ANNEX III

LABELLING AND PACKAGE LEAFLET

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

TILMICOSIN CALIER 250 mg/ml Solution for use in drinking water/milk (DE, EL, ES, HU, PT)
TILMICOSINA CALIER 250 mg/ml Solution for use in drinking water/milk (IT)

2. Composition

Each ml contains:

Active substance:
Tilmicosin (as phosphate) ..... 250 mg

Excipients:
Propyl gallate (E 310) ..... 0.2 mg
Disodium edetate ..... 2 mg

Light amber clear solution.

3. Target species

Chickens (except hens producing eggs for human consumption), turkeys, pigs and calves (non-ruminant)

4. Indications for use

Pigs: For the treatment and metaphylaxis of respiratory disease in pig herds, associated with *Actinobacillus pleuropneumoniae, Mycoplasma hyopneumoniae* and *Pasteurella multocida.*

The presence of the disease in the group/flock must be established before the product is used.

Chickens (except hens producing eggs for human consumption): For the treatment and metaphylaxis of respiratory disease in chicken flocks, associated with *Mycoplasma gallisepticum* and *M. synoviae.*

The presence of the disease in the group/flock must be established before the product is used.

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

The presence of the disease in the group/flock must be established before the product is used.

Calves: For the treatment and metaphylaxis of bovine respiratory disease, associated with *Mannheimia haemolytica, Mycoplasma bovis, M. Dispar* and *Pasteurella multocida*

The presence of the disease in the group/flock must be established before the product is used.

5. Contraindications

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

6. Special warnings

Special warnings:
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 the veterinary medicinal product has to be adapted in a way that the recommended dosage will be taken up by the animals or different medication should be considered.

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

Special precautions for safe use in the target species:
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.

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

An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

Do not exceed the stated dose or duration of treatment.

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.

Special precautions for the protection of the environment:
Tilmicosin is toxic to cyanobacteria.

Pregnancy and lactation:
The safety of tilmicosin has not been established in animals used for breeding purposes.

Interaction with other medicinal products and other forms of interaction:
None known.

Overdose:
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.

Special restrictions for use and special conditions for use:
This veterinary medicinal product is intended to be used for the preparation of medicated water/milk.

Administration by a veterinary surgeon or under their direct responsibility.

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

7. Adverse events

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

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Decreased drinking

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system <{national system details}.>

8. Dosage for each species, routes and method of administration

In drinking water/milk use.
The product must be diluted in drinking water (pigs, chickens, turkeys) or milk replacer (calves) before the administration.

Pigs: To be included in the drinking water to provide a daily dose of 15-20 mg/kg bodyweight for 5 days.

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.

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.

To ensure a correct dosage, body weight should be determined as accurately as possible.

Medicated water should be the only source of drinking. Medicated water must be renewed every 24 hours. Medicated milk replacer should be prepared freshly every 6 hours.

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

The use of suitably calibrated measuring equipment is recommended.

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:

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

Animals with acute or severe clinical conditions that cannot drink, should receive adequate parenteral treatment.

9. Advice on correct administration

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 the veterinary medicinal product has to be

adapted in a way that the recommended dosage will be taken up by the animals or different medication should be considered.

10. Withdrawal periods

Meat and offal:

Pigs: 14 days
Chickens: 12 days
Turkeys: 19 days
Calves: 42 days

Not for use in birds producing or intended to produce eggs for human consumption. Do not use within 14 days of the start of the laying period.

Not authorised for use in animals producing milk for human consumption.

11. Special storage precautions

Keep out of the sight and reach of children.

As packaged for sale:
This veterinary medicinal product does not require any special temperature storage conditions.
Protect from light.

After first opening the immediate packaging:
Do not store above 25ºC.
Protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the carton {Exp}. The expiry date refers to the last day of that month.

Shelf life after first opening the container: 6 months.
Shelf life after dilution in water according to directions: 24 hours
Shelf life after reconstitution in milk according to directions: 6 hours

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or <household waste>.

This veterinary medicinal product should not enter water courses as tilmicosin phosphate 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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Package sizes:
Bottle of 1 L
Bottle of 5 L

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

DD month YYYY

Detailed information on this veterinary medicinal product is available in the Union Product Database.

16. Contact details

To be completed nationally.

17. Other information

Tilmicosin is very persistent and toxic to cyanobacteria.