FINAL APPROVED PACKAGE INSERT FOR

TILMOVET 250 mg/ml

VETERINARY MEDICINE

SCHEDULING STATUS

S4

PROPRIETY NAMES AND DOSAGE FORMS

Tilmovet 250 mg/ml Concentrate for Oral Solution

COMPOSITION

Each millilitre contains Tilmicosin 250 mg

Excipients:

Disodium edetate, propyl gallate, phosphoric acid (concentrated), water for injection.

PHARMACOLOGICAL CLASSIFICATION

C.17.1.4. Macrolides and lincosamides

PHARMACOLOGICAL ACTION

Pharmacodynamics

Tilmicosin is mainly a bactericidal, semi-synthetic antibiotic of the macrolide group. It is believed to affect bacterial protein synthesis.

Tilmicosin has a wide spectrum of activity against Gram-positive organisms and is particularly active against *Pasteurella*, *Actinobacillus* (*Haemophilus*) and *Mycoplasma* organisms of bovine, porcine and avian origin. Tilmicosin has some activity against certain Gram-negative micro-organisms. Cross resistance between tilmicosin and other macrolide antibiotics has been observed. Macrolides inhibit

protein synthesis by reversibly binding to the 50S ribosomal subunit. Bacterial growth is inhibited by induction of the separation of peptidyl transfer RNA from the ribosome during the elongation phase.

Ribosomal methylase, encoded by the *erm* gene, can precipitate resistance to macrolides by alteration of the ribosomal binding site.

The gene that encodes for an efflux mechanism, *mef*, also brings about a moderate degree of resistance.

Resistance is also brought about by an efflux pump that actively rids the cells of the macrolide. This efflux pump is chromosomally mediated by genes referred to as *acrAB* genes. Resistance of *Pseudomonas* species and other Gram-negative bacteria, *Enterococcus spp.* and *Staphylococcus spp.* may be precipitated by chromosomally controlled alteration of permeability or uptake of the drug.

Pharmacokinetics

When administered orally with drinking water to chickens, turkeys, and pigs, tilmicosin is absorbed and moves rapidly out of the serum into areas with a low pH. This results in very low serum concentrations, but detectable levels of tilmicosin are found in the lung tissue as early as 6 hours after starting the treatment. In both chickens and turkeys, tilmicosin is also detected in pooled air sac tissue as early as 6 hours after starting the treatment. In swine, tilmicosin is also known to be concentrated in alveolar macrophages.

INDICATIONS PER SPECIES

Pigs:

For the treatment and prevention of respiratory infections associated with *Mycoplasma hyopneumoniae*, *Pasteurella multocida* and *Actinobacillus pleuropneumoniae* when the disease has been diagnosed at herd level.

Fowl:

For the treatment and control of respiratory infections in fowls associated with M*ycoplasma gallisepticum*, *Mycoplasma synoviae* and other organisms sensitive to tilmicosin.

CONTRA-INDICATIONS

Do not use in cases of hypersensitivity to the active substance or in cases of known resistance to tilmicosin. Do not allow horses and other equines access to drinking water containing tilmicosin. Do not use in ruminants with active rumen function.

WARNINGS AND/OR WITHDRAWAL PERIOD IN THE CASE OF FOOD-PRODUCING ANIMALS

KEEP OUT OF REACH OF CHILDREN AND UNINFORMED PERSONS.

- Water containing **Tilmovet 250 mg/ml** must be withdrawn from fowls 12 days prior to slaughter of fowls treated with **Tilmovet 250 mg/ml**.
- Water containing **Tilmovet 250 mg/ml** must be withdrawn from swine 14 days prior to slaughter of swine treated with **Tilmovet 250 mg/ml**.
- For oral use in swine and fowls only.
- Do not administer undiluted.
- Medicated drinking water must be freshly prepared every 24 hours and is stable when stored below 30°C.
- When mixing and handling **Tilmovet 250 mg/ml,** use a dust mask. Operators should wash contaminated parts of skin thoroughly with soap and water, should skin contact occur. If accidental eye contact occurs, immediately rinse thoroughly with clean water. If irritation persists, seek medical attention.
- Tilmicosin should not be administered by injection to pigs. The product contains disodium edetate.
- The uptake of medicated water can be altered because of illness. If the uptake is insufficient, alternative treatment may be required.

SAFETY IN PREGNANCY AND LACTATION

The safety of **Tilmovet 250 mg/ml,** has not been established during pregnancy and lactation. Use only in accordance with risk/benefit assessment by the responsible veterinarian.

Withdrawal periods

Pigs:

Meat and offal: 14 days.

Fowl:

Meat and offal: 12 days.

Eggs:

Not authorised for use in layers (producing eggs for human consumption).

DOSAGE AND DIRECTIONS FOR USE PER AGE AND SPECIES

For oral use only. The product must be diluted in drinking water before administration.

Pigs:

15 - 20 mg tilmicosin per kg bodyweight for **5 days**, i.e., 6 - 8 ml of **Tilmovet 250 mg/ml** for 100 kg bodyweight corresponding to **80 ml** of product per 100 litres of drinking water for 5 days.

Fowl:

15-20 mg tilmicosin per kg bodyweight for **3 days**, i.e., 6-8 ml of **Tilmovet 250 mg/ml** for 100 kg bodyweight corresponding to **30 ml** of product per 100 litres of drinking water for 3 days.

One 960 ml bottle is sufficient to medicate 1200 litres of drinking water for pigs or 3200 litres of drinking water for broilers, turkeys, and pullets.

Drinking water containing **Tilmovet 250 mg/ml** should be freshly prepared every 24 hours, only using clean water.

If signs of disease do not improve significantly within 3 - 5 days, the diagnosis should be re-evaluated, and treatment changed.

08/08/2022

To avoid underdosing, body weight should be determined as accurately as possible. The uptake of medicated water depends on the clinical condition of the animals. To obtain the correct dosage, the concentration of the product must be adjusted accordingly.

Do not administer to pigs in a wet feeding system.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS FOR USE PER SPECIES

Tilmovet 250 mg/ml is for oral use in swine and fowls only.

Special precautions for use in animals

Inappropriate use of **Tilmovet 250 mg/ml** may increase the prevalence of bacterial resistance to tilmicosin and may decrease the effectiveness of treatment with tilmicosin-related substances. Use of the **Tilmovet 250 mg/ml** should be based on susceptibility testing and official and local antimicrobial policies must be considered. Do not allow horses or other equines access to drinking water containing tilmicosin.

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

People with known hypersensitivity to tilmicosin should avoid contact with the product. The veterinary medicinal product may cause irritation or sensitisation through skin contact.

Avoid skin and eye contact. Wear protective gloves and protective clothing when handling the veterinary medicinal product. Wash hands after use.

In case of contact with skin or eyes, rinse thoroughly with clean water. If irritation persists and in case of accidental ingestion, seek veterinary advice and notify the registration holder.

INTERACTIONS

Cross-resistance between **Tilmovet 250 mg/ml**, other macrolide antibiotics and lincosamides have been observed.

Tilmovet 250 mg/ml may cause a decrease in antibacterial activity of β-lactam antibiotics. Do not use **Tilmovet 250 mg/ml** and bacteriostatic antimicrobial agents concurrently.

KNOWN SIGNS OF OVERDOSE AND PARTICULARS OF ITS TREATMENT PER SPECIES

Pigs drink less water when a dose of 300 to 400 mg/litre (1,5 to 2 times the recommended dose) is administered. While this will result in less intake of tilmicosin, it might lead to dehydration of the animals. Replace with untreated water when needed.

No symptoms were observed in fowls treated at 375 mg/litre for 5 days. A dose of 75 mg/litre for 10 days resulted in less consistent faeces.

No symptoms of overdose were noticed in turkeys treated at 375 mg/litre of drinking water for 3 days.

No symptoms were observed at 75 mg/litre for 6 days.

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 material derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

IDENTIFICATION

A clear yellow to amber solution.

PRESENTATION

Tilmovet 250 mg/ml is packed in a high-density white polyethylene bottle (HDPE) of 960 ml, with a vertical see-through bar and a graduated scale. The bottle is closed with a white polypropylene (PP) screw cap, with a multiple-layer induction sealing insert inside.

STORAGE INSTRUCTIONS

Store in a dry, dark place at or below 30°C, in the original container. The product can be stored up to 2 years.

Once opened, the product can be stored up to 3 months at or below 30°C in the original container.

Protect from light after dilution in drinking water. The medicated water can be stored up to 24 hours after preparation of **Tilmovet 250 mg/ml**.

REGISTRATION NUMBER

20/17.1.4/15

NAME AND BUSINESS ADDRESS OF HOLDER OF THE CERTIFICATE OF REGISTRATION

HUVEPHARMA SOUTH AFRICA (Pty) Ltd

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DATE OF NOTIFICATION OF APPROVAL OF THIS SCIENTIFIC PROFESSIONAL INFORMATION

25 July 2022

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