[Version 9,03/2022]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Doxylin 50% WSP, powder for oral solution in pre-ruminant calves, pigs and chickens (BE, BG, CY, IT, LV, LU, NL, SK)
Doxylin 50%, powder for oral solution in pre-ruminant calves, pigs and chickens (PT, EE)
Doxylin 500 mg/g, powder for oral solution in pre-ruminant calves, pigs and chickens (HU, RO)
Doxylin Vet, powder for oral solution in pre-ruminant calves, pigs and chickens (DK)
Doxylin Vet 500 mg/g, powder for oral solution in pre-ruminant calves, pigs and chickens (FI, LT)
Doxylin 500 mg/g, powder for use in drinking water/milk for pre-ruminant calves, pigs and chickens (IE)
Doxymed 50, 500 mg/g, powder for oral solution in pre-ruminant calves, pigs and chickens (PL)
Doxymed 500 mg/g, powder for use in drinking water/milk for calves, pigs and chickens (AT)
Doxymed Vet 500 mg/g, powder for use in drinking water/milk for calves, pigs and chickens (NO, SE)
Doxycycline 50% Dopharma, powder for oral solution in pre-ruminant calves, pigs and chickens (EL)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Per gram:

Active substance:

Doxycycline hyclate: 500 mg
(equivalent to 433 mg doxycycline)

Excipients:

Qualitative composition of excipients and other constituents
Citric acid
Lactose

Slightly yellowish powder.

3. CLINICAL INFORMATION

3.1 Target species

Pre-ruminant calves, pigs, chickens.

3.2 Indications for use for each target species

For the treatment of the following specified infections of the respiratory tract and the alimentary tract caused by micro-organisms susceptible to doxycycline.

Pre-ruminant calves:
- Bronchopneumonia and pleuropneumonia caused by *Pasteurella spp*., *Streptococcus spp*., *Arcanobacterium 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*.

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

3.3 Contraindications

Do not use in cases of hypersensitivity to tetracyclines or to any of the excipients.
Do not administer to animals with severe liver- or kidney insufficiency.

3.4 Special warnings

A high resistance rate of E. coli, isolated from chickens, against tetracyclines has been documented. Therefore the veterinary medicinal 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 (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.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Use of the veterinary medicinal product should be based on identification and susceptibility testing of the target
pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.

Use of the veterinary medicinal product should be in accordance with official, national and regional antimicrobial
policies.

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

During the handling of the veterinary medicinal product, skin contact and inhalation has to be avoided, taking into account the risk of sensitization and contact dermatitis. For that purpose wear gloves and a dust mask.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

None known.

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 the national competent authority via the national reporting system. See also the last section of the package leaflet 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.
Tetracyclines can chelate cations (e.g. Mg, Mn, Fe and Al) and this may lead to decreased bioavailability

3.9 Administration routes and dosage

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

Pre-ruminant calves:	10 mg doxycycline hyclate / kg body weight / day, corresponding to 20 mg of veterinary medicinal product per kg body weight, for 3-5 consecutive days, divided over 2 administrations.
Pigs:	10 mg doxycycline hyclate / kg body weight / day, corresponding to 20 mg of veterinary medicinal product per kg body weight, for 3-5 consecutive days.
Chickens:	25 mg doxycycline hyclate / kg body weight / day, corresponding to 50 mg of veterinary medicinal product per kg body weight, for 3-5 consecutive days.

For the administration through the drinking water, the exact daily amount of veterinary medicinal 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:

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

To ensure a correct dosage body weight should be determined as accurately as possible.
The intake of medicated water depends on the clinical conditions of the animals. In order to obtain the correct dosage, the concentration in drinking water may have to be adjusted accordingly.
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 - approximately 100 grams of veterinary medicinal 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 medicated milk replacer should be used immediately.

3.10 Symptoms of overdose (and where applicable, emergency procedures and 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.

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: 7 days
Pigs: 8 days
Chickens: 5 days
Not for use in birds producing eggs for human consumption.
Not authorised for use in animals producing milk for human consumption.

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 aminoacetyl-tRNA to the acceptor site on the mRNA ribosome complex and prevents coupling of amino acids to the elongating peptide chains.
Doxycycline inhibits bacteria, Mycoplasma, Chlamydia, Rickettsia, and certain Protozoa.

Four resistance mechanisms acquired by microorganisms 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 microorganisms with acquired resistance to tetracyclines.

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 and penetration of doxycycline throughout most body tissues is good.
Following absorption, tetracyclines are hardly metabolized. In contrast to the other tetracyclines, doxycycline is mainly excreted via the faeces.

Calves
After a dosage of 10 mg/kg body weight/day during 5 days, an elimination halftime varying between 15 and 28 hours was found. The doxycycline plasma level reached an average of 2.2 to 2.5 µg/ml.

Pigs
In pigs, no accumulation of doxycycline in plasma was found after treatment via the drinking water. Mean plasma values of 0.44 ± 0.12 µg/ml after 3 days of medication with an average dose of 10 mg/kg body weight were found.

Poultry
Steady state plasma concentrations of 2.05 ± 0.47 µg/ml were reached within 6 hours after start of the medication and varied between 1.28 and 2.18 µg/ml with a dosage of 25 mg/kg body weight during 5 days.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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:
- securitainer: 36 months;
- bucket: 24 months.
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: use immediately.

5.3 Special precautions for storage

Store below 25ºC.
Do not refrigerate or freeze.
Protect from frost.

5.4 Nature and composition of immediate packaging

- Securitainer: white polypropylene container, covered with a low-density polyethylene lid.
The securitainer contains 1 kg of veterinary medicinal product.
- Bucket: white polypropylene bucket provided with a polypropylene lid.
The bucket contains 1, 2.5 or 5 kg of veterinary medicinal product.
Not all pack sizes may be marketed.

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

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

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.