

*[Version 9.1,11/2024]*

**ANNEX I**  
**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Doxylin 100%, powder for use in drinking water/milk for cattle and pigs (NL, BE, DE, EE, EL, LT, LV)

Doxylin 1000 mg/g, powder for use in drinking water/milk for cattle and pigs (IT, HU, RO)

Doxylin, 867 mg/g, powder for use in the drinking water/milk for cattle and pigs (FR)

DoxyMed (DK), 1000 mg/g, powder for use in the drinking water/milk for cattle and pigs (PL)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:

### Active substances:

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

Yellow, crystalline powder.

## 3. CLINICAL INFORMATION

### 3.1 Target species

Cattle (pre-ruminating calf), pigs.

### 3.2 Indications for use for each target species

Pre-ruminating calves:

- Bronchopneumonia and pleuropneumonia caused by *Pasteurella* spp., *Streptococcus* spp., *Trueperella pyogenes*, *Histophilus somni* and *Mycoplasma* spp.

Pigs:

- Atrophic rhinitis caused by *Pasteurella multocida* and *Bordetella bronchiseptica*;  
- Bronchopneumonia caused by *Pasteurella multocida*, *Streptococcus suis* and *Mycoplasma hyorhinis*;  
- Pleuropneumonia caused by *Actinobacillus pleuropneumoniae*.

### 3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance.

Do not use in animals with severe liver- or kidney insufficiency.

### 3.4 Special warnings

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

It is necessary to administer medicated milk to calves on an individual basis. Also the separation of doxycycline in the milk replacer has to be taken into account. In order to prevent this, leave the mixer on during the tapping of the milk.

### 3.5 Special precautions for use

Special precautions for safe use in the target species:

Due to likely variability (time, geographical) in susceptibility of bacteria for doxycycline, bacteriological sampling and susceptibility testing of micro-organisms from diseased animals on farm are highly 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.

Resistance to tetracyclines has been reported in pig respiratory pathogens (*A. pleuropneumoniae*, *S. suis*) and calf pathogens (*Pasteurella* spp.) in some EU countries.

As eradication of the target pathogens may not be achieved, medication should therefore be combined with good management practices, e.g. good hygiene, proper ventilation, no overstocking.

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

People with known hypersensitivity to the tetracycline class of antibiotics should administer the veterinary medicinal product with caution.

To prevent sensitization and contact dermatitis during preparation and administration of the medicated drinking water, skin and eye contact with the veterinary medicinal product and inhalation of dust particles should be avoided. Personal protective equipment consisting of impermeable gloves (e.g. rubber or latex) and an appropriate dust mask (e.g. disposable half-mask respirator conforming to European Standard EN149) should be worn when handling 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, seek medical advice immediately and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes, or difficulty with breathing are more serious symptoms and require urgent medical attention.

Do not smoke, eat or drink while handling the veterinary medicinal product.

Special precautions for the protection of the environment:

Not applicable.

### 3.6 Adverse events

Cattle (pre-ruminating calf), pigs:

Rare (1 to 10 animals / 10 000 animals treated):	Photosensitivity Allergic reactions
Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Myocardial degeneration <sup>1</sup>

<sup>1</sup> In pre-ruminating calves. Acute (mostly fatal), following single or multiple dosages. Since mostly this is caused by overdosage, it is important to measure the dosage accurately.

If suspected adverse reactions occur, treatment should be discontinued.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet or the immediate packaging for respective contact details.

### 3.7 Use during pregnancy, lactation or lay

#### Pregnancy and lactation:

Due to deposit of doxycycline in young bone tissue, use of the veterinary medicinal product should be limited during pregnancy and lactation.

### 3.8 Interaction with other medicinal products and other forms of interaction

Do not use in conjunction with bactericidal antibiotics, such as penicillins and 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.

### 3.9 Administration routes and dosage

Calves: in milk (replacer) use.

Pigs: in drinking water use.

#### Dosage:

Calves: 10 mg of doxycycline hyclate/kg of body weight/day, for 3-5 consecutive days, divided over 2 administrations.

Pigs: 10 mg of doxycycline hyclate/kg of body weight/day, for 3-5 consecutive days.

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

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

To ensure a correct dosage body weight should be determined as accurately as possible.

The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage, the concentration doxycycline hyclate may need to be adjusted accordingly.

The use of suitably calibrated measuring equipment is recommended. The daily amount is to be added to the drinking water such that all medication will be consumed in 24 hours. Medicated drinking water should be freshly prepared every 12 hours. It is recommended to prepare a concentrated pre-solution - max. 400 grams of veterinary medicinal product per 10 litres of drinking water - and to dilute this further to therapeutic concentrations if required. Alternatively, the concentrated solution can be used in a proportional water medicator.

Solubility of the veterinary medicinal product is pH dependent and 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 16°d and pH more than 8.

Do not store the drinking water in metallic containers.

The medicated milk replacer should be used within 6 hours.

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

In calves an acute, sometimes fatal myocardial degeneration can occur following overdose (see also 3.6). Symptomatic treatment should be initiated if necessary.

### **3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance**

Not applicable.

### **3.12 Withdrawal periods**

Meat and offal:

Calves: 14 days.

Pigs: 8 days.

## **4. PHARMACOLOGICAL INFORMATION**

### **4.1 ATCvet code: QJ01AA02**

### **4.2 Pharmacodynamics**

Doxycycline is a broad-spectrum antibiotic. It inhibits bacterial protein synthesis intracellularly by binding on the 30-S ribosome subunits. This interferes with binding of aminoacyl-tRNA to the acceptor site on the mRNA ribosome complex and prevents coupling of amino acids to the elongating peptide chains.

Doxycycline inhibits bacteria, Mycoplasmata, Chlamydia, Rickettsia, and certain Protozoa.

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 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 micro-organisms with acquired resistance to tetracyclines.

MIC values for tetracycline:

<b>Pathogen</b>	<b>MIC<sub>50</sub></b>	<b>MIC<sub>90</sub></b>
Mannheimia haemolytica (Bo)	0.5	8
Pasteurella multocida (Bo)	0.5	2
Pasteurella multocida (Su)	0.5	2
Actinobacillus pleuropneumoniae (Su)	1	16
Streptococcus suis (Su)	16	32

### **4.3 Pharmacokinetics**

Doxycycline is quickly and almost completely absorbed from the intestine. The presence of food in the intestine has no effect on the actual absorption of doxycycline. The distribution of doxycycline in the body and penetration of doxycycline throughout most body tissues is good.

Following absorption, tetracyclines are hardly metabolised. In contrast to the other tetracyclines, doxycycline is mainly excreted via the faeces.

## **5. PHARMACEUTICAL PARTICULARS**

### **5.1 Major incompatibilities**

No information is available on potential interactions or incompatibilities of this veterinary medicinal product administered orally by mixing into drinking water or liquid feed containing biocidal products. In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

## **5.2 Shelf life**

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

Shelf life after first opening the immediate packaging: 3 months.

Shelf life after dissolution in drinking water according to directions: 12 hours.

Shelf life after dissolution in milk replacer according to directions: 6 hours.

## **5.3 Special precautions for storage**

Keep the container tightly closed in order to protect from light and moisture.

## **5.4 Nature and composition of immediate packaging**

White polypropylene container of 100 grams or 1 kg, covered with a low-density polyethylene closure.

White polypropylene container (bucket) of 1, 2 or 5 kg, covered with a polypropylene closure.

Not all pack sizes may be marketed.

## **5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products**

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

## **6. NAME OF THE MARKETING AUTHORISATION HOLDER**

Dopharma Research B.V.

## **7. MARKETING AUTHORISATION NUMBER(S)**

## **8. DATE OF FIRST AUTHORISATION**

Date of first authorisation:

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

## **10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS**

Veterinary medicinal product subject to prescription.

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

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE**

**Polypropylene container**

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Doxylin 100%, powder for use in drinking water/milk

**2. STATEMENT OF ACTIVE SUBSTANCES**

Doxycycline hyclate: 1000 mg/g  
(equivalent to doxycycline 867 mg/g)

**3. PACKAGE SIZE**

100 g, 1 kg, 2 kg or 5 kg

**4. TARGET SPECIES**

Cattle (pre-ruminating calf), pigs

**5. INDICATIONS**

**6. ROUTES OF ADMINISTRATION**

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

**7. WITHDRAWAL PERIODS**

Withdrawal periods:  
Meat and offal:  
Calves: 14 days.  
Pigs: 8 days.

**8. EXPIRY DATE**

Exp. {mm/yyyy}

Shelf life after dissolution in drinking water according to directions: 12 hours.  
Shelf life after dissolution in milk replacer according to directions: 6 hours.  
Once opened use within 3 months.  
Once opened, use by ... \_\_/\_\_/\_\_

**9. SPECIAL STORAGE PRECAUTIONS**

Keep the container tightly closed in order to protect from light and 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**

Dopharma Research B.V.

**14. MARKETING AUTHORISATION NUMBERS**

**15. BATCH NUMBER**

Lot {number}

**B. PACKAGE LEAFLET**

## PACKAGE LEAFLET

### 1. Name of the veterinary medicinal product

Doxylin 100%, powder for use in drinking water/milk for cattle and pigs

### 2. Composition

#### Active substances:

Doxycycline hyclate 1000 mg/g  
(equivalent to doxycycline 867 mg/g)

Yellow, crystalline powder.

### 3. Target species

Cattle (pre-ruminating calves) and pigs.

### 4. Indications for use

Pre-ruminating calves:

- Bronchopneumonia and pleuropneumonia caused by *Pasteurella* spp., *Streptococcus* spp., *Trueperella pyogenes*, *Histophilus somni* and *Mycoplasma* spp.

Pigs:

- Atrophic rhinitis caused by *Pasteurella multocida* and *Bordetella bronchiseptica*;  
- Bronchopneumonia caused by *Pasteurella multocida*, *Streptococcus suis* and *Mycoplasma hyorhinis*;  
- Pleuropneumonia caused by *Actinobacillus pleuropneumoniae*.

### 5. Contraindications

Do not use in cases of hypersensitivity to the active substance.  
Do not use in animals with severe liver- or kidney insufficiency.

### 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 or medicated milk replacer, animals should be treated parenterally.

It is necessary to administer medicated milk to calves on an individual basis. Also the separation of doxycycline in the milk replacer has to be taken into account. In order to prevent this, leave the mixer on during the tapping of the milk.

#### Special precautions for safe use in the target species:

Due to likely variability (time, geographical) in susceptibility of bacteria for doxycycline, bacteriological sampling and susceptibility testing of micro-organisms from diseased animals on farm are highly 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.

Resistance to tetracyclines has been reported in pig respiratory pathogens (*A. pleuropneumoniae*, *S. suis*) and calf pathogens (*Pasteurella* spp.) in some EU countries.

As eradication of the target pathogens may not be achieved, medication should therefore be combined with good management practices, e.g. good hygiene, proper ventilation, no overstocking.

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

People with known hypersensitivity to the tetracycline class of antibiotics should administer the veterinary medicinal product with caution.

To prevent sensitization and contact dermatitis during preparation and administration of the medicated drinking water, skin and eye contact with the veterinary medicinal product and inhalation of dust particles should be avoided. Personal protective equipment consisting of impermeable gloves (e.g. rubber or latex) and an appropriate dust mask (e.g. disposable half-mask respirator conforming to European Standard EN149) should be worn when handling 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, seek medical advice immediately and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes, or difficulty with breathing are more serious symptoms and require urgent medical attention.

Do not smoke, eat or drink while handling the veterinary medicinal product.

Pregnancy and lactation:

Due to deposit of doxycycline in young bone tissue, use of the veterinary medicinal product should be limited during pregnancy and lactation.

Interaction with other medicinal products and other forms of interaction:

Do not use in conjunction with bactericidal antibiotics, such as penicillins and 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:

In calves an acute, sometimes fatal myocardial degeneration can occur following overdose (see also the section Adverse events). Symptomatic treatment should be initiated if necessary.

Major incompatibilities:

No information is available on potential interactions or incompatibilities of this veterinary medicinal product administered orally by mixing into drinking water or liquid feed containing biocidal products. In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

**7. Adverse events**

Cattle (pre-ruminating calf), pigs:

Rare (1 to 10 animals / 10 000 animals treated):	Photosensitivity Allergic reactions
Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Myocardial degeneration <sup>1</sup>

<sup>1</sup> In pre-ruminating calves. Acute (mostly fatal), following single or multiple dosages. Since mostly this is caused by overdosage, it is important to measure the dosage 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.

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

Calves: 10 mg of doxycycline hyclate/kg of body weight/day, for 3-5 consecutive days, divided over 2 administrations.

Pigs: 10 mg of doxycycline hyclate/kg of body weight/day, for 3-5 consecutive days.

Calves: in milk (replacer) use.

Pigs: in drinking water use.

## **9. Advice on correct administration**

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

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

To ensure a correct dosage body weight should be determined as accurately as possible.

The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage, the concentration doxycycline hyclate may need to be adjusted accordingly.

The use of suitably calibrated measuring equipment is recommended. The daily amount is to be added to the drinking water such that all medication will be consumed in 24 hours. Medicated drinking water should be freshly prepared every 12 hours. It is recommended to prepare a concentrated pre-solution - max. 400 grams of veterinary medicinal product per 10 litres of drinking water - and to dilute this further to therapeutic concentrations if required. Alternatively, the concentrated solution can be used in a proportional water medicator.

Solubility of the veterinary medicinal product is pH dependent and 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 16°d and pH more than 8.

Do not store the drinking water in metallic containers.

The medicated milk replacer should be used within 6 hours.

## **10. Withdrawal periods**

Meat and offal:

Calves: 14 days.

Pigs: 8 days.

## **11. Special storage precautions**

Keep out of the sight and reach of children.

Keep the container tightly closed in order to protect from light and 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: 3 months.

Shelf life after dissolution in drinking water according to directions: 12 hours.

Shelf life after dissolution in milk replacer according to directions: 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**

### **Pack sizes:**

- Container: 100 grams, 1 kg.

- Bucket: 1, 2, 5 kg.

Not all pack sizes may be marketed.

## **15. Date on which the package leaflet was last revised**

DD/MM/YYYY

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 and contact details to report suspected adverse events:

Dopharma Research B.V.

Zalmweg 24

NL-4941 VX Raamsdonksveer

Tel: +31-162-582000

[pharmacovigilance@dopharma.com](mailto:pharmacovigilance@dopharma.com)

Manufacturer responsible for batch release:

Dopharma B.V.

Zalmweg 24

NL-4941 VX Raamsdonksveer

Local representative and contact details to report suspected adverse events:

{Name}

{Address}  
{Country} – {Town} – {Code}  
Tel: + {Telephone number}  
{E-mail}

**<17. Other information>**

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

**PP Container/bucket**

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Doxylin 100%, powder for use in drinking water/milk for cattle and pigs.

**2. COMPOSITION**

Doxycycline hyclate 1000 mg/g  
(equivalent to doxycycline 867 mg/g)

Yellow, crystalline powder.

**3. PACKAGE SIZE**

100 grams, 1 kg, 2 kg, 5 kg

**4. TARGET SPECIES**

Cattle (pre-ruminating calves) and pigs.

**5. INDICATIONS FOR USE**

**Indications for use**

Pre-ruminating calves:

- Bronchopneumonia and pleuropneumonia caused by *Pasteurella* spp., *Streptococcus* spp., *Trueperella pyogenes*, *Histophilus somni* and *Mycoplasma* spp.

Pigs:

- Atrophic rhinitis caused by *Pasteurella multocida* and *Bordetella bronchiseptica*;  
- Bronchopneumonia caused by *Pasteurella multocida*, *Streptococcus suis* and *Mycoplasma hyorhinis*;  
- Pleuropneumonia caused by *Actinobacillus pleuropneumoniae*.

**6. CONTRAINDICATIONS**

**Contraindications**

Do not use in cases of hypersensitivity to the active substance.  
Do not use in animals with severe liver- or kidney insufficiency.

**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 or medicated milk replacer, animals should be treated parenterally.

It is necessary to administer medicated milk to calves on an individual basis. Also the separation of doxycycline in the milk replacer has to be taken into account. In order to prevent this, leave the mixer on during the tapping of the milk.

Special precautions for safe use in the target species:

Due to likely variability (time, geographical) in susceptibility of bacteria for doxycycline, bacteriological sampling and susceptibility testing of micro-organisms from diseased animals on farm are highly 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.

Resistance to tetracyclines has been reported in pig respiratory pathogens (*A. pleuropneumoniae*, *S. suis*) and calf pathogens (*Pasteurella* spp) in some EU countries.

As eradication of the target pathogens may not be achieved, medication should therefore be combined with good management practices, e.g. good hygiene, proper ventilation, no overstocking.

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

People with known hypersensitivity to the tetracycline class of antibiotics should administer the veterinary medicinal product with caution.

To prevent sensitization and contact dermatitis during preparation and administration of the medicated drinking water, skin and eye contact with the veterinary medicinal product and inhalation of dust particles should be avoided. Personal protective equipment consisting of impermeable gloves (e.g. rubber or latex) and an appropriate dust mask (e.g. disposable half-mask respirator conforming to European Standard EN149) should be worn when handling 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, seek medical advice immediately and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes, or difficulty with breathing are more serious symptoms and require urgent medical attention.

Do not smoke, eat or drink while handling the veterinary medicinal product.

Pregnancy and lactation:

Due to deposit of doxycycline in young bone tissue, use of the veterinary medicinal product should be limited during pregnancy and lactation.

Interaction with other medicinal products and other forms of interaction:

Do not use in conjunction with bactericidal antibiotics, such as penicillins and cephalosporins.

Absorption of doxycycline can be decreased in the presence of high quantities of calcium, iron, magnesium or aluminium in the diet. Do not administered 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:

In calves an acute, sometimes fatal myocardial degeneration can occur following overdose. (See also the section Adverse events). Symptomatic treatment should be initiated if necessary.

Major incompatibilities:

No information is available on potential interactions or incompatibilities of this veterinary medicinal product administered orally by mixing into drinking water or liquid feed containing biocidal products. In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

## 8. ADVERSE EVENTS

### Adverse events

Cattle (pre-ruminating calf), pigs:

Rare (1 to 10 animals / 10 000 animals treated):	Photosensitivity Allergic reactions
Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Myocardial degeneration <sup>1</sup>

<sup>1</sup> In pre-ruminating calves. Acute (mostly fatal), following single or multiple dosages. Since mostly this is caused by overdosage, it is important to measure the dosage 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.

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

### Dosage for each species, routes and method of administration

Calves 10 mg of doxycycline hyclate/kg of body weight/day, for 3-5 consecutive days, divided over 2 administrations.

Pigs: 10 mg of doxycycline hyclate/kg of body weight/day, for 3-5 consecutive days.

Calves: in milk (replacer) use.

Pigs: in drinking water use.

## 10. ADVICE ON CORRECT ADMINISTRATION

### Advice on correct administration

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

$$\frac{\text{mg of veterinary medicinal product / kg of body weight / day}}{\text{Mean body weight (kg) of animals to be treated}}$$

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Mean daily water consumption (litre) per animal

= .... mg of veterinary medicinal product per litre of drinking water

To ensure a correct dosage body weight should be determined as accurately as possible.

The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage, the concentration doxycycline hyclate may need to be adjusted accordingly.

The use of suitably calibrated measuring equipment is recommended. The daily amount is to be added to the drinking water such that all medication will be consumed in 24 hours. Medicated drinking water should be freshly prepared every 12 hours. It is recommended to prepare a concentrated pre-solution – max. 400 grams of veterinary medicinal product per 10 litres of drinking water - and to dilute this further to therapeutic concentrations if required. Alternatively, the concentrated solution can be used in a proportional water medicator.

Solubility of the veterinary medicinal product is pH dependent and 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 16°d and pH more than 8.

Do not store the drinking water in metallic containers.

The medicated milk replacer should be used within 6 hours.

## **11. WITHDRAWAL PERIODS**

### **Withdrawal periods**

Calves (Meat and offal): 14 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 container tightly closed in order to protect from light and 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

### Pack sizes

- Container: 100 grams, 1 kg.
- Bucket: 1, 2, 5 kg.

Not all pack sizes may be marketed.

## 16. DATE ON WHICH THE LABEL WAS LAST REVISED

### Date on which the label was last revised

DD/MM/YYYY

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 and contact details to report suspected adverse events:

Dopharma Research B.V.  
Zalmweg 24  
NL-4941 VX Raamsdonksveer  
Tel: +31-162-582000  
[pharmacovigilance@dopharma.com](mailto:pharmacovigilance@dopharma.com)

#### Manufacturer responsible for batch release:

Dopharma B.V.  
Zalmweg 24  
NL-4941 VX Raamsdonksveer

#### Local representatives and contact details to report suspected adverse events:

{Name}  
{Address}  
{Country} – {Town} – {Code}  
Tel: + {Telephone number}  
{E-mail}

## 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: 3 months.

Shelf-life after dissolution in drinking water: 12 hours.

Shelf-life after dissolution in milk replacer: 6 hours.

<b>21. BATCH NUMBER</b>
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Lot {number}