

## PACKAGE LEAFLET

**TILMIPRIL 300 mg/ml SOLUTION FOR INJECTION FOR CATTLE AND SHEEP [IT, PT, ES]**

Tilmicosin

**MICORION 300 mg/ml SOLUTION FOR INJECTION FOR CATTLE AND SHEEP [CZ, PL]**

Tilmicosin

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

Marketing authorisation holder:

VETPHARMA ANIMAL HEALTH, S.L.

Gran Via Carles III, 98, 7<sup>a</sup>

08028 Barcelona

Spain

Manufacturer responsible for batch release:

INDUSTRIAL VETERINARIA, S.A.

Esmeralda, 19

08950 Esplugues de Llobregat

Spain

### 2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tilmipril 300 mg/ml solution for injection for cattle and sheep [IT, PT, ES]

Tilmicosin

Micorion 300 mg/ml solution for injection for cattle and sheep [CZ, PL]

Tilmicosin

### 3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS

Each ml contains:

**Active substance:**

Tilmicosin.....300 mg

**Excipients:**

Propylene glycol.....250 mg

Clear, yellowish to brown-yellowish 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 case 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.

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

## **7. TARGET SPECIES**

Cattle and sheep

## **8. DOSAGE FOR EACH SPECIES, ROUTE AND METHOD OF ADMINISTRATION**

**For subcutaneous injection only.**

Use 10 mg tilmicosin per kg body weight (corresponding to 1 ml of the product per 30 kg body weight).

**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 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 taken into account when this veterinary medicinal product is used.

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

The use of this veterinary medicinal product should be based on susceptibility tests.

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

Avoid introduction of contamination into vial during use. Do not use the product if you notice any foreign particulate matter and/or abnormal physical appearance.

**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.

Store below 25°C

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

Do not freeze.

Do not use after the expiry date stated on the label.

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

## 12. SPECIAL WARNINGS

### Special warnings for each target species

#### Sheep

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

Do not administer to lambs weighing less than 15 kg since there is a risk of overdose toxicity.

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 veterinary medicinal product should only be administered by a veterinary surgeon.
- Never carry a syringe loaded with this veterinary medicinal product 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 this veterinary medicinal product.
- 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:

- Avoid contact with skin and eyes. Rinse any splashes from skin or eyes immediately with water.
- May cause sensitisation by skin contact. 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: ... *relevant national number stated (to be completed nationally)* [INCLUDE THE NAME OF THE COMPETENT AUTHORITY IN EACH COUNTRY AND THE TELEPHONE NUMBER]

### Use during pregnancy, lactation or lay

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 doses of 10, 30 and 50 mg/kg of body weight, each injected three times at 72 hour intervals did not cause any deaths. As expected, oedema at the site of injection was noted. The only lesion observed at necropsy was minimal myocardial necrosis in the 50 mg/kg group.

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**

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

**14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED**

**15. OTHER INFORMATION**

Not all pack sizes may be marketed.