ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ZOOTYL 945 000 IU/g powder for use in drinking water for pigs, chickens and turkeys

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:
Active substance:
Tylosin tartrate 945 000 IU

A white to medium yellow powder.

3. CLINICAL INFORMATION

3.1 Target species

Chicken (broilers, layer hens), turkeys and pigs.

3.2 Indications for use for each target species

Chicken (broilers, layer hens): Treatment and metaphylaxis of chronic respiratory disease (CRD). Treatment of necrotic enteritis caused by *Clostridium perfringens*.
Turkeys: Treatment and metaphylaxis of infectious sinusitis.
Pigs: Treatment of porcine proliferative enteritis or ileitis, caused by *Lawsonia intracellularis.*
The presence of the disease in the herd should be established before metaphylactic treatment.

3.3 Contraindications

Do not use in cases of hypersensitivity to tylosin or other macrolides or to any of the excipients.
Do not use in cases of known resistance to tylosin or cross-resistance to other macrolides (MLS-resistance).
Do not use in animals vaccinated with tylosin-sensitive vaccines either at the same time or within one week previously.
Do not administer to animals with hepatic damage.
Do not use in horses.

3.4 Special warnings

Do not leave or dispose of water containing tylosin tartrate where it may be accessible to either animals not under treatment or to wildlife.

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 to tylosin, bacteriological sampling and susceptibility testing are recommended.
Under dosing and/or treating for an insufficient length of time are considered to promote the development of resistance in bacteria and should be avoided.
Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to tylosin and other macrolides.
Official, national and regional procedures relating to use of antimicrobial agents should be taken into account.
Animals with acute infections may have a reduced water and feed consumption and should be treated with a suitable injectable veterinary medicinal product first.

A high rate of *in vitro* resistance has been demonstrated in European strains of *Brachyspira hyodysenteriae* implying that the product will not be sufficiently efficacious against swine dysentery.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Tylosin may induce irritation. Macrolides, such as tylosin, may also cause hypersensitivity (allergy) following injection, inhalation, ingestion or contact with skin or eye. Hypersensitivity to tylosin may lead to cross reactions to other macrolides and vice versa. Allergic reactions to these substances may occasionally be serious and therefore direct contact should be avoided.
People with known hypersensitivity to Tylosin tartrate should avoid contact with the veterinary medicinal product.
Personal protective equipment consisting of wear overalls, safety glasses, impervious gloves and wear either a disposable half mask respirator conforming to European Standard EN149 or a non-disposable respirator to European Standard EN140 with a filter to EN143 should be worn when handling the veterinary medicinal product. Wash hands after use.
In the event of accidental skin contact, wash thoroughly with soap and water. In case of accidental eye contact, flush the eyes with plenty of clean, running water.
Do not handle the product if you are allergic to ingredients in the product.
If you develop symptoms following exposure, such as skin rash, you should seek medical advice immediately and show the combined label and package leaflet to the physician.. Swelling of the face, lips and eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.

Special precautions for the protection of the environment:
Not applicable.

Other precautions:
To limit the development of antimicrobial resistance, it's advisable to perform periodic susceptibility testing.
The inappropriate use of the veterinary medicine may increase the prevalence of bacteria resistant to tylosin and may decrease the effectiveness of treatment with other macrolides, lincosamides and streptogramin B due to potential of cross-resistance.

3.6 Adverse events

Pigs

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Rectal oedema[1*], anal prolapse[1*, 2*], pruritus[1*], reddening of the skin[1*], diarrhoea[1*]

[1*] These reversible signs appeared 48-72 hours after initiation of treatment.

[2*] Mild anal prolapse.

Chicken and turkeys
No specific adverse reactions have been identified in chicken and turkeys.

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 combined label and package leaflet for respective contact details..

3.7 Use during pregnancy, lactation or lay

No adverse effects to tylosin have been seen in fertility, multi-generation or teratology studies.
No studies have been performed on the target species. Use only accordingly to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

Antagonism with lincosamides and aminoglycosides.

3.9 Administration routes and dosage

In drinking water use.

- CHICKEN:
- Treatment and metaphylaxis of chronic respiratory disease (CRD): 43800 – 87600 IU/kg bw/day (corresponding to 50 – 100 mg product/ kg bw).
- Metaphylaxis of CRD:

  Broilers:
  1st week – for 3 days
  4th week - for 1 day

  Layers:
  1st week – for 3 days
  4th week – for 1 day
  9th to 12th week – for 2 days
  18th to 20th week – for 2 days
- Treatment of CRD: Broilers and layers: for 3 to 5 days.

- Treatment of necrotic enteritis: 8800 – 17500 IU/kg bw/day (corresponding to 10 – 20 mg product/ kg bw) for 3 days.

- TURKEYS:
- Treatment and metaphylaxis of infectious sinusitis: 43800 – 87600 IU/kg bw/day (corresponding to 50 – 100 mg product/ kg bw).
- Metaphylaxis:
  1st week – for 5 days
  4nd week – for 1 day
- Treatment: for 5 days.

- PIGS:
- Treatment of ileitis: 4380 – 8760 IU/kg bw/day (corresponding to 5 – 10 mg product/ kg bw) for 7 days.

All species:
To ensure a correct dosage, body weight should be determined as accurately as possible. The use of suitably calibrated measuring equipment is recommended. The intake of medicated water depends on the clinical condition of the animals. In order to obtain the correct dosage, the concentration of tylosin tartrate may need to be adjusted accordingly. 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:

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

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.

The medicated water must be renewed every 24 hours.
If individual animals show signs of a serious infection such as a reduced water or feed intake, then they should be treated individually, such as by injection..

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

There are no known toxic effects of overdose associated with the use of the product. Do not exceed the recommended dose.

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:
Chiken and pigs - zero days.
Turkeys – 1 day
Eggs: zero days

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01FA90

4.2 Pharmacodynamics

Tylosin is a macrolide antibiotic produced by a strain of *Streptomyces fradiae*. It exerts its antimicrobial effect by inhibiting protein synthesis of susceptible micro-organisms.
The tylosin spectrum of activity includes Gram-positive bacteria including *Clostridium perfringens* and some Gram-negative strains such as *Pasteurella* and *Mycoplasma* spp. at concentrations of 16µg/ml or less.

4.3 Pharmacokinetics

Absorption: Tylosin reaches maximal blood levels between 1 to 3 hours after oral administration. Minimal or no blood levels remain 24 hours after an oral dose.
Distribution: After oral dose given to pigs, tylosin was found in all tissues, between 30 minutes and two hours after administration, except for the brain and spinal cord.
Biotransformation and elimination: It was demonstrated that most of the excreted material is to be found in faeces and consists of tylosin (factor A), relomycin (factor D) and dihydrodesmycosin.

Environmental properties

Tylosin is toxic for terrestrial plants and cyanobacteria.

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: 3 years
Shelf life after first opening the immediate packaging: 28 days
Shelf life after reconstitution according to directions: 24 hours

5.3 Special precautions for storage

Store in the original package.
Store in a dry place.

5.4 Nature and composition of immediate packaging

Polyester(PET)/Adhesive/Aluminium foil (ALU)/Polyethylene (PE) bags closed by thermo-sealing. The inner layer is PE.

Pack sizes:
100 g (contain 94 500 000 IU)
1 kg (contain 945 MIU)
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.
The veterinary medicinal product should not enter water courses as tylosin tartrate may be dangerous for fish and other aquatic organisms. 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

ZOOPAN - Produtos Pecuários, S.A.

7. MARKETING AUTHORISATION NUMBER(S)

VMA 00085

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 1st July 2020.

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).