

## **PARTICULARS TO APPEAR ON THE OUTER PACKAGE {Carton}**

### **1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Apotil 300 mg/ml Solution for Injection

### **2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES**

Tilmicosin 300 mg/ml

### **3. PHARMACEUTICAL FORM**

Solution for injection

### **4. PACKAGE SIZE**

50ml, 100ml, 250ml

### **5. TARGET SPECIES**

Sheep and cattle

### **6. INDICATION(S)**

#### **Cattle**

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

Treatment of interdigital necrobacillosis (bovine pododermatitis, foul in the foot)

#### **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*.

### **7. METHOD AND ROUTE(S) OF ADMINISTRATION**

SUBCUTANEOUS ROUTE

Read the package leaflet before use.

### **8. WITHDRAWAL PERIOD**

**Cattle:**

Meat and offal: 70 days

Milk: 36 days

**Sheep:**

Meat and offal; 42 days

Milk: 18 days

**9. SPECIAL WARNING(S), IF NECESSARY**

**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 Apotil 300 mg/ml solution for injection 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 Apotil 300 mg/ml solution for injection.
- 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 and eyes immediately with water.
- May cause sensitisation by skin contact. Wash hands after use.

**10. EXPIRY DATE**

Shelf life after first broaching: 28 days.

One opened use by ...

**11. SPECIAL STORAGE CONDITIONS**

Keep the vial in the outer carton.

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

**12. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS 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.

**13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IF APPLICABLE [Distribution category]**

POM-V

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

**14. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”**

KEEP OUT OF THE SIGHT AND REACH OF CHILDREN

**15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Nimrod Veterinary Products  
Staverton Court  
Staverton  
Cheltenham  
Gloucestershire  
GL51 0UX

**16. MARKETING AUTHORISATION NUMBER(S)**

**Vm 36308/4000**

**17. MANUFACTURER’S BATCH NUMBER**

**PACKAGE LEAFLET FOR:**

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

Nimrod Veterinary Products  
Staverton Court  
Staverton  
Cheltenham  
Gloucestershire  
GL51 0UX

**Manufacturer for the batch release**

Industrial Veterinaria, S.A.  
Esmeralda, 19  
08950 Esplugues de Llobregat  
Spain

**2. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Apotil 300 mg/ml Solution for Injection

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

Tilmicosin 300 mg/ml

**4. INDICATION(S)**

**Cattle**

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

Treatment of interdigital necrobacillosis (bovine pododermatitis, foul in the foot)

**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

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

## **7. TARGET SPECIES**

Cattle and sheep

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

**For subcutaneous administration only.**

Use 10 mg tilmicosin per kg body weight (corresponding to 1 ml Apotil 300 mg/ml 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 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:**

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

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

Avoid introduction of contamination into vial during use. Do not use Apotil 300 mg/ml if you notice any foreign particulate matter and/or abnormal physical appearance.

**10. WITHDRAWAL PERIOD(S)**

**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

**11. SPECIAL STORAGE PRECAUTIONS**

Keep out of the sight and reach of children. Protect from direct sunlight.

Do not store above 30 °C

Protect from light

Keep vial in outer container

Do not use this veterinary medicinal product after the expiry date which is stated on the label and the carton after EXP. The expiry date refers to the last day of that month. Shelf-life after first opening the container: 28 days.

When the container is broached (opened) for the first time, using the in-use shelf-life specified on this package leaflet, the date on which any product remaining in the

carton should be discarded should be worked out. This discard date should be written in the space provided.

## 12. SPECIAL WARNING(S)

### Special precautions for use in animals

Do not administer intravenously. Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.

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

For Animal Treatment Only

**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 Apotil 300 mg/ml solution for injection 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 Apotil 300 mg/ml solution for injection.
- 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 and 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: 0844 8920111

**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.

**Interaction with other medicinal products and other forms of interaction**

Interactions between macrolides and ionophores have been observed in some species. 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 product should be disposed of in accordance with local requirements.

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

**15. OTHER INFORMATION**

POM – V To be supplied only on veterinary prescription

*Vm 36308/4000*

Containers of 50 ml, 100 ml and 250 ml



Clinical containers of 6, 10 and 12 units of 50 ml, 100 ml and 250 ml

Not all pack sizes may be marketed

**MINIMUM PARTICULARS TO APPEAR ON THE LABEL: Concertina Labels.**

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

Tilmicosin 300 mg/ml

**4. PHARMACEUTICAL FORM**

Solution for injection

**5. PACKAGE SIZE**

**6. INDICATION(S)**

**7. CONTRAINDICATIONS**

**8. ADVERSE REACTIONS**

**9. TARGET SPECIES**

Cattle and Sheep

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

Route of administration: Subcutaneous

For dosing and all other warnings see package leaflet..

**11. ADVICE ON CORRECT ADMINISTRATION**

Once opened use by ....

**12. 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 (in accordance with section 4.7 above), 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 (in accordance with section 4.7 above), milk should not be used for human consumption until 18 days after lambing.

**13. SPECIAL STORAGE PRECAUTIONS**

**14. SPECIAL WARNING(S)**

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Physicians treating patients exposed to this compound are advised to discuss clinical management with the National Poison Information Service on: 0844 892 0111

**15. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY**

**16. DATE ON WHICH THE LABEL WAS LAST APPROVED**

**18. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE**

*[Distribution category]*

POM-V

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

**19. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”**

Keep out of the sight and reach of children

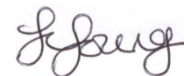
**20. MARKETING AUTHORISATION NUMBER(S)**

Vm 36308/4000

**21. MANUFACTURER’S BATCH NUMBER**

Reviewed: January 2018

**Approved: 08/01/2018**

A handwritten signature in black ink, appearing to read "J. Berg".