SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Soludox 500 mg/g powder for use in drinking water for turkeys

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g powder contains:
Active substance:
Doxycycline hyclate 500 mg, corresponding to 433 mg doxycycline
Excipients:
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for use in drinking water.
Yellow crystalline powder.

4. CLINICAL PARTICULARS

4.1 Target species

Turkeys (broilers, breeders).

4.2 Indications for use, specifying the target species

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

4.3 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 and/or renal dysfunction.
Do not use when tetracycline resistance has been detected in the flock due to the potential for cross-resistance.

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, turkeys should be treated parenterally.

4.5 Special precautions for use

Special precautions for use in animals
Official, national and regional antimicrobial policies should be taken into account when the product is used.

Use of the product deviating from the instructions given in the SPC 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.
Due to likely variability (time, geographical) in susceptibility of bacteria for doxycycline bacteriological sampling and susceptibility testing are recommended. In particular susceptibility of *O.rhinotracheale* may differ from country to country and even farm to farm.
Use of the product should be based on culture and sensitivity of micro-organisms from diseased cases on 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.
Avoid administration in oxidised drinking equipment.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
This product may cause contact dermatitis and/or hypersensitivity reactions if contact is made with the skin or eyes (powder and solution) or if the product is inhaled.
If you know you are allergic to the tetracycline class of antibiotics, special care should be taken when handling this product or the medicated solution.
During preparation and administration of the medicated drinking water, skin contact with the product and inhalation of dust particles should be avoided. Wear impermeable gloves (e.g. rubber or latex) and an appropriate dust mask (e.g. disposable half-mask respirator conforming to European Standard EN149) when applying the product.
In the event of 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 product.
If you develop symptoms following exposure such as skin rash, you should seek medical advice and show this warning 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 product.
Take measures to avoid producing dust when incorporating the product into water.
Avoid direct contact with skin and eyes when handling the product to prevent sensitisation and contact dermatitis.

4.6 Adverse reactions (frequency and seriousness)

As for all tetracyclines, on rare occasions (more than 1 but less than 10 animals in 10,000 animals) allergic reactions and photosensitivity may occur. If suspected adverse reactions occur, treatment should be discontinued.

4.7 Use during pregnancy, lactation or lay

Laboratory studies in rats and rabbits have not produced any evidence of a teratogenic, foetotoxic or maternotoxic effect. Do not use in birds in lay and within 4 weeks before the start of the laying period.

4.8 Interaction with other medicinal products and other forms of interaction

Do not administer in conjunction with bactericidal antibiotics such as beta-lactams as tetracyclines are bacteriostatic antimicrobials. 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 or 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 product is pH-dependent and it will precipitate out if mixed in alkaline solutions.

4.9 Amounts to be administered and administration route

Administer orally in the drinking water.
Dosage: 25 mg doxycycline corresponding to 29 mg doxycycline hyclate per kg of body weight daily (equivalent to 58 mg product per kg of body weight), administered in the drinking water for 5 consecutive days.
The product should be administered continuously in the drinking water during the whole period of treatment. Based on the dosage to be used, and the number and weight of the birds to be treated, the exact daily amount of product required can be calculated.
The following formula can be used to calculate the concentration of the product in drinking water:

$$\frac{\text{58 mg product / kg body weight / day} \times \text{mean body weight (kg) of birds to be treated}}{\text{mean daily water consumption (l) per bird}} = \text{.... mg product per l drinking water}$$

To ensure a correct dosage, body weight should be determined as accurately as possible. The uptake of medicated drinking water depends on the clinical condition of the birds. 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 is to be added to the drinking water such that all medication will be consumed within 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 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 product is pH-dependent and it may precipitate out 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 birds should not have access to water sources other than the medicated water.

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

No adverse effects were observed after administration of doxycycline to turkeys at the fivefold therapeutic dose for up to 10 days. 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 periods

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

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Tetracyclines.
ATCvet code: QJ 01 AA 02.

5.1 Pharmacodynamic properties

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. In particular, cell-division and the formation of the cell wall are impaired.
Doxycycline is a broad-spectrum antibiotic.
The MIC90 of doxycycline against *Mycoplasma 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.
Four resistance mechanisms acquired by microorganisms 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.

5.2 Pharmacokinetic particulars

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.
The harmacokinetics of doxycycline after single oral administration to turkeys is 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, and it exhibits an elimination half-life in turkeys of 7.9 to 10.8 hours. The protein binding ratio at therapeutic plasma concentrations is in the range of 70 to 85%. The bioavailability in turkeys may vary between 25 and 64%, also depending on 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 product at dosages of 25 mg doxycycline/kg in turkeys for 5 days, the average plasma concentrations over the whole treatment period were reported 2.24±1.02 µg/ml in turkeys. PK/PD analysis of fAUC/MIC90 data resulted in >24 h values that meet the requirements for tetracyclines.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tartaric acid

6.2 Major incompatibilities

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

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: 6 months.
Shelf life after dilution or reconstitution according to directions: 24 hours.

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.
Keep the bag tightly closed after first opening in order to protect from moisture.

6.5 Nature and composition of immediate packaging

Bags of 1 kg.
Sachets of 100 grams packed per 10 in a carton box.
1000 g bag: polyester, polyethylene, aluminium, polyethylene and an inner layer of polyethylene.
1000 g bag: polyethylene terephtalic acid, aluminium, polyamide and an inner layer of polyethylene.
100 g sachet: polyester, polyethylene, aluminium and an inner layer of ionomer (surlyn).
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. MARKETING AUTHORISATION HOLDER

Eurovet Animal Health B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands

8. MARKETING AUTHORISATION NUMBER

Vm 16849/4046

9. DATE OF FIRST AUTHORISATION

28 August 2012

10. DATE OF REVISION OF THE TEXT

October 2017

Approved: 12/10/2017