LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Bag

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Doxx-Sol 500 mg/g powder for use in drinking water/milk replacer for pre-ruminant calves, pigs and chickens
Doxycycline hyclate

2. STATEMENT OF ACTIVE SUBSTANCES

1 gram contains:
Doxycycline hyclate 500 mg (equivalent to 433 mg doxycycline)

3. PHARMACEUTICAL FORM

Powder for use in drinking water/milk replacer

4. PACKAGE SIZE

1 kg
(5 kg)

5. TARGET SPECIES

Cattle (pre-ruminant calves), pigs, chickens, (broilers, breeders, replacement pullets)

6. INDICATION

7. METHOD AND ROUTE OF ADMINISTRATION

Oral use, after dissolution in drinking water/milk replacer.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD (S)

Withdrawal periods

Meat and offal:
Calves: 7 days
Pigs: 8 days
Chickens: 5 days
Not for use in birds producing or intended to produce eggs for human consumption.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

Exp <<EXP month/year>>
Shelf life after first opening of the immediate packaging: 3 months.
Shelf life after reconstitution in drinking water: 24 hours.
Shelf life after reconstitution in milk replacer: 4 hours.

Once opened, use by:

11. SPECIAL STORAGE CONDITIONS

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

Disposal: Read the package leaflet.

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

Huvepharma NV
Uitbreidingstraat 80
2600 Antwerp
Belgium

16. MARKETING AUTHORISATION NUMBER

Vm 30282/4022

17. MANUFACTURER'S BATCH NUMBER

Batch <<number>>

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:

Doxx-Sol 500 mg/g powder for use in drinking water/milk replacer for pre-ruminant calves, pigs and chickens

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

Marketing authorisation holder:
Huvepharma NV
Uitbreidingstraat 80
2600 Antwerp
Belgium

Manufacturer responsible for the batch release:
Biovet JSC
39 Petar Rakov Str.
4550 Peshtera
Bulgaria

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Doxx-Sol 500 mg/g powder for use in drinking water/milk replacer for pre-ruminant calves, pigs and chickens

Doxycycline hyclate

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

Each gram contains:
Active substance:
Doxycycline hyclate 500 mg (equivalent to 433 mg doxycycline)

Yellowish powder.
Clear solution when dissolved in water

4. INDICATION(S)

Treatment of the following specified infectious diseases of the respiratory tract and the alimentary tract caused by micro-organisms susceptible to doxycycline

Cattle (Pre-ruminant calves:)
- Bronchopneumonia and pleuropneumonia caused by *Pasteurella spp*., *Streptococcus spp*., *Trueperella pyogenes,s*, *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*.

Chickens (broilers, breeders, replacement pullets):
- Infections of the respiratory tract caused by *Mycoplasma spp*., *Escherichia coli*, *Haemophilus paragallinarum* and *Bordetella avium*;
- Enteritis caused by *Clostridium perfringens* and *Clostridium colinum*.

5. CONTRAINDICATIONS

Do not use in known cases of known hypersensitivity to tetracyclines or to any of the excipients.
Do not administer to animals with serious liver or kidney insufficiency.
Do not use when tetracycline resistance has been detected in the herd/flock due to the potential for cross resistance
Do not use in ruminating cattle.

6. ADVERSE REACTIONS

As for all tetracyclines, on rare occasions allergic reactions and photosensitivity may occur. If suspected adverse reactions occur, treatment should be discontinued
If you notice any serious effects or other effects not mentioned in this leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

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 1,000 animals treated)

- rare (more than 1 but less than 10 animals in 10,000 animals treated)

- very rare (less than 1 animal in 10,000 animals treated, including isolated reports)

7. TARGET SPECIES

Cattle (pre-ruminant calves), pigs, chickens, (broilers, breeders, replacement pullets)

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

Cattle (Pre-ruminant calves): for use in milk replacer
10 mg doxycycline hyclate (corresponding to 20 mg of product) /kg body weight / day, divided over 2 administrations, for 3-5 consecutive days

Pigs:
for use in drinking water
10 mg doxycycline hyclate (corresponding to 20 mg of product) /kg body weight / day, / kg body weight/day, for 3-5 consecutive days.

Chickens (broilers, breeders, replacement pullets): for use in drinking water
25 mg doxycycline hyclate (corresponding to 50 mg of product) /kg body weight / day, / kg body weight/day, for 3-5 consecutive days.

To be administered orally through the milk-replacer and/or the drinking water.

9. ADVICE ON CORRECT ADMINISTRATION

For the administration through the drinking water, the exact daily amount of product should be calculated, based on the recommended dose, and the number and weight of the animals to be treated, according to the following formula:

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

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

The uptake of medicated water is dependent on the clinical conditions of the animals. In order to obtain the correct dosage, the concentration in drinking water may have to be adjusted. The use of suitably calibrated weighing equipment is recommended if part packs are used.
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 24 hours.

It is recommended to prepare a concentrated pre-solution - not exceeding 100 grams product per litre drinking water - and to dilute this further to therapeutic concentrations if required. Alternatively, the concentrated solution can be used in a proportional water medicator. The water should be stirred until full dissolution of the product is obtained.
Milk replacer: The veterinary medicinal product must first be dissolved in water before adding the milk powder. The medicated milk replacer should be used immediately and should be freshly prepared after 4 hours at the latest.
Sufficient access to the system of water supply should be available for the animals to be treated to ensure adequate water consumption. No other source of drinking water should be available during the medication period. At the end of treatment period the water supply should be cleaned adequately to avoid the uptake of remaining quantities in sub-therapeutic doses.
The solubility of doxycycline decreases at higher pH. Therefore, the product should not be used in hard alkaline water since precipitation might occur depending on the product concentration. Delayed precipitation might also occur.

10. WITHDRAWAL PERIODS

Meat and offal:
Calves: 7 days
Pigs: 8 days
Chickens: 5 days

Not for use in birds producing or intended to produce eggs for human consumption.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Do not use this veterinary medicinal product after expiry date which is stated on the label after exp. The expiry date refers to the last day of the month
Shelf life after first opening the container: 3 months.
Shelf life after reconstitution in drinking water: 24 hours.
Shelf life after reconstitution in milk replacer: 4 hours.

12. SPECIAL WARNINGS

Special precautions for use in animals

A high resistance rate of *E. coli*, isolated from chickens, against tetracyclines has been documented. Resistance to tetracyclines has also been reported in pig respiratory pathogens (*A. pleuropneumoniae*, *S. suis*) and calf pathogens (*Pasteurella* spp.) in some EU countries.

Use of the product should be based on identification and susceptibility testing of the target pathogens. If it is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target bacteria at farm level, or at local/regional level.

Use of 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.

Official, national and regional antimicrobial policies should be taken into account when the product is used.

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:

Take measures to avoid producing dust when incorporating the product into water. 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.
People with known hypersensitivity to tetracyclines should avoid contact with the veterinary medicinal product. 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. Do not smoke, eat or drink while handling 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 and lactation

The safety of the veterinary medicinal product has not been established in pregnant or lactating sows.

Laboratory studies in rats and rabbits have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects

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

Use only according to the benefit/risk assessment by the responsible veterinarian.

Interactions with other medicinal products and other forms of interaction

Do not use in conjunction with bactericidal antibiotics, such as penicillins and cephalosporins.
Do not administer concurrently with feed overloaded with polyvalent cations such as Ca^{2+}, Mg^{2+}, Zn^{2+} and Fe^{3+} because the formation of doxycycline complexes with these cations is possible. Do not administer together with antacids, kaolin and iron preparations. It is advised that the interval between administration of the product and administration of products containing polyvalent cations should be 1-2 hours because the latter limit the absorption of doxycycline.
Doxycycline increases the action of anticoagulants.
Overdose (symptoms, emergency procedures, antidotes)

In calves acute, sometimes fatal myocardial degeneration can occur following single or multiple dosages. Since mostly this is caused by overdosage, it is important to measure the dosage accurately.
If suspected toxic reactions do occur due to extreme overdose, the medication should be discontinued and appropriate symptomatic treatment should be initiated if necessary.

Incompatibilities

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

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

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

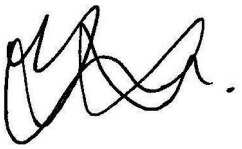
14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

December 2019

15. OTHER INFORMATION

Bag size 1 kg, 5 kg.
Not all pack sizes may be marketed.

To be completed nationally



Approved: 17 February 2020