

B. PACKAGE LEAFLET

PACKAGE LEAFLET
TILMINJECT 300 mg/ml Solution for Injection for Cattle and Sheep

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release:

LABORATORIOS CALIER, S.A.
C/ Barcelonès, 26 (P.I. el Ramassar)
LES FRANQUESES DEL VALLÈS, (Barcelona)
SPAIN

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

TILMINJECT 300 mg/ml Solution for Injection for Cattle and Sheep.
Tilmicosin

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each ml contains:

Active substance:

Tilmicosin 300 mg

Excipients:

Propylene Glycol (E 1520) 250 mg

Clear yellow-orange solution.

4. INDICATIONS

Cattle

Treatment of bovine respiratory disease associated with *Mannheimia haemolytica* and *Pasteurella multocida*.

Treatment of interdigital necrobacillosis.

Sheep

Treatment of respiratory tract infections caused by *Mannheimia haemolytica* and *Pasteurella multocida*.

Treatment of foot rot in sheep caused by *Dichelobacter nodosus* and *Fusobacterium necrophorum*.

Treatment of acute ovine mastitis caused by *Staphylococcus aureus* and *Mycoplasma agalactiae*.

5. CONTRAINDICATIONS

Do not administer intravenously.
Do not administer intramuscularly
Do not administer to lambs weighing less than 15 kg.
Do not administer to primates.
Do not administer to pigs.
Do not administer to horses and donkeys.
Do not administer to goats.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

6. ADVERSE REACTIONS

Occasionally, a soft diffuse swelling may occur at the injection site but this disappears within five to eight days. In rare cases recumbency, incoordination and convulsions have been observed.

Deaths of cattle have been observed following a single intravenous dose of 5 mg/kg body weight and following the subcutaneous injection of doses of 150 mg/kg body weight at 72 hour intervals. In pigs, intramuscular injection at 20 mg/kg body weight has caused deaths. Sheep have died following a single intravenous injection of 7.5 mg/kg body weight.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

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 inform your veterinary surgeon.

7. TARGET SPECIES

Cattle and sheep.

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

For subcutaneous injection only.

Use a single dose of 10 mg tilmicosin per kg body weight (corresponding to 1 ml Tilminject per 30 kg body weight).

If no improvement is noted within 48 hours, the diagnosis should be confirmed.

Avoid introduction of contamination into vial during use. The vial should be inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, discard the vial.

Cattle:

Method of administration:

Withdraw the required dose from the vial and remove the syringe from the needle, leaving the needle in the vial. When a group of animals has to be treated, leave the needle in the vial to remove the subsequent doses.

Restrain the animal and insert a separate needle subcutaneously at the injection site, preferably in a skinfold over the rib cage behind the shoulder. Attach the syringe to the needle and inject into the base of the skinfold. Do not inject more than 20 ml per injection site.

Sheep:

Method of administration:

Accurate weighing of lambs is important to avoid overdosing. The use of a 2 ml syringe or smaller improves accurate dosing.

Withdraw the required dose from the vial and remove the syringe from the needle, leaving the needle in the vial.

Restrain the sheep whilst leaning over the animal and insert a separate needle subcutaneously into the injection site, which should be in a skinfold over the rib cage behind the shoulder. Attach the syringe to the needle and inject into the base of the skin fold. Do not inject more than 2 ml per injection site.

9. ADVICE ON CORRECT ADMINISTRATION

Official, national and regional antimicrobial policies should be considered when the product is used.

To avoid self-injection do not use automatic injection equipment.

Wherever possible, the use of the product should be based on susceptibility testing.

To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing.

Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to tilmicosin and may decrease the effectiveness of treatment with other macrolide antimicrobials, due to the potential for cross-resistance.

10. WITHDRAWAL PERIOD

Cattle:

Meat and offal: 70 days

Milk: 36 days

If the product is administered to cows during the dry period or to pregnant dairy heifers, milk should not be used for human consumption until 36 days after calving.

Sheep:

Meat and offal; 42 days

Milk: 18 days

If the product is administered to ewes during the dry period or to pregnant ewes, milk should not be used for human consumption until 18 days after lambing.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Keep the vial in the outer carton in order to protect from light.

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

Shelf life after first opening of the container: 28 days.

12. SPECIAL WARNING(S)

Special precautions for use in target species

The clinical trials did not demonstrate a bacteriological cure in sheep with acute mastitis caused by *Staphylococcus aureus* and *Mycoplasma agalactiae*.

Accurate weighing of lambs is important to avoid overdose. The use of a 2 ml or smaller syringe will facilitate accurate dosing.

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

Operator Safety Warnings:

INJECTION OF TILMICOSIN IN HUMANS CAN BE FATAL – EXERCISE EXTREME CAUTION TO AVOID ACCIDENTAL SELF-INJECTION AND FOLLOW THE ADMINISTRATION INSTRUCTIONS AND THE GUIDANCE BELOW, PRECISELY

- This product should only be administered by a veterinary surgeon.
- Never carry a syringe loaded with Tilminject 300 mg/ml Solution for injection for cattle and ovine with the needle attached. The needle should be connected to the syringe only when filling the syringe or administering the injection. Keep the syringe and needle separate at all other times.
- Do not use automatic injection equipment.
- Ensure that animals are properly restrained, including those in the vicinity.
- Do not work alone when using Tilminject 300 mg/ml Solution for injection for cattle and ovine.
- In case of self-injection SEEK IMMEDIATE MEDICAL ATTENTION and take the vial or the package leaflet with you. Apply a cold pack (not ice directly) to the injection site.

Additional operator safety warnings:

The product is slightly irritant to the skin and eye. Avoid splashes on the skin and eyes. Personal protective equipment consisting of impervious gloves and protective glasses should be worn when handling the veterinary medicinal product. In the event of accidental contact with the skin or eyes, rinse thoroughly with water. If irritation persists, seek medical advice. Wash hands after use.

NOTE TO THE PHYSICIAN

INJECTION OF TILMICOSIN IN HUMANS HAS BEEN ASSOCIATED WITH FATALITIES.

The cardiovascular system is the target of toxicity, and this toxicity may be due to calcium channel blockade. Administration of intravenous calcium chloride should only be considered if there is positive confirmation of exposure to tilmicosin.

In dog studies, tilmicosin induced a negative inotropic effect with consequent tachycardia, and a reduction in systemic arterial blood pressure and arterial pulse pressure.

DO NOT GIVE ADRENALIN OR BETA-ADRENERGIC ANTAGONISTS SUCH AS PROPRANOLOL.

In pigs, tilmicosin-induced lethality is potentiated by adrenalin.

In dogs, treatment with intravenous calcium chloride showed a positive effect on the left ventricular inotropic state and some improvements in vascular blood pressure and tachycardia.

Pre-clinical data and an isolated clinical report suggest that calcium chloride infusion may help to reverse tilmicosin induced changes in blood pressure and heart rate in humans.

Administration of dobutamine should also be considered due to its positive inotropic effects although it does not influence tachycardia.

As tilmicosin persists in tissues for several days, the cardiovascular system should be closely monitored and supportive treatment provided.

Physicians treating patients exposed to this compound are advised to discuss clinical management with the National Poison Information Service on:

Pregnancy

The safety of the veterinary medicinal product has not been established during pregnancy. Use only according to the benefit/risk assessment by the responsible veterinarian

Overdose (symptoms, emergency procedures, antidotes):

In cattle subcutaneous injections of 10, 30 and 50 mg/kg body weight, repeated three times with a 72 hours interval, did not cause death. As expected, oedema developed at the site of injection. The only lesion observed at autopsy was a necrosis of the myocardium in the group treated with 50 mg/kg body weight.

Doses of 150 mg/kg body weight, administered subcutaneously with an interval of 72 hours caused death. Oedema at the site of injection was observed and at autopsy a light necrosis of the myocardium was the only lesion determined. Other symptoms observed were: difficulty in moving, reduced appetite and tachycardia.

In sheep single injections (approximately 30 mg/kg body weight) may cause a slight increase of the rate of respiration. Higher doses (150 mg/kg body weight) caused ataxia, lethargy and the inability to raise the head.

Deaths occurred after one single intravenous injection of 5 mg/kg body weight in cattle and 7.5 mg/kg in sheep body weight.

Incompatibilities:

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

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste. Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Package sizes:

Carton box with 1 vial of 100 ml

Carton box with 1 vial of 250 ml

Not all pack sizes may be marketed.

Tilmicosin is persistent in soils.

Not all pack sizes may be marketed.

For animal treatment only to be supplied only on veterinary prescription.

For use by veterinary surgeons only

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

