BOX

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Hymatil 300 mg/ml solution for injection for cattle and sheep
Tilmicosin

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each ml contains: Tilmicosin 300 mg; Propylene glycol 250 mg.

3. PHARMACEUTICAL FORM

Solution for injection.

4. PACKAGE SIZE

50 ml
100 ml
250 ml
6 x 50 ml
6 x 100 ml
6 x 250 ml
10 x 50 ml
10 x 100 ml
10 x 250 ml
12 x 50 ml
12 x 100 ml
12 x 250 ml

5. TARGET SPECIES

Cattle and sheep

6. INDICATION(S)

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*.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

FOR SUBCUTANEOUS INJECTION ONLY.
Read the package leaflet before use.

Official, national and regional antimicrobial policies should be taken into account when the product is used.
To avoid self-injection do not use automatic injection equipment.
The use of the product should be based on susceptibility tests.
Avoid introduction of contamination into the 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.
Use 10 mg tilmicosin per kg body weight (corresponding to 1 ml Hymatil per 30 kg body weight).
Do not treat lamb 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.
If no improvement is noted within 48 hours, the diagnosis should be confirmed

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

Do not administer intravenously. Intravenous injection in cattle and sheep has been fatal.
Do not administer intramuscularly.
Do not administer to lambs weighing less than 15 kg.
Do not administer to horses, donkeys, pigs, goats or primates. Injection of the product in goats and pigs has been fatal.
Do not use in case of hypersensitivity to the active substance or to any of the excipients.

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 Hymatil 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 Hymatil.
- 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.

NOTE TO PHYSICIAN: Please see package leaflet for details.

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.

10. EXPIRY DATE

EXP
Once broached, use within 28 days.

11. SPECIAL STORAGE CONDITIONS

Store below 25ºC.Keep the vial in the outer carton in order to protect from light.
Do not freeze.

12. SPECIAL 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 product should be disposed of in accordance with national requirements.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only.
To be supplied only on veterinary prescription.
Administration only by a veterinary surgeon.

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

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

INDUSTRIAL VETERINARIA, S.A.
Esmeralda, 19
E-08950 Esplugues de Llobregat (Barcelona) Spain.

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Batch

LABEL VIAL OF 50 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Hymatil 300 mg/ml solution for injection for cattle and sheep
Tilmicosin

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Each ml contains: Tilmicosin 300 mg; Propylene glycol, 250 mg.

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

50 ml

4. ROUTE(S) OF ADMINISTRATION

FOR SUBCUTANEOUS INJECTION ONLY.
Read package leaflet before use.

5. WITHDRAWAL PERIOD

See package leaflet for details.

6. BATCH NUMBER

Batch

7. EXPIRY DATE

EXP
Once broached, use within 28 days.
Once opened do not be store above 25 °C and use by _____

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.
To be supplied only on veterinary prescription.
Administration only by a veterinary surgeon.

9. SPECIAL WARNING(S), IF NECESSARY

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 Hymatil 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 Hymatil.
- 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.

NOTE TO THE PHYSICIAN: Please see package leaflet for details.

LABEL VIAL OF 100 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Hymatil 300 mg/ml solution for injection for cattle and sheep
Tilmicosin

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each ml contains: Tilmicosin 300 mg; Propylene glycol, 250 mg.

3. PHARMACEUTICAL FORM

Solution for injection.

4. PACKAGE SIZE

100 ml

5. TARGET SPECIES

Cattle and sheep

6. INDICATION

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*.

7. METHOD AND ROUTE OF ADMINISTRATION

FOR SUBCUTANEOUS INJECTION ONLY.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

See package leaflet for details.

9. SPECIAL WARNING(S), IF NECESSARY

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 Hymatil 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 Hymatil.
- 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.

NOTE TO THE PHYSICIAN: Please see package leaflet for details.

10. EXPIRY DATE

EXP {month/year}
Once broached, use within 28 days.
Once opened use by:

11. SPECIAL STORAGE CONDITIONS

Store below 25ºC.Keep the vial in the outer carton in order to protect from light.
Do not freeze.

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 product should be disposed of in accordance with national requirements.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only.

To be supplied only on veterinary prescription.
Administration only by a veterinary surgeon.

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

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Industrial Veterinaria, S.A.
Esmeralda, 19
E-08950 Esplugues de Llobregat (Barcelona) Spain.

16. MARKETING AUTHORISATION NUMBER

{number}

17. MANUFACTURER'S BATCH NUMBER

Batch {number}

LABEL VIAL OF 250 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Hymatil 300 mg/ml solution for injection for cattle and sheep
Tilmicosin

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each ml contains: Tilmicosin 300 mg; Propylene glycol, 250 mg.

3. PHARMACEUTICAL FORM

Solution for injection.

4. PACKAGE SIZE

250 ml

5. TARGET SPECIES

Cattle and sheep

6. INDICATION

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*.

7. METHOD AND ROUTE OF ADMINISTRATION

FOR SUBCUTANEOUS INJECTION ONLY.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

See package leaflet for details

9. SPECIAL WARNING(S), IF NECESSARY

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 Hymatil 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 Hymatil.
- 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.

NOTE TO THE PHYSICIAN: Please see package leaflet for details.

10. EXPIRY DATE

EXP {month/year}
Once broached, use within 28 days.
Once opened use by:

11. SPECIAL STORAGE CONDITIONS

Store below 25ºC.Keep the vial in the outer carton in order to protect from light.
Do not freeze.

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 product should be disposed of in accordance with national requirements.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only.
To be supplied only on veterinary prescription.
Administration only by a veterinary surgeon.

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

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Industrial Veterinaria, S.A.
Esmeralda, 19
E-08950 Esplugues de Llobregat (Barcelona) Spain

16. MARKETING AUTHORISATION NUMBER

{number}

17. MANUFACTURER'S BATCH NUMBER

Batch {number}

PACKAGE LEAFLET
HYMATIL 300 mg/ml solution for injection for cattle and sheep
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:
INDUSTRIAL VETERINARIA, S.A.
Esmeralda, 19
08950 Esplugues de Llobregat (Barcelona) Spain

Manufacturer responsible for batch release:
Industrial Veterinaria, S.A.
Esmeralda 19
08950 Esplugues de Llobregat (Barcelona) Spain

aniMedica GmbH
Im Südfeld 9
48308 Senden-Bösensell Germany

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Hymatil 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.....250 mg
Clear, yellowish to brown-yellowish solution.

4. INDICATION(S)

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(S) AND METHOD OF ADMINISTRATION

FOR SUBCUTANEOUS INJECTION ONLY
Use 10 mg tilmicosin per kg body weight (corresponding to 1 ml Hymatil 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 the product is used.
To avoid self-injection do not use automatic injection equipment.
The use of the 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 Hymatil 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 25ºC.
Keep the vial in the outer carton in order to protect from light.
Do not freeze.
Do not use after the expiry date which is stated on the label.
Shelf-life after first opening the immediate packaging: 28 days.

12. SPECIAL WARNING(S)

Special warnings for each target species:
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 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 Hymatil 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 Hymatil.
- 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 Poisons Information Service on: (indicate here the telephone number of the centre).

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 could be 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 body weight in sheep.

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.
Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

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.

When the container is broached (opened) for the first time, using the in-use shelf-life which is specified on this package leaflet, the date on which any product remaining in the container should be discarded should be worked out. This discard date should be written in the space provided on the label.