Summary of product characteristics

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Soludox 500 mg/g powder for use in drinking water for pigs and chickens
Soludox 433 mg/g powder for use in drinking water for pigs and chickens (France only)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g powder contains:

Active substance:
Doxycycline hyclate 500 mg, corresponding to 433 mg doxycycline
France: Doxycycline 433 mg, corresponding to 500 mg doxycycline hyclate

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

Pigs and chickens (broiler, pullet, breeder).

4.2 Indications for use, specifying the 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)*.

4.3 Contraindications

Do not use in case of known hypersensitivity to tetracyclines or to any of the excipients.
Do not use in animals with an impaired liver function.
Do not use in animals with renal disorders.

4.4 Special warning 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.

4.5 Special precautions for use

Special precautions for use in animals
Due to likely variability (time, geographical) in susceptibility of bacteria for doxycycline, and that susceptibility of *A. pleuropneumoniae* and *O. rhinotracheale* in particular may differ from country to

country and even farm to farm, bacteriological sampling and susceptibility testing are recommended. Use of the 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 tetracyclines should avoid contact with the veterinary medicinal product. 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)

Tetracyclines may - in very rare cases - induce photosensitivity and allergic reactions. If suspected adverse reactions occur, treatment should be discontinued. Inform your veterinary surgeon if adverse reactions occur that are not stated.

4.7 Use during pregnancy, lactation or lay

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.
In the absence of specific studies the use of the product is not recommended during pregnancy or lactation.

4.8 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.

4.9 Amounts to be administered and administration route

To be administered orally in the drinking water.

The recommended dose in pigs is:
12.5 mg doxycycline hyclate (25 mg 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 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 product) per kg body weight per day for 3-4 consecutive days in case of infections caused by *O. rhinotracheale*.

Based on the dose to be used, and the number and weight of the animals 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 required in drinking water:

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

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 pigs/chickens. 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 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 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 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.

4.10 Overdose (symptoms, emergency procedures, 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.

4.11 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 authorised for use in birds producing eggs for human consumption.
Do not use within 4 weeks before the onset of the laying period.

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 the bacteria. Cell-division and the formation of the cell wall in particular are impaired.
Tetracyclines are bacteriostatic antibiotics with activity against a wide range of aerobic and anaerobic gram-positive and gram-negative bacteria. They are also effective against Mycoplasmata.
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 against doxycycline may also vary; susceptibility figures of *A. pleuropneumoniae* in particular 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.

5.2 Pharmacokinetic particulars

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/g 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tartaric acid

6.2 Incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.
The solubility of the product is pH dependent and it will precipitate if mixed in an alkaline solution.
Do not store the drinking water in metallic containers.

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: 9 months.
Shelf life after dilution or reconstitution according to directions: 24 hours.

6.4 Special precautions for storage

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

6.5 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 of 100 g, 250 g, 500 g, 1 kg and 10x100 g in a carton box.
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 product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Eurovet Animal Health BV
Handelsweg 25
5531 AE Bladel
The Netherlands

8. MARKETING AUTHORISATION NUMBER

(NL/V/0141/001/R/001)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

Labelling and package leaflet

LABEL TEXT
SINGLE SACHETS/BAGS

1x 100g/250g/500g/1kg

The full text will be printed on the single sachet/bag
Format used is especially for this type of labelling

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE
=
LEAFLET

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Soludox 500 mg/g powder for use in drinking water for pigs and chickens
Doxycycline hyclate
France only: Soludox 433 mg/g powder for use in drinking water for pigs and chickens
Doxycycline

2. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS

1 g powder contains:

Active substance:	
Doxycycline hyclate	500 mg, corresponding to 433 mg doxycycline
France: Doxycycline	*433 mg, corresponding to 500 mg doxycycline hyclate*
Excipients:	
Tartaric acid	500 mg

3. PHARMACEUTICAL FORM

Powder for use in drinking water.

4. PACKAGE SIZE

100 g *(250 g, 500 g, 1 kg)*

5. TARGET SPECIES

Pigs and chickens (broiler, pullet, breeder).

6. INDICATIONS

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)*.

7. CONTRAINDICATIONS

Do not use in case of known hypersensitivity to tetracyclines or to any of the excipients.
Do not use in animals with an impaired liver function.
Do not use in animals with renal disorders.

8. ADVERSE REACTIONS

Tetracyclines may - in very rare cases - induce photosensitivity and allergic reactions. If suspected adverse reactions occur, treatment should be discontinued.

If you notice any serious effects or other effects not mentioned on this packaging , please inform your veterinary surgeon.

9. DOSAGE FOR EACH SPECIES, ROUTES AND METHOD OF ADMINISTRATION

To be administered orally in the drinking water.

The recommended dose in pigs is:
12.5 mg doxycycline hyclate (25 mg 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 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 product) per kg body weight per day for 3-4 consecutive days in case of infections caused by *O. rhinotracheale*

Based on the dose to be used, and the number and weight of the animals 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 required in drinking water:

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

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 pigs/chickens. 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 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 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 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.

10. 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 authorised for use in birds producing eggs for human consumption.
Do not use within 4 weeks before the onset of the laying period.

11. SPECIAL WARNINGS

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.

Special precautions for use in animals:

Due to likely variability (time, geographical) in susceptibility of bacteria for doxycycline, susceptibility of *A. pleuropneumoniae* and *O. rhinotracheale* in particular may differ from country to country and even farm to farm, bacteriological sampling and susceptibility testing are recommended. Use of the product should be based on 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 tetracyclines should avoid contact with the veterinary medicinal product. 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.

Use 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.

In the absence of specific studies the use of the product is not recommended during pregnancy or lactation.

Interactions with other medicinal products and other forms of interaction:

Do not combine with antibiotics that are bactericidal, like 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.

Overdose (symptoms, emergency procedures, 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.

Incompatibilities:

In the absence of compatibility studies, this product must not be mixed with other veterinary medicinal products. The solubility of the product is pH dependent and it will precipitate if mixed in an alkaline solution. Do not store the drinking water in metallic containers.

12. EXPIRY DATE

EXP: {month/year}

Shelf life after first opening the packaging: 9 months.

Shelf life after dilution or reconstitution according to directions: 24 hours.

Once opened use by __/__/__

13. SPECIAL STORAGE PRECAUTIONS

Keep the bag tightly closed after first opening in order to protect from moisture.
Do not use this veterinary medicinal product after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

14. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

15. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only.
To be supplied only on veterinary prescription.

16. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

17. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release:
Eurovet Animal Health BV
Handelsweg 25
5531 AE Bladel
The Netherlands

18. MARKETING AUTHORISATION NUMBER(S)

19. MANUFACTURER'S BATCH NUMBER

Lot: {number}

20. DATE ON WHICH THE TEXT WAS LAST APPROVED

21. OTHER INFORMATION

Pack sizes: 100 g, 10x100 g, 250 g, 500 g and 1 kg
Not all pack sizes may be marketed.
For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

LABELLING 10 x 100 g

Carton box for the 10x100 g Alufoil sachets
with label for 100 g sachets
and leaflet

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARTON 10 X 100 g only

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Soludox 500 mg/g powder for use in drinking water for pigs and chickens
Doxycycline hyclate
France only: Soludox 433 mg/g powder for use in drinking water for pigs and chickens
Doxycycline

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

1 g powder contains:

Active substance:	
Doxycycline hyclate	500 mg, corresponding to 433 mg doxycycline
France: Doxycycline	*433 mg, corresponding to 500 mg doxycycline hyclate*
Excipients:	
Tartaric acid	500 mg

3. PHARMACEUTICAL FORM

Powder for use in drinking water.

4. PACKAGE SIZE

10x100 g

5. TARGET SPECIES

Pigs and chickens (broiler, pullet, breeder).

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

To be administered orally in the drinking water.
Read the package leaflet before use.

8. 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 authorised for use in birds producing eggs for human consumption.
Do not use within 4 weeks before the onset of the laying period.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP: {month/year}
Shelf life after first opening of the packaging: 9 months.
Shelf life after dilution or reconstitution according to directions: 24 hours.
Once opened use by: __/__/__

11. SPECIAL STORAGE CONDITIONS

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

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only.
To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eurovet Animal Health BV
Handelsweg 25
5531 AE Bladel
The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Lot: {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Aluminium Foil Sachet 100 g (packed per 10)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Soludox 500 mg/g powder for use in drinking water for pigs and chickens
Doxycycline hyclate
France only: Soludox 433 mg/g powder for use in drinking water for pigs and chickens
Doxycycline

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

1 g powder contains:

Active substance:

Doxycycline hyclate	500 mg, corresponding to 433 mg doxycycline
France: Doxycycline	*433 mg, corresponding to 500 mg doxycycline hyclate*

Excipients:

Tartaric acid	500 mg

3. PHARMACEUTICAL FORM

Powder for use in drinking water.

4. PACKAGE SIZE

100 g

5. TARGET SPECIES

Pigs and chickens (broiler, pullet, breeder).

6. INDICATIONS

7. METHOD AND ROUTE(S) OF ADMINISTRATION

To be administered orally in the drinking water.

8. 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 authorised for use in birds producing eggs for human consumption.
Do not use within 4 weeks before the onset of the laying period.

9. SPECIAL WARNINGS, IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP: {month/year}
Shelf life after first opening of the packaging: 9 months.
Shelf life after dilution or reconstitution according to directions: 24 hours.
Once opened use by__/__/__

11. SPECIAL STORAGE CONDITIONS

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

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only.
To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eurovet Animal Health BV
Handelsweg 25
5531 AE Bladel
The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Lot: {number}

PACKAGE LEAFLET FOR:
Soludox 500 mg/g powder for use in drinking water for pigs and chickens

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release:
Eurovet Animal Health BV
Handelsweg 25
5531 AE Bladel
The Netherlands

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Soludox 500 mg/g powder for use in drinking water for pigs and chickens
Doxycycline hyclate
France only: Soludox 433 mg/g powder for use in drinking water for pigs and chickens
Doxycycline.

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

1 g powder contains:

Active substance:	
Doxycycline hyclate	500 mg, corresponding to 433 mg doxycycline
France: Doxycycline	*433 mg, corresponding to 500 mg doxycycline hyclate*
Excipients:	
Tartaric acid	500 mg

4. INDICATIONS

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)*.

5. CONTRAINDICATIONS

Do not use in case of known hypersensitivity to tetracyclines or to any of the excipients.
Do not use in animals with an impaired liver function.
Do not use in animals with renal disorders.

6. ADVERSE REACTIONS

Tetracyclines may - in very rare cases - induce photosensitivity and allergic reactions. If suspected adverse reactions occur, treatment should be discontinued.
If you notice any serious effects or other effects not mentioned in this package leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Pigs and chickens (broiler, pullet, breeder).

8. DOSAGE FOR EACH SPECIES, ROUTE AND METHOD OF ADMINISTRATION

To be administered orally in the drinking water.

The recommended dose in pigs is:
12.5 mg doxycycline hyclate (25 mg 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 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 product) per kg body weight per day for 3-4 consecutive days in case of infections caused by *O. rhinotracheale*

9. ADVICE ON CORRECT ADMINISTRATION

Based on the dose to be used, and the number and weight of the animals 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 required in drinking water:

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

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 pigs/chickens. 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 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 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 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.

10. WITHDRAWAL PERIOD

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 authorised for use in birds producing eggs for human consumption.
Do not use within 4 weeks before the onset of the laying period.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Keep the bag tightly closed after first opening in order to protect from moisture.

Do not use this veterinary medicinal product after the expiry date which is stated on the label after EXP.
The expiry date refers to the last day of that month.
Shelf life after first opening the packaging: 9 months.
Shelf life after dilution or reconstitution according to directions: 24 hours.

12. SPECIAL WARNINGS

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.
Special precautions for use in animals:
Due to likely variability (time, geographical) in susceptibility of bacteria for doxycycline, and that susceptibility of *A. pleuropneumoniae* and *O. rhinotracheale* in particular may differ from country to country and even farm to farm, bacteriological sampling and susceptibility testing are recommended. Use of the product should be based on 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 tetracyclines should avoid contact with the veterinary medicinal product.
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.
Use 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.
In the absence of specific studies the use of the product is not recommended during pregnancy or lactation.
Interactions with other medicinal products and other forms of interaction:
Do not combine with antibiotics that are bactericidal like 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.
Overdose (symptoms, emergency procedures, 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.
Incompatibilities:
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products. The solubility of the product is pH dependent and it will precipitate if mixed in alkaline solution. Do not store the drinking water in metallic containers.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Pack sizes: 100 g, 10x100 g, 250 g, 500 g and 1 kg.
Not all pack sizes may be marketed.
For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.