Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Pulmotil AC Concentrate for oral solution for use in drinking water or milk replacer

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Tilmicosin (as phosphate) 250 mg/ml

Excipients:
Propyl gallate
Disodium edetate

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Concentrate for Oral Solution for use in drinking water or milk replacer.
Clear yellow to amber coloured solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Chickens (except hens producing eggs for human consumption)
Turkeys
Pigs
Calves (non ruminant)

4.2 Indications for use, specifying the target species

Pigs: For the treatment and prevention of respiratory disease in pig herds, associated with *Mycoplasma hyopneumoniae, Pasteurella multocida, Actinobacillus pleuropneumoniae* and other organisms susceptible to tilmicosin.

Chickens: For the treatment and prevention of respiratory disease in chicken flocks, associated with *Mycoplasma gallisepticum* and *M. synoviae*.

Turkeys: For the treatment and prevention of respiratory disease in turkey flocks, associated with *Mycoplasma gallisepticum* and *M. synoviae*.

Calves: For the treatment and prevention of bovine respiratory disease, associated with *Mannheimia haemolytica, Pasteurella multocida, Mycoplasma bovis, M. dispar* and other organisms susceptible to tilmicosin.

4.3 Contraindications

Do not allow horses and other equines access to drinking water containing tilmicosin.
Do not use in case of hypersensitivity to tilmicosin or to any of the excipients.

4.4 Special warnings for each target species

Important: Must be diluted before administration to animals.

Pigs, chickens and turkeys: Water consumption should be monitored in order to guarantee adequate dosing. In case water consumption does not match quantities for which recommended concentrations were calculated, the concentration of Pulmotil AC has to be adapted in a way that the recommended dosage will be taken up by the animals or different medication should be considered.

4.5 Special precautions for use

Special precautions for use in animals
For oral use only. Contains disodium edetate; do not inject.
Severely ill individuals tend to drink less and may need simultaneous treatment, preferably by parenteral medication.
Inappropriate use of the product may increase the prevalence of bacteria resistant to tilmicosin and may decrease the effectiveness of treatment with tilmicosin-related substances. The use of the product should be based on susceptibility tests.
Medicated drinking water or milk replacer should be prepared fresh every 24 hours.
Official, national and regional antimicrobial policies should be taken into account when the product is used.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
- Tilmicosin may induce irritation. Macrolides, such as tilmicosin, may also cause hypersensitivity (allergy) following injection, inhalation, ingestion or contact with skin or eye. Hypersensitivity to tilmicosin 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.
- To avoid exposure during preparation of the medicated drinking water, wear overalls, safety glasses, and impervious gloves. Do not eat, drink or smoke when handling this product. Wash hands after use.
- In the case of accidental ingestion, wash out mouth immediately with water and seek medical advice. 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 and show the physician this warning. Swelling of the face, lips and eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.

4.6 Adverse reactions (frequency and seriousness)

In very rare cases, a decrease in water intake has been observed.

4.7 Use during pregnancy, lactation or lay

The safety of tilmicosin has not been established in animals used for breeding purposes.

4.8 Interaction with other medicinal products and other forms of interactions

None known.

4.9 Amounts to be administered and administration route

Pigs: To be included in the drinking water to provide a daily dose of 15-20 mg/kg bodyweight for 5 days, which may be achieved by the inclusion of 200 mg tilmicosin per litre (80 ml Pulmotil AC per 100 litres).

Chickens and Turkeys (except hens producing eggs for human consumption): To be included in the drinking water at a daily dose of 15-20 mg/kg bodyweight in chickens and 10-27 mg/kg bodyweight in turkeys for 3 days, which may be achieved by the inclusion of 75 mg tilmicosin per litre (30 ml Pulmotil AC per 100 litres).

Calves: To be included in milk replacer only, at a dose of 12.5 mg/kg bodyweight and given twice daily for 3-5 consecutive days, which may be achieved by the inclusion of 1 ml of product every 20 kg bodyweight.

One 240 ml bottle of Pulmotil AC is sufficient to medicate 300 litres of drinking water for pigs or 800 litres of drinking water for chickens or turkeys. One 960 ml bottle is sufficient to medicate 1200 litres of drinking water for pigs or 3200 litres of drinking water for chickens or turkeys.

One 240 ml bottle and 960 ml bottle of Pulmotil AC are sufficient to medicate in milk replacer respectively 12 to 20 and 48 to 80 veal calves each of 40 kg bodyweight depending on the duration of treatment.

The uptake of medicated drinking water/milk replacer depends on the clinical condition of the animals. In order to obtain a correct dosage the concentration of tilmicosin should be adjusted accordingly.

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

When pigs are offered drinking water containing 300 or 400 mg/litre (equivalent to 22.5-40 mg/kg bodyweight or 1.5-2 times the recommended concentration) commonly animals exhibit a reduced water intake. Although this has a self-limiting effect on tilmicosin intake, it could, in extreme circumstances, result in dehydration. This can be corrected by the removal of the medicated drinking water and replacement with fresh unmedicated water.

No symptoms of overdose have been seen in chickens given drinking water containing levels of tilmicosin up to 375 mg/litre (equivalent to 75-100 mg/kg bodyweight or 5 times the recommended dose) for 5 days; daily treatment with 75 mg/litre (equivalent to the maximum recommended dose) for 10 days resulted in a reduction in faecal consistency.

No symptoms of overdose have been seen in turkeys given drinking water containing levels of tilmicosin up to 375 mg/litre (equivalent to 50-135 mg/kg bodyweight or 5 times the recommended dose) for 3 days; daily treatment with 75 mg/litre (equivalent to the maximum recommended dose) for 6 days also produced no symptoms of overdose.

No symptoms of overdose, with exception of a slight decrease in the milk consumption, have been seen in calves given twice daily doses 5 times the maximum recommended dose or for twice the maximum recommended duration of treatment.

4.11 Withdrawal period(s)

Pigs - 14 days
Chickens - 12 days
Turkeys – 19 days
Calves - 42 days
Not authorised for use in laying birds producing eggs for human consumption. Do not use within 14 days of onset of the laying
Not for use in lactating animals.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: antibacterials for systemic use, tilmicosin.
ATC vet code: QJ01FA91

5.1 Pharmacodynamic properties

Tilmicosin is a semi-synthetic antibiotic of the macrolide group and is believed to affect protein synthesis. It has bacteriostatic action but at high concentrations it may be bactericidal. This antibacterial activity is predominantly against Gram-positive microorganism with activity against certain gram-negative ones and Mycoplasma of a bovine, porcine, ovine and avian origin. In particular, its activity has been demonstrated against the following microorganism:

- *Pigs: Mycoplasma hyopneumoniae, Pasteurella multocida* and *Actinobacillus pleuropneumoniae*
- *Chickens and turkeys: Mycoplasma gallisepticum* and *Mycoplasma synoviae*
- *Calves: Mannheimia haemolytica, Pasteurella multocida, Mycoplasma bovis* and *M. dispar*.

Scientific evidence suggests that macrolides act synergistically with the host immune system. Macrolides appear to enhance phagocyte killing of bacteria. Tilmicosin has been shown to inhibit *in vitro* the replication of the Porcine Reproductive and Respiratory Syndrome virus in alveolar macrophages in a dose dependent fashion.

Cross-resistance between tilmicosin and other macrolides and lincomycin has been observed.

5.2 Pharmacokinetic particulars

Whilst blood concentrations of tilmicosin are low, there is pH-dependent macrophage accumulation of tilmicosin in inflamed tissues.

Pigs: After oral administration of 200 mg tilmicosin/l drinking water, the average active substance concentrations detected in lung tissue, alveolar macrophages and bronchial epithelium 5 days after the start of treatment were 1.44 µg/ml, 3.8 µg/ml and 7.4 µg/g respectively.

Poultry: As early as 6 hours after oral administration of 75 mg tilmicosin/l drinking water, the average active substance concentrations detected in lung and alveolar tissue were 0.63 µg/g and 0.30 µg/g respectively. 48 hours after the start of treatment, the tilmicosin concentrations in lung and alveolar tissue were 2.3 µg/g and 3.29 µg/g respectively.

Calves: As early as 6 hours after oral administration of 25 mg tilmicosin/kg body weight/day in milk replacer, an average active substance concentration of 3.1 µg/g was detected in lung tissue. 78 hours after the start of treatment, the tilmicosin concentration in lung tissue was 42.7 µg/g. Therapeutically effective concentrations of tilmicosin were measured up to 60 hours after treatment.

Turkeys: After oral administration of 75 mg tilmicosin/l drinking water, the average active substance concentrations detected in lung tissue, air sac tissue and plasma 5 days after the start of treatment were 1.89 µg/ml, 3.71 µg/ml and 0.02 µg/g respectively. The highest mean tilmicosin concentration detected for lung tissues was 2.19 µg/g at 6 days; for air sac tissue it was 4.18 µg/g at 2 days and in the plasma it was 0.172 µg/g at 3 days.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium edetate
Propyl gallate
Phosphoric acid (for pH adjustment)
Purified water

6.2 Major 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: 2 years.
Shelf-life after first opening the immediate packaging: 3 months.
Shelf-life after dilution or reconstitution according to directions: 24 hours.

6.4 Special precautions for storage

Do not store above 30°C.
Protect from direct sunlight.

6.5 Nature and composition of immediate packaging

The primary container is a polyethylene naphthalate (PEN) amber coloured bottle containing 240 ml or 960 ml of Pulmotil AC, with a polypropylene screw top and polyethylene/aluminium/polyethylene terephthalate seal.
A graduated polypropylene cup is also supplied. Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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 national requirements.
Veterinary medicinal product must not be disposed of via waste water or the drainage systems.
Manure from treated animals should not be deposited on the same field in successive years.

7 MARKETING AUTHORISATION HOLDER

Elanco GmbH
Heinz-Lohmann-Strasse 4
27472 Cuxhaven
Germany

8 MARKETING AUTHORISATION NUMBER(S)

VPA22020/011/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 5th February 1992
Date of last renewal: 4th February 2009

10 DATE OF REVISION OF THE TEXT

November 2018