ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

TILMODIL 300 mg/ml Solution for Injection

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Tilmicosin 300 mg/ml

3. PACKAGE SIZE

50ml
100ml

4. TARGET SPECIES

Cattle and sheep.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

FOR SUBCUTANEOUS INJECTION ONLY

Read the package leaflet before use.

7. WITHDRAWAL PERIODS

Cattle:
Meat and offal: 70 days
Milk: 36 days
Sheep:
Meat and offal: 42 days
Milk: 18 days

8. EXPIRY DATE

Exp. {mm/yyyy}

Shelf life after first opening the immediate packaging: 28 days
Once broached, use by…

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 °C. Protect from direct sunlight.

10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Emdoka

14. MARKETING AUTHORISATION NUMBERS

Vm 34534/5008

15. BATCH NUMBER

Batch {number}

16. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

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

- To avoid self-injection do not use automatic injection equipment.
- This product should only be administered by a veterinary surgeon.
- Never carry a syringe loaded with the 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.
- Ensure that animals are properly restrained, including those in the vicinity.
- Do not work alone when using the veterinary medicinal product.
- In case of human injection SEEK IMMEDIATE MEDICAL ATTENTION and take the vial or the package insert with you. Apply a cold pack (not ice directly) to the injection site.

Additional operator safety warnings and NOTE TO THE PHYSICIAN:
Please see package leaflet for details.

17. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: Read package leaflet

18. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

POM-V

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE LABEL for Vial of 50ml and 100ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

TILMODIL 300 mg/ml Solution for Injection

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Tilmicosin 300 mg

3. TARGET SPECIES

Cattle and sheep.

4. ROUTES OF ADMINISTRATION

FOR SUBCUTANEOUS INJECTION ONLY.

5. WITHDRAWAL PERIODS

Cattle:
Meat and offal: 70 days
Milk: 36 days
Sheep:
Meat and offal: 42 days
Milk: 18 days

6. EXPIRY DATE

Exp. {mm/yyyy}
Once broached use within 28 days.

7. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 °C. Protect from direct sunlight. Keep the vial in the outer carton.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Emdoka

9. BATCH NUMBER

Batch {number}

10. 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 on the inside of the label or the package leaflet precisely.

Operator safety warnings, NOTE TO THE PHYSICIAN: Please see package leaflet for details.

11. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: Read package leaflet

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

For animal treatment only.
POM-V

B. PACKAGE LEAFLET

PARTICULARS TO APPEAR ON THE PACKAGE LEAFLET:

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

TILMODIL 300 mg/ml Solution for Injection for cattle and sheep

2. COMPOSITION

One ml contains:

Active substance:
Tilmicosin 300 mg

Excipients:
Propylene glycol 250 mg

Clear, yellowish to brown-yellowish solution.

3. TARGET SPECIES

Cattle and sheep

4. INDICATIONS FOR USE

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, pigs, horses, donkeys and goats.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

6. SPECIAL WARNING(S)

Special warnings:

Sheep

The clinical trials did not demonstrate a bacteriological cure in sheep with acute mastitis caused by *Staphyloccocus 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 for safe use in the target species:

Official, national and regional antimicrobial policies should be taken into account when the product is used.

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

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 macrolides and lincomycin due to the potential for cross-resistance.

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

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

- To avoid self-injection do not use automatic injection equipment.
- This product should only be administered by a veterinary surgeon.
- Never carry a syringe loaded with the 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.
- Ensure that animals are properly restrained, including those in the vicinity.
- Do not work alone when using the veterinary medicinal product.
- In case of human injection SEEK IMMEDIATE MEDICAL ATTENTION and take the vial or the package insert with you. Apply a cold pack (not ice directly) to the injection site.

Additional operator safety warnings:

- Avoid contact with 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 adrenaline.

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: *[To be completed nationally]*

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.

Interaction with other medicinal products and other forms of interaction:
Interactions between macrolides and ionophores have been observed in some species.

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.

6. Adverse reactions:

Sheep and Cattle:

Undetermined frequency (cannot be estimated from the available data)	Injection site swelling[1] Death[2]
Rare (1 to 10 animals / 10,000 animals treated):	Recumbency, incoordination and convulsions
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Dyspnoea (difficult breathing)[3]

[1] Soft and diffuse. Disappears within five to eight days
[2] 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.
[3] Can lead to acute death. Such cases may relate to relative overdosing and/or inadvertent intramuscular injection.

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 authosrisation holder using the contact details at the end of this package leaflet, or via the national reporting system.

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

FOR SUBCUTANEOUS INJECTION ONLY.
Use 10 mg tilmicosin per kg body weight (corresponding to 1 ml veterinary medicinal product per 30 kg body weight).

To ensure a correct dosage, bodyweight should be determined as accurately as possible to avoid under-dosing.

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 the product is used.
Wherever possible, the use of the product should be based on susceptibility testing.
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 macrolides and lincomycin due to the potential for cross-resistance.
To avoid self-injection do not use automatic injection equipment.
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 veterinary medicinal product if you notice any foreign particulate matter and/or abnormal physical appearance.
Do not broach the vial more than 25 times.

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
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.

Do not store above 25 °C. Protect from direct sunlight.
Do not use this veterinary medicinal product after the expiry date which is stated on the label after Exp.
Shelf-life after first opening the immediate packaging: 28 days.

12. SPECIAL PRECAUTIONS FOR DISPOSAL

Medicines should not be disposed of via the wastewater.
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. 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

Vm 34534/5008

Pack sizes: Cardboard box containing one amber glass vial of 50 or 100ml.
Not all pack sizes may be marketed.

15. PID LINK (Do not print heading)

[The following statement must be included where reference to the European Union Product Database is included on the product information. This statement is relevant to both UK(GB) and UK(NI) products:]

Find more product information by searching for the 'Product Information Database' on www.gov.uk.

16. CONTACT DETAILS

Marketing authorisation holder:
Emdoka, John Lijsenstraat 16, B-2321 Hoogstraten, Belgium

Manufacturer responsible for batch release: Produlab Pharma bv, NL-4941 SJ Raamsdonksveer, Nederland

Local representatives and contact details to report suspected adverse reactions:

DUGV (UK) Ltd.
Union House
111 New Union Street
Coventry, CV1 2NT

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

17. OTHER INFORMATION

POM-V
For animal treatment only.

Gavin Hall
Approved: 01 July 2024