycycline hyclate (40 mg veterinary medicinal product) per kg body weight per day for 3-4 consecutive days in case of infections caused by *O. rhinotracheale.*

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

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

To ensure a correct dosage, body weight should be determined as accurately as possible.
The intake of medicated drinking water depends on the clinical condition of the animals. In order to obtain the correct dosage the concentration of doxycycline has to be adjusted accordingly. The use of suitably calibrated weighing equipment is recommended if part packs are used. The daily amount of veterinary medicinal product required is to be added to the drinking water such that all medication will be consumed in 24 hours. Medicated drinking water should be refreshed or replaced every 24 hours. It is recommended to prepare a concentrated pre-solution - approximately 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.
Solubility of the veterinary medicinal product is pH dependent and it may precipitate if it is mixed in hard alkaline drinking water. Use at minimum concentrations of 200 mg powder per litre drinking water in areas with hard alkaline drinking water (hardness above 10.2 °d and pH more than 8.1).
During the treatment period animals should not have access to water sources other than the medicated water.

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

Overdoses up to 1.6 times the label recommended dose resulted in no clinical signs that could be attributed to treatment. Poultry tolerate double overdoses of doxycycline (40 mg/kg body weight) without any clinical effect.

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

Pigs:
Meat and offal: 4 days.

Chickens:
Meat and offal: 3 days, following a dose rate of 10 mg/kg body weight for 4 days.
Meat and offal: 9 days, following a dose rate of 20 mg/kg body weight for 4 days.
Not for use in birds producing eggs for human consumption.
Do not use within 4 weeks before the start of the laying period.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code : QJ01AA02

4.2 Pharmacodynamics

Doxycycline belongs to the group of the tetracycline antibiotics. These antibiotics have a broad-spectrum of antimicrobial activity, sharing the same basic structure of polycyclic naphthacenecarboxamide.
Doxycycline is primarily a bacteriostatic drug. It exerts its action by inhibiting the protein synthesis of the bacterial cell. Inhibition of bacterial protein synthesis results in disturbance of all functions necessary for the life of bacteria. Cell-division and the formation of the cell wall in particular are impaired.
Doxycycline is a broad-spectrum antibiotic, active against a large number of Gram-positive and Gram-negative, aerobe and anaerobe micro-organisms, Mycoplasmata, Chlamydiae and Rickettsiae.
For *Ornithobacterium rhinotracheale,* results demonstrate a great variation from high to low susceptibility, depending on the geographical region where isolates came from.
In pig pathogens resistance to doxycycline may also vary; in particular, susceptibility figures of *A. pleuropneumoniae* may differ from country to country and even farm to farm.
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 transposons). 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 micro-organisms with acquired resistance to tetracyclines.

4.3 Pharmacokinetics

Doxycycline is absorbed in the stomach and the first part of the duodenum. Compared to the older tetracyclines, the absorption of doxycycline is less affected by the presence of bivalent cations in food. Bioavailability in non-fasted pigs is approximately 21%.
Following oral administration at a dose of 12.8 mg/kg body weight, steady state concentrations during medication range between a C_{min} of 0.40 µg/ml in the early morning to a C_{max} of 0.87 µg/ml in the late afternoon in pigs.
Following administration of doxycycline hyclate at an actual dose of 21 mg/kg body weight to chickens, mean plasma concentrations above 1 µg/ml were reached within 6 hours and lasted for 6 hours after cessation of medication. From 24 hours up to 96 hours after start of treatment, the doxycycline plasma concentrations exceeded 2 µg/ml. Following administration of doxycycline hyclate at an actual dose of 10 mg/kg body weight, steady state plasma concentrations ranged from 0.75 to 0.93 µg/ml between 12 and 96 hours after start of medication.
Because doxycycline is highly lipid soluble, it has a good tissue penetration. Respiratory tract tissue: plasma ratios of 1.3 (healthy lungs), 1.9 (pneumonic lungs) and 2.3 (nasal mucosa) have been reported for doxycycline. Plasma protein binding is high (over 90%).
Doxycycline is scarcely metabolised. Doxycycline is primarily excreted with the faeces.

Environmental properties

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.
No information is available on potential interactions or incompatibilities of this veterinary medicinal product administered orally by mixing into drinking water containing biocidal products or other substances used in drinking water.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: 9 months.
Shelf life after dilution or reconstitution according to directions: 24 hours.

5.3 Special precautions for storage

Keep the sachet tightly closed after first opening in order to protect from moisture.

5.4 Nature and composition of immediate packaging

The packs consists of one of the following laminates:
- Polyester / polyethylene / aluminium / polyethylene and an inner layer of polyethylene.
- Polyester / polyethylene / aluminium and an inner layer of ionomer (surlyn).
- Polyethylene terephtalic acid / aluminium / polyamide and an inner layer of polyethylene.

Pack sizes:
100 g, 250 g, 500 g and 1 kg sachet.
Carton box with 10x100 g sachets.

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

Eurovet Animal Health B.V.,

7. MARKETING AUTHORISATION NUMBER(S)

VPA10989/072/001

8. DATE OF FIRST AUTHORISATION

09/02/2018

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

01/09/2025

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).