# SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT.

**ES : DOXI – 10 S.P. PREMIX**
BG, PL, RO : Doxi SP 100 mg/g premix for porcine

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION.

**Active substance**

Doxycycline (hyclate) .....100 mg/g.

**Excipients**

For a full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM.

Premix for medicated feeding stuff

## 4. CLINICAL PARTICULARS

### 4.1. Target species

Porcine (fattening pigs)

### 4.2. Indications for use, specifying the target species

Porcine (fattening pigs): treatment of porcine respiratory complex caused *by Pasteurella multocida, Bordetella bronchyseptica* and/or *Mycoplasma hyopneumoniae.*

For any infectious process a bacteriological confirmation of the diagnosis is recommended and a sensitivity test for the bacteria causing the process should be performed.

### 4.3. Contraindications

Do not administer to animals with known hypersensitivity to tetracyclines.
Do not administer to animals with hepatic disturbances.
Do not use in case of known resistance to tetracyclines

## 4.4. Special warnings

Sick animals may have reduced appetite if necessary be medicated parenterally

## 4.5. Special precautions for use

### i) Special precautions for use in animals

For any infectious process a bacteriological confirmation of the diagnosis is recommended and a sensitivity test for the bacteria causing the process should be performed.

### ii) 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.
- Handle the veterinary medicinal product with care to avoid dust inhalation and contact with skin and eyes during incorporation of premix into feed, as well as when administering the medicated feed to animals, by taking specific precautions:
  - Take the appropriate measures to avoid dust dissemination during the incorporation of the premix into feed.
  - Wear a dust mask (in compliance with EN140FFP1), gloves, overalls and approved safety glasses.
  - Avoid contact with skin and eyes. Rinse thoroughly with water in case of exposure.
  - Do not smoke, eat or drink when handling the veterinary medicinal product.
  - If you develop symptoms following exposure such as skin rash, you should seek medical advice and show the present warning to the doctor. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.

## 4.6. Adverse reactions (frequency and seriousness)

- As for all tetracyclines, photosensitization as well as allergic reactions may occur.
- Prolonged treatments can lead to digestive disturbances and intestinal disbiosis.

## 4.7. Use during pregnancy, lactation or lay

In studies performed with experimental animals (mice and rabbit) toxic effects were not observed. The safety of the product has not been demonstrated in pregnant or lactating sows, therefore its use is not recommended in these animals.

## 4.8. Interactions with other medicinal products and other forms of interaction

Doxycycline absorption is diminished by the presence of high concentrations of calcium, iron, magnesium and aluminium in the diet. Do not administer along with

antiacids, kaolin or iron preparations.
It is advised that the interval between the administrations of other products containing polyvalent cations should be 1-2 hours because the limit the absorption of tetracyclines.
Do not combine with bactericidal antimicrobial agents as penicillin and cephalosporins
Doxycycline increases the action of anticoagulants.

### 4.9. Amounts to be administered and administration route

In-feed use.

13 mg of doxycycline / kg b.w. / day, during 8 days, approximately 250 g of doxycycline / tonne feed, for an estimated average consumption of 50 g of feed / kg b.w. / day, (equivalent to 2.5 kg of the product / tonne feed).

The dosage of the product to be incorporated in feed should be established according to the following formula:

130 mg the product / (kg b.w. * day) * (average body weight of animals in kg) / (average feed daily intake in kg)

Feed consumption will depend on the clinical condition of the animal. In order to obtain a correct dosage, the concentration of the antimicrobial agent should be adjusted taking into account the daily feed intake at the onset of treatment.

The product may be administered in pellets as well as non-pelleted feed. Recommended granulation conditions are: vapour during 15 minutes at a temperature not exceeding 80 ºC and pressure of 2.5 atm.

### 4.10. Overdose (symptoms, emergency procedures, antidotes), if necessary

Not described.

### 4.11. Withdrawal period

Pigs: meat and offal: 5 days

## 5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Tetracyclines
ATCvet code: QJ01AA02

### 5.1. Pharmacodynamic properties

Doxycycline is a bacteriostatic antibacterial that acts by interfering with bacterial protein synthesis in sensitive species.

Doxycycline is a semi-synthetic tetracycline derived from oxytetracycline, that acts on 30 S subunit of bacterial ribosome, to which it is reversibly bound, blocking the union of aminoacil-RNAt (transference RNA) to the complex formed by RNAm and ribosomes, preventing the addition of new aminoacids to the growing peptide chain and interfering in protein synthesis.

Doxycycline has a broad spectrum of activity (gram-positive and gram-negative bacteria).

It is active against:

*Mycoplasma spp*
*Bordetella spp*
*Pasteurella multocida*

*In-vitro* sensitivity to Doxycycline of porcine strains of *Pasteurella multocida* and *Bordetella bronchiseptica,* as well as *Mycoplasma hyopneumoniae,* have been determined, being $MIC_{90}$ 0.517 μg/ml, 0.053 μg/ml and 0.200 μg/ml, respectively.

According to the guidelines NCCLS, strains are considered sensitive to Doxycycline when MICs ≤ 4 μg/ml and resistant when MICs ≥ 16 μg/ml

At least two mechanisms of resistance to tetracyclines exist. The most important mechanism is due to a decrease in cellular accumulation of the drug, caused by the establishment of an elimination route by pumping the antibacterial or as a result of an alteration in transport system, that limits the uptake of energy-dependent tetracycline. The alteration in the transport system is caused by inducible proteins coded by plasmids and transposons. The other mechanism is due to a decrease of the affinity of ribosomes to Tetracycline-$Mg^{2+}$ complex, caused by chromosome mutations.

## 5.2. Pharmacodynamic particulars

Bioavailability after oral and i.m. administration is very high. When administered by oral route values higher than 70% are reached in most species. Feed can slightly modify oral bioavailability of Doxycycline. Under fasting conditions the drug has a bioavailability about 10-15% higher than when feed is administered to the animal.

Doxycycline is widely distributed in the organism thanks to its physico-chemical characteristics, since it is highly liposoluble. It reaches well-irrigated tissues, as well as peripheral tissues. It concentrates in liver, kidney and bones, as well as in intestines; since it has an enterohepatic cycle. In lung, concentrations higher than in plasma are reached. Therapeutic concentrations have been found in aqueous humor, myocardium, reproductive tissues, brain and mammary gland. Binding to plasmatic proteins is 90-92%.

About 40% of the drug is widely metabolized and excreted by feces (biliar and intestinal route), the main part as microbiologically inactive conjugates.

After the administration of 200, 400 and 800 mg Doxycycline/kg feed (dosage of 7, 13 and 26 mg/kg b.w.), minimum and maximum concentrations at steady state ($Css_{min}$ – $Css_{max}$) were 0.4 – 0.9, 0.7 – 1.2, 1.6 – 3.2 μg/ml, respectively.

After the administration of 250 mg doxycycline/kg feed (with the product), minimum and maximum concentrations at steady state ($Css_{min}$ – $Css_{max}$) were 2.27 and 1.44 g/ml, respectively.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1. List of excipients

- Refined arachis oil
- Almond and hazelnut shell

### 6.2. Incompatibilities

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

### 6.3. Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale : 24 months
Shelf-life after incorporation into meal or pelleted feed: 3 months
Shelf-life after first opening the immediate packaging: 3 months

### 6.4. Special precautions for storage

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

### 6.5. Nature and composition of immediate packaging

1 kg and 25 kg aluminium bags, thermosealed.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

## 7. MARKETING AUTHORISATION HOLDER.

S.P VETERINARIA S.A.
Ctra. Reus-Vinyols, km 4,1
43330 RIUDOMS
TARRAGONA
Spain

## 8. MARKETING AUTHORISATION NUMBER:

## 9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

## 10. DATE OF REVISION OF THE TEXT

## PROHIBITION OF SALE, SUPPLY AND/OR USE

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