

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE - COMBINED LABEL AND PACKAGE LEAFLET

250 g, 500 g, 1 kg

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Centidox 1000 mg/g, powder for use in drinking water or milk (replacer) for cattle and pigs

2. COMPOSITION

Each g contains:

Active substance:

Doxycycline 867 mg
(equivalent to 1000 mg of doxycycline hyclate)

Yellow powder.

3. PACKAGE SIZE

250 g
500 g
1 kg

4. TARGET SPECIES

Cattle (calf) and pig.

5. INDICATIONS FOR USE

Indications for use

Treatment and metaphylaxis of respiratory diseases caused by *Pasteurella multocida* and *Mycoplasma* spp. susceptible to doxycycline. The presence of the clinical disease in the herd should be established before the veterinary medicinal product is used.

6. CONTRAINDICATIONS

Contraindications

Do not use in animals with an active microbiological digestion in the rumen.
Do not use in cases of hypersensitivity to doxycycline or other tetracyclines.
Do not use in animals with hepatic disorders.
Do not use in animals with renal disorders.

7. SPECIAL WARNINGS

Special warnings

Special warnings:

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

Special precautions for safe use in the target species:

Administer the medicated milk per calf individually. It should be taken into account that de-mixing may occur in the milk (replacer). To prevent this happening, the mixer should be kept turned on during tapping of the milk.

Due to likely variability (time, geographical) in susceptibility of bacteria for doxycycline, bacteriological sampling and susceptibility testing are recommended. If this is not possible, therapy should be based on local (regional and farm level) epidemiological information about susceptibility of the target bacteria as well as by taking into account official national antimicrobial policies.

Inappropriate use of the veterinary medicinal product 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.

Avoid administration in oxidised drinking equipment.

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

People with known hypersensitivity to doxycycline or other tetracyclines should avoid contact with the veterinary medicinal product.

During preparation and administration of the medicated drinking water, skin contact with the veterinary medicinal 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 veterinary medicinal 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 veterinary medicinal 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 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.

Pregnancy and lactation:

Laboratory studies have not produced any evidence of a teratogenic, foetotoxic or maternotoxic effect. In the absence of specific studies, the use of the veterinary medicinal product is not recommended during pregnancy or lactation.

Interaction 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 or iron preparations. It is advised that the interval between the administration of other veterinary medicinal products containing polyvalent cations should be 1-2 hours, because they limit the absorption of tetracyclines.

Doxycycline increases the action of anticoagulants.

Overdose:

Overdosing in calves could in some cases result in an acute, sometimes fatal heart muscle degeneration, see also 'Adverse events'.

Major incompatibilities:

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

The solubility of the veterinary medicinal product is pH dependent and it will precipitate if mixed in an alkaline solution.

Do not store the drinking water in metallic containers.

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.

8. ADVERSE EVENTS

Adverse events

Cattle (calf) and pig:

Rare (1 to 10 animals / 10,000 animals treated):	Allergic reaction Photosensitivity
Undetermined frequency (cannot be estimated from the available data)	Cardiomyopathy ^a

^a In calf: Acute, sometimes fatal, heart muscle degeneration can occur after one or more administrations. Since in most cases this is related to overdosing, it is important to measure the dose accurately.

If suspected adverse reactions occur, treatment should be discontinued.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed on this label, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or its local representative using the contact details on this label, or via your national reporting system: {national system details}.

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

Dosage for each species, routes and method of administration

Calves: In milk (replacer) use.

Pigs: In drinking water use.

Dosage:

Calves: 10 mg doxycycline hyclate per kg body weight per day for 5 days

Pigs: 10 mg doxycycline hyclate per kg body weight per day for 5 days

10. ADVICE ON CORRECT ADMINISTRATION

Advice on correct administration

Calves:

Based on the dose to be used, and the number and weight of the calves to be treated, the exact daily amount of veterinary medicinal product required can be calculated. To ensure a correct dosage, body weight should be determined as accurately as possible to avoid under-dosing. The use of suitably calibrated weighing equipment is recommended if part packs are used.

The following formula can be used to calculate the concentration of the veterinary medicinal product per litre milk (replacer):

$$\frac{10 \text{ mg veterinary medicinal product per kg body weight per day} \times \text{average body weight (kg) of animals to be treated}}{\text{average daily milk (replacer) consumption l/animal}} = \dots \text{ mg veterinary medicinal product per litre milk (replacer)}$$

After reconstitution with (artificial) milk the solution should be consumed within 6 hours.
The medicated milk (replacer) should not contain less than 100 mg veterinary medicinal product per litre.

Pigs:

A concentrated drinking water solution should be given twice daily (morning/evening) such that half of the total daily dose is consumed per medication period of 4 hours. This drinking water solution should contain at a minimum 400 mg veterinary medicinal product per litre drinking water. Based on the dose to be used, the minimum concentration of 400 mg veterinary medicinal product per litre, mean drinking water consumption, and the number and weight of the pigs to be treated, the exact amount of medicated drinking water required can be calculated. To ensure a correct dosage, body weight should be determined as accurately as possible. The use of suitably calibrated weighing equipment is recommended if part packs are used. For example, a solution containing 400 mg veterinary medicinal product per litre drinking water is sufficient, when given one litre twice per day, to administer the full treatment dose of 10 mg/kg for pigs of 80 kg body weight consuming 100 ml drinking water per kg body weight.

Medicated drinking water solution should be consumed within 4 hours. Do not prepare more medicated drinking water than will be consumed within that 4 hour period. It is advisable to restrict drinking water for approximately 2 hours (less in hot weather) prior to the medication period and to ensure there are enough drinking points for adequate water consumption for all pigs to be treated. No other source of drinking water should be available during the medication period. Once all the medicated water has been drunk, turn the drinking water system back on.

Solubility of the veterinary medicinal product is pH dependent and in areas with hard alkaline water, formation of complexes may occur in the drinking water. The veterinary medicinal product should not be used in very hard water above 17.5°d and pH more than 8.1.

11. WITHDRAWAL PERIODS

Withdrawal periods

Calves:

Meat and offal: 16 days

Pigs:

Meat and offal: 8 days

12. SPECIAL STORAGE PRECAUTIONS

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.

13. SPECIAL PRECAUTIONS FOR DISPOSAL

Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

14. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

15. MARKETING AUTHORISATION NUMBERS AND PACK SIZES

Marketing authorisation numbers

Pack sizes

100 g, 250 g, 500 g, 1000 g or 10x100 g in a carton box.

Not all pack sizes may be marketed.

16. DATE ON WHICH THE LABEL WAS LAST REVISED

Date on which the label was last revised

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

17. CONTACT DETAILS

Contact details

Marketing authorisation holder, manufacturer responsible for batch release and contact details to report suspected adverse events:

Manufacturer responsible for batch release:

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

Local representatives and contact details to report suspected adverse events:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

18. OTHER INFORMATION

Other information

19. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

20. EXPIRY DATE

Exp {mm/yyyy}

Once opened use by ...

Shelf life after first opening the immediate packaging: 6 months

Shelf life after dissolution according to directions:

Solutions in water: 4 hours.

Milk solutions: 6 hours.

21. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

booklet label (outside) 100 g sachet
carton box for the 10x100 g sachets with separate leaflet

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Centidox 1000 mg/g, powder for use in drinking water or milk (replacer)

2. STATEMENT OF ACTIVE SUBSTANCES

Each g contains:

Doxycycline 867 mg
(equivalent to 1000 mg of doxycycline hyclate)

3. PACKAGE SIZE

100 g
10x100 g

4. TARGET SPECIES

Cattle (calf) and pig.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Calves: In milk (replacer) use.
Pigs: In drinking water use.

7. WITHDRAWAL PERIODS

Withdrawal periods:

Calves:

Meat and offal: 16 days

Pigs:

Meat and offal: 8 days

8. EXPIRY DATE

Exp. {mm/yyyy}

Once opened, use within 6 months.

Shelf life after dissolution according to directions:

Solutions in water: 4 hours.

Milk solutions: 6 hours.

Once opened use by ...

9. SPECIAL STORAGE PRECAUTIONS

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

10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

label 100 g sachet (in carton box of 10x100 g, with separate leaflet)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Centidox 1000 mg/g, powder for use in drinking water or milk (replacer)

2. STATEMENT OF ACTIVE SUBSTANCES

Each g contains:

Doxycycline 867 mg
(equivalent to doxycycline hyclate 1000 mg)

3. TARGET SPECIES

Cattle (calf) and pig.

4. ROUTES OF ADMINISTRATION

Calves: In milk (replacer) use.

Pigs: In drinking water use.

Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal periods:

Calves:

Meat and offal: 16 days

Pigs:

Meat and offal: 8 days

6. EXPIRY DATE

Exp. {mm/yyyy}

Once opened, use within 6 months.

Shelf life after dissolution according to directions:

Solutions in water: 4 hours.

Milk solutions: 6 hours.

Once opened use by ...

7. SPECIAL STORAGE PRECAUTIONS

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

8. NAME OF THE MARKETING AUTHORISATION HOLDER

9. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

**booklet label (inside) 100 g sachet
leaflet in carton box for the 10x100 g sachets**

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Centidox 1000 mg/g, powder for use in drinking water or milk (replacer) for cattle and pigs

2. Composition

Each g contains:

Active substance:

Doxycycline 867 mg
(equivalent to 1000 mg of doxycycline hyclate)

Yellow powder.

3. Target species

Cattle (calf) and pig.

4. Indications for use

Treatment and metaphylaxis of respiratory diseases caused by *Pasteurella multocida* and *Mycoplasma* spp. susceptible to doxycycline. The presence of the clinical disease in the herd should be established before the veterinary medicinal product is used.

5. Contraindications

Do not use in animals with an active microbiological digestion in the rumen.
Do not use in cases of hypersensitivity to doxycycline or other tetracyclines.
Do not use in animals with hepatic disorders.
Do not use in animals with renal disorders.

6. Special warnings

Special warnings:

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

Special precautions for safe use in the target species:

Administer the medicated milk per calf individually. It should be taken into account that de-mixing may occur in the milk (replacer). To prevent this happening, the mixer should be kept turned on during tapping of the milk.

Due to likely variability (time, geographical) in susceptibility of bacteria for doxycycline, bacteriological sampling and susceptibility testing are recommended. If this is not possible, therapy should be based on local (regional and farm level) epidemiological information about susceptibility of the target bacteria as well as by taking into account official national antimicrobial policies.

Inappropriate use of the veterinary medicinal product 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.

Avoid administration in oxidised drinking equipment.

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

People with known hypersensitivity to doxycycline or other tetracyclines should avoid contact with the veterinary medicinal product.

During preparation and administration of the medicated drinking water, skin contact with the veterinary medicinal 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 veterinary medicinal 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 veterinary medicinal 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 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.

Pregnancy and lactation:

Laboratory studies have not produced any evidence of a teratogenic, foetotoxic or maternotoxic effect. In the absence of specific studies, the use of the veterinary medicinal product is not recommended during pregnancy or lactation.

Interaction 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 or iron preparations. It is advised that the interval between the administration of other veterinary medicinal products containing polyvalent cations should be 1-2 hours, because they limit the absorption of tetracyclines.

Doxycycline increases the action of anticoagulants.

Overdose:

Overdosing in calves could in some cases result in an acute, sometimes fatal heart muscle degeneration, see also 'Adverse events'.

Major incompatibilities:

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

The solubility of the veterinary medicinal product is pH dependent and it will precipitate if mixed in an alkaline solution.

Do not store the drinking water in metallic containers.

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7. Adverse events

Cattle (calf) and pig:

Rare (1 to 10 animals / 10,000 animals treated):	Allergic reaction Photosensitivity
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Undetermined frequency (cannot be estimated from the available data)	Cardiomyopathy ^a
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^a In calf: Acute, sometimes fatal, heart muscle degeneration can occur after one or more administrations. Since in most cases this is related to overdosing, it is important to measure the dose accurately.

If suspected adverse reactions occur, treatment should be discontinued.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or its local representative using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

8. Dosage for each species, routes and method of administration

Calves: In milk (replacer) use.

Pigs: In drinking water use.

Dosage:

Calves: 10 mg doxycycline hyclate per kg body weight per day for 5 days

Pigs: 10 mg doxycycline hyclate per kg body weight per day for 5 days

9. Advice on correct administration

Calves:

Based on the dose to be used, and the number and weight of the calves to be treated, the exact daily amount of veterinary medicinal product required can be calculated. To ensure a correct dosage, body weight should be determined as accurately as possible to avoid under-dosing. The use of suitably calibrated weighing equipment is recommended if part packs are used.

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The medicated milk (replacer) should not contain less than 100 mg veterinary medicinal product per litre.

Pigs:

A concentrated drinking water solution should be given twice daily (morning/evening) such that half of the total daily dose is consumed per medication period of 4 hours. This drinking water solution should contain at a minimum 400 mg veterinary medicinal product per litre drinking water. Based on the dose to be used, the minimum concentration of 400 mg veterinary medicinal product per litre, mean drinking water consumption, and the number and weight of the pigs to be treated, the exact amount of medicated drinking water required can be calculated. To ensure a correct dosage, body weight should be determined as accurately as possible. The use of suitably calibrated weighing equipment is recommended if part packs are used. For example, a solution containing 400 mg veterinary medicinal product per litre drinking water is sufficient, when given one litre twice per day, to administer the full treatment dose of 10 mg/kg for pigs of 80 kg body weight consuming 100 ml drinking water per kg body weight.

Medicated drinking water solution should be consumed within 4 hours. Do not prepare more medicated drinking water than will be consumed within that 4 hour period. It is advisable to restrict drinking water for approximately 2 hours (less in hot weather) prior to the medication period and to ensure there are enough drinking points for adequate water consumption for all pigs to be treated. No other source of drinking water should be available during the medication period. Once all the medicated water has been drunk, turn the drinking water system back on.

Solubility of the veterinary medicinal product is pH dependent and in areas with hard alkaline water, formation of complexes may occur in the drinking water. The veterinary medicinal product should not be used in very hard water above 17.5°d and pH more than 8.1.

10. Withdrawal periods

Calves:

Meat and offal: 16 days

Pigs:

Meat and offal: 8 days

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 of the immediate packaging: 6 months.

Shelf life after dissolution according to directions:

Solutions in water: 4 hours.

Milk solutions: 6 hours.

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

100 g, 250 g, 500 g, 1000 g or 10x100 g in a carton box.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

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

16. Contact details

Marketing authorisation holder, manufacturer responsible for batch release and contact details to report suspected adverse events:

Manufacturer responsible for batch release:

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

Local representatives and contact details to report suspected adverse events:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

17. Other information