ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Label for 200 g container and 1 Kg container

1.NAME OF THE VETERINARY MEDICINAL PRODUCT

Doxipulvis 500 mg/g Powder for Use in Drinking Water / Milk Replacer
Doxycycline hyclate

2.STATEMENT OF THE ACTIVE SUBSTANCES

Each gram contains:

Active substance:

Doxycycline 500.0 mg
(As doxycycline hyclate 577.1 mg)

3.PHARMACEUTICAL FORM

Powder for use in drinking water/milk replacer

4.PACKAGE SIZE

200 g
1 Kg

5.TARGET SPECIES

Cattle (pre-ruminant calves), pigs, chickens (broilers, breeders) and turkeys (broilers, breeders)

6.INDICATION(S)

7.METHOD AND ROUTE(S) OF ADMINISTRATION

To be administered orally in milk replacer, drinking water or liquid feed.

Calves, pigs:

10 mg of doxycycline per kg of body weight per day (equivalent to 11.54 mg of doxycycline hyclate/kg bw /day) by oral route, during 3 to 5 days, or 0.2 g of powder

per 10 kg of body weight per day, during 3-5 consecutive days, to be dissolved in drinking water, milk or liquid feed; to be adjusted according to actual feed intake of the animals, in order to meet the weight dosage.

Chickens and turkeys:

10 mg of doxycycline per kg of body weight per day (equivalent to 11.54 mg of doxycycline hyclate/kg bw /day), equivalent to 0.02 g of soluble powder per kg of body weight during 3 to 5 consecutive days, to be dissolved in drinking water.

The exact daily amount of oral powder based on the recommended dose and the number and weight of the animals to be treated should be calculated according to the following formula:

$$\frac{\text{0.02 g of powder per kg of body weight per day} \times \text{body weight (kg) of the animals to be treated}}{\text{Average water intake per animal (litres)}} = \text{… g of powder per litre of drinking water}$$

To ensure accuracy of the dose, the body weight should be determined as precisely as possible.

The intake of water containing the drug substance depends on the clinical condition of the animals. To obtain the correct dose, it may be necessary to adjust the concentration in the drinking water.

8.WITHDRAWAL PERIOD(S)

Withdrawal period:

Meat and offal:

- Cattle (Calves): 14 days
- Pigs: 6 days
- Chicken: 7 days
- Turkeys: 12 days

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

9.SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP:

Shelf life after first opening the immediate packaging: 1 month
Shelf life after dilution in drinking water according to directions: 12 hours
Shelf life after dilution in milk replacer according to directions: 1 hour
Shelf life after dilution in liquid feed according to directions: use immediately
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

Once opened, use by ...

11. SPECIAL STORAGE CONDITIONS

This veterinary medicinal product does not require any special storage conditions.

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

Disposal: read package leaflet.

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

For animal treatment only. To be supplied only on veterinary prescription
Administration by a veterinary surgeon or under their direct responsibility.

IE: POM Prescription Only Medicine.

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

SP Veterinaria SA
Ctra. Reus
Vinyols km 4.1 – Riudoms (43330)
Spain

16. MARKETING AUTHORISATION NUMER(S)

Vm 36967/5001

17. MANUFACTURE'S BATCH NUMBER

B. PACKAGE LEAFLET

PACKAGE LEAFLET

DOXIPULVIS 500 MG/G POWDER FOR USE IN DRINKING WATER/MILK REPLACER

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

Marketing authorisation holder and manufacturer responsible for batch release:
SP Veterinaria SA
Ctra. Reus
Vinyols km 4.1 – Riudoms (43330)
Spain

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Doxipulvis 500 mg/g Powder for Use in Drinking Water / Milk Replacer
Doxycycline hyclate

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

Each gram contains:

Active substance:

Doxycycline (hyclate) 500.0 mg
(As doxycycline hyclate 577.1 mg)

Yellow fine powder

4. INDICATION(S)

In calves:
- Treatment and metaphylaxis of respiratory and digestive infections caused by germs susceptible to doxycycline.

In pigs:
- Treatment and metaphylaxis of respiratory infections caused by germs susceptible to doxycycline.

In chickens and turkey:
- Treatment and metaphylaxis of respiratory infections due to micro-organisms susceptible to doxycycline.

In the case of metaphylaxis, the presence of the disease in the group must be established before the product is used.

5. CONTRAINDICATIONS

Do not use in cases of hypersensitivity to the active substance, to other tetracyclines or to any of the excipients.
Do not use when tetracycline resistance has been detected in the herd/flock due to the potential for cross resistance.
Do not use in animals with renal or hepatic disorders.
Do not use in ruminating cattle.

6. ADVERSE REACTIONS

Gastrointestinal disturbances, allergic reactions and photosensitisation may occur very rarely.

If suspected adverse reactions occur, treatment should be discontinued.

The frequency of adverse reactions is defined using the following convention:
- Very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- Common (more than 1 but less than 10 animals in 100 animals treated)
- Uncommon (more than 1 but less than 10 animals in 1000 animals treated)
- Rare (more than 1 but less than 10 animals in 10000 animals treated)
- Very rare (less than 1 animal in 10000 animals treated, including isolated reports)

Alternatively you can report via your national reporting system {national system details}. For details regarding the national system please contact NCA.

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 inform your veterinary surgeon.

7. TARGET SPECIES

Cattle (pre-ruminant calves), pigs, chickens (broilers, breeders) and turkeys (broilers, breeders)

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

To be administered orally in milk replacer, drinking water or liquid feed.

Calves, pigs:

10 mg of doxycycline per kg of body weight per day (equivalent to 11.54 mg of doxycycline hyclate/kg bw /day) by oral route, during 3 to 5 days, or 0.2 g of powder per 10 kg of body weight per day, during 3-5 consecutive days, to be dissolved in drinking water, milk or liquid feed; to be adjusted according to actual feed intake of the animals, in order to meet the weight dosage.

Chickens and turkeys:

10 mg of doxycycline per kg of body weight per day (equivalent to 11.54 mg of doxycycline hyclate/kg bw /day), equivalent to 0.02 g of soluble powder per kg of body weight during 3 to 5 consecutive days, to be dissolved in drinking water.

The exact daily amount of oral powder based on the recommended dose and the number and weight of the animals to be treated should be calculated according to the following formula:

$$\frac{\text{0.02 g of powder per kg of body weight per day} \times \text{body weight (kg) of the animals to be treated}}{\text{Average water intake per animal (litres)}} = \ldots \text{ g of powder per litre of drinking water}$$

To ensure accuracy of the dose, the body weight should be determined as precisely as possible.

The intake of water containing the drug substance depends on the clinical condition of the animals. To obtain the correct dose, it may be necessary to adjust the concentration in the drinking water.

9. ADVICE ON CORRECT ADMINISTRATION

The use of suitably calibrated weighing equipment is recommended if part packs are used. The daily amount of powder should be added to the drinking water so that the drug is consumed in 24 hours divided in two administrations. Drinking water containing the drug substance has to be freshly prepared every 12 hours. It is recommended to prepare a concentrated solution (approximately 10 g of product per litre of water) which can be diluted later, if necessary, to the therapeutic

concentration. It is also possible to distribute the concentrated solution using a metering pump.

The product should not be prepared at a concentration below 0.1 g of powder/L of hard water/ milk and at pH above 8.2.
The solubility of the product has been tested at the maximum concentration of 400 g/L.

The medicated water should be the only source of drinking water, throughout the treatment period. Water uptake should be monitored at frequent intervals during medication.
Sufficient access to the system of water supply should be available for the animals to be treated to ensure adequate water consumption. The medicated water must not be prepared or stored in a metal container. After the end of the medication period, the water supply system should be cleaned appropriately to avoid intake of sub-therapeutic amounts of the active substance.

The temperature of the milk replacer should not be above 38ºC prior to the introduction of the finished product.
The milk replacer should be prepared no more than one hour prior to the addition of the product and the medicated milk replacer should be used immediately.

When administering in liquid feed, first dissolve the product in water and then add feed. The preparation should be used immediately. Care should be taken that the intended dose will be completely ingested.

10. WITHDRAWAL PERIOD(S)

Meat and offal:

- Cattle (Calves): 14 days
- Pigs: 6 days
- Chicken: 7 days
- Turkeys: 12 days

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

11. SPECIAL STORAGE PRECAUCIONS

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special storage conditions.
Shelf life after first opening the immediate packaging: 1 month

Shelf life after dilution in drinking water according to directions: 12 hours
Shelf life after dilution in milk replacer according to directions: 1 hour
Shelf life after dilution in liquid feed according to directions: use immediately
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

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, calves and pigs should be treated parenterally.

Special precautions for use in animals:

Due to the likely variability (time, geographical) in the occurrence of resistance of bacteria against doxycycline, bacteriological sampling and susceptibility testing of micro-organisms form diseased animals are highly recommended.
A high resistance rate for *Escherichia coli*, isolated from chickens against tetracyclines has been documented. Therefore, the product should be used for the treatment of infections caused by *E. coli* only after susceptibility testing has been carried out. Resistance to tetracyclines has also been reported in pig respiratory pathogens (*Actinobacillus pleuropneumoniae*, *Streptococcus suis*) and calf pathogens (*Pasteurella* spp.) in some EU countries.
Official and local antimicrobial policies should be taken into account when the product is used.
Use the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to doxycycline and may decrease the effectiveness of treatment with other tetracyclines due to the potential for cross-resistance.
As the eradication of target pathogens may not be achieved, medication should be combined with good animal husbandry practices such as proper sanitation, adequate ventilation, no overstocking.

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

- This product may cause contact dermatitis and/or hypersensitivity reactions if contact is made with the skin or eyes (powder and solution), or if the powder is inhaled.
- 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.
- 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 or a non – disposable respirator to European Standard EN140 with a filter to EN143) 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.

Pregnancy / Lactation / Lay / Fertility:

Doxycycline showed no evidence of teratogenic or embryotoxic effects in laboratory animals.
In mammals, doxycycline crosses the placental barrier. Due to a lower affinity for calcium, doxycycline results in less staining of teeth compared to tetracycline.
Doxycycline is found in breast milk.
The safety of the veterinary medicinal product has not been established during pregnancy and lactation. In pregnant and lactating animals use only in accordance to the benefit/risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:
Divalent or trivalent cations (Mg, Fe, Al, Ca) can chelate tetracyclines. Tetracyclines should not be administered with antiacids, gels based on aluminum, preparations based on vitamins or minerals, since insoluble complexes are formed, which reduces the absorption of the antibiotic.
Do not use in conjunction with bactericidal antibiotics, such as penicillins or cephalosporins.

Doxycycline increases the action of anticoagulants.

Overdose (symptoms, emergency procedures, antidotes):
Not described. If suspected toxic reactions occur, the medication should be discontinued and appropriate symptomatic treatment should be initiated.

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

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

Medicines should not be disposed of via wastewater.
Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

October 2021

15. OTHER INFORMATION

Package size:

200 g
1 Kg

Not all pack sizes may be marketed.

Approved 26 June 2023