

**Part IB-2**

**LABELLING**

CENTIDOX 1000 mg/g  
POWDER FOR USE IN DRINKING WATER OR MILK (REPLACER)  
FOR CATTLE AND PIGS

**The full text will be printed on the Sachet or Carton box  
Format used is required by Dutch law for this type of labelling**

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE**  
=  
**LEAFLET**

**Alufoil sachet: 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  
Doxycycline hyclate

**2. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS**

1 g powder contains:

**Active substance:**

Doxycycline hyclate                      1000 mg equivalent to 867 mg doxycycline base

**3. PHARMACEUTICAL FORM**

Powder for use in drinking water or milk (replacer).

**4. PACKAGE SIZE**

250 g, 500 g, 1 kg

**5. TARGET SPECIES**

Cattle (calves) and pigs.

**6. INDICATIONS**

Calves and pigs:

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 product is used.

**7. CONTRAINDICATIONS**

Do not use in animals with an active microbiological digestion in the rumen.

Do not use in case of known hypersensitivity to tetracyclines.

Do not use in animals with hepatic disorders.

Do not use in animals with renal disorders.

**8. ADVERSE REACTIONS**

In calves an acute, sometimes fatal, heart muscle degeneration occurs after one or more administrations. Since in most cases this is related to overdosing, it is important to accurately measure the dose.

Tetracyclines may - in 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 leaflet/text, please inform your veterinary surgeon.

## 9. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

### 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

### Mode of administration:

Calves: orally, dissolve in the milk (replacer)

Pigs: orally in the drinking water

### Calves:

Based on the dose to be used, and the number and weight of the calves to be treated, the exact daily amount of product 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 product per litre milk (replacer):

$$\frac{10 \text{ mg doxycycline hyclate per kg body weight per day} \times \text{Mean body weight (kg) of animals to be treated}}{\text{Mean daily milk (replacer) consumption (l) per animal}} = \dots \text{ mg product per l milk (replacer)}$$

After reconstitution with (artificial) milk the solution should be consumed within 6 hours. The medicated milk (replacer) should not contain less than 100 mg 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 product per litre drinking water. Based on the dose to be used, the minimum concentration of 400 mg 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 to avoid under-dosing. The use of suitably calibrated weighing equipment is recommended if part packs are used. For example, a solution containing 400 mg 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 product is pH dependent and in areas with hard alkaline water, formation of complexes may occur in the drinking water. The product should not be used in very hard water above 17.5°d and pH more than 8.1.

## 10. WITHDRAWAL PERIOD

Calves:

Meat and offal: 16 days

Pigs:

Meat and offal: 8 days

## **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/milk, animals should be treated parenterally.

### Special precautions for use in animals:

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 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 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 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 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 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):

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

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.

## **12. EXPIRY DATE**

Shelf life after first opening the immediate packaging: 6 months

Shelf life after dilution or reconstitution according to directions:

Solutions in water: 4 hours.

Milk solutions: 6 hours.

EXP: {month/year}

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**

xx-xx-2015

**21. OTHER INFORMATION**

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

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.

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE AND THE IMMEDIATE PACKAGE**

label 100 g alufoil sachet (in carton box of 10x100 g, with separate leaflet)  
booklet label (outside) 100 g alufoil sachet  
carton box for the 10x100 g alufoil sachets with separate 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  
Doxycycline hyclate

**2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES**

1 g powder contains:

**Active substance:**

Doxycycline hyclate                      1000 mg equivalent to 867 mg doxycycline base

**3. PHARMACEUTICAL FORM**

Powder for use in drinking water or milk (replacer)

**4. PACKAGE SIZE**

100 g, 10x100 g

**5. TARGET SPECIES**

Cattle (calves) and pigs.

**6. INDICATIONS**

**7. METHOD AND ROUTE(S) OF ADMINISTRATION**

Calves: orally, dissolve in the milk(replacer).  
Pigs: orally in the drinking water.  
Read the package leaflet before use.

**8. WITHDRAWAL PERIOD**

Calves: Meat and offal: 16 days

Pigs: Meat and offal: 8 days

## **9. SPECIAL WARNINGS**

Read the package leaflet before use.

## **10. EXPIRY DATE**

EXP: {month/year}

Shelf life after first opening of the immediate packaging: 6 months. Shelf life after dilution or reconstitution according to directions: Solutions in water: 4 hours. Milk solutions: 6 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}

**B. PACKAGE LEAFLET**

**booklet label (inside) 100 g sachet**

**leaflet in carton box for the 10x100 g alufoil sachets**



## 7. TARGET SPECIES

Cattle (calves) and pigs.

## 8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

### 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

### Mode of administration:

Calves: orally, dissolve in the milk (replacer)

Pigs: orally in the drinking water

## 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 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 product per litre milk (replacer):

$$\frac{10 \text{ mg doxycycline hyclate per kg body weight per day} \times \text{Mean body weight (kg) of animals to be treated}}{\text{Mean daily milk (replacer) consumption (l) per animal}} = \dots \text{ mg product per l milk (replacer)}$$

After reconstitution with (artificial) milk the solution should be consumed within 6 hours.

The medicated milk (replacer) should not contain less than 100 mg 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 product per litre drinking water. Based on the dose to be used, the minimum concentration of 400 mg 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 to avoid under-dosing. The use of suitably calibrated weighing equipment is recommended if part packs are used. For example, a solution containing 400 mg 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 product is pH dependent and in areas with hard alkaline water, formation of complexes may occur in the drinking water. The product should not be used in very hard water

above 17.5°d and pH more than 8.1.

## **10. WITHDRAWAL PERIOD**

### 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 the immediate packaging: 6 months.

Shelf life after dilution or reconstitution according to directions:

Solutions in water: 4 hours.

Milk solutions: 6 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/milk, animals should be treated parenterally.

### Special precautions for use in animals:

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 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 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, lactation or lay:

Laboratory studies have not produced any evidence of a teratogenic, foetotoxic or maternotoxic effect. In the absence of specific studies, the use of the 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 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):

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

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.

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

Any unused veterinary medicinal product or waste material 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**

xx-xx-2015

**15. OTHER INFORMATION**

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

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.