DATA SHEET

Apotil™ 300 mg/ml Solution for Injection

Presentation A clear yellow solution for injection, containing 300 mg tilmicosin per ml.

Uses For the treatment of pneumonia in cattle and sheep, associated with *Mannheimia haemolytica, Pasteurella multocida,* and other microorganisms sensitive to tilmicosin. For the treatment of ovine mastitis associated with *Staphylococcus aureus* and *Mycoplasma agalactiae*. For the treatment of interdigital necrobacillosis in cattle (bovine pododermatitis, foul in the foot) and ovine footrot.

Dosage and administration To be used only in sheep over 15 kg and cattle, administered only by subcutaneous injection. Give a single subcutaneous injection of 1 ml of Apotil per 30 kg bodyweight (equivalent to 10 mg tilmicosin per kg) as indicated below.

Cattle, method of administration *Withdraw* the required dose from the vial and remove the syringe from the needle. If a group of animals is to be treated, leave the needle in the vial as a draw-off needle for subsequent doses. Restrain the animal and insert a separate needle subcutaneously into the injection site. Injection in a fold of skin over the rib cage behind the shoulder is preferred. Connect the syringe to the needle and inject into the base of the skin fold. 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 or smaller syringe improves the accuracy of 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 fold of skin over the rib cage behind the shoulder. Connect the syringe to the needle and inject into the base of the skin fold. Do not inject more than 2 ml per injection site.

If no improvement is noted within 48 hours, the diagnosis should be confirmed. Avoid introducing contaminants into the vial whilst using it. It should be inspected for foreign particulate matter and abnormal appearance. If either be observed, discard the vial.

Contra-indications, warnings, etc. FOR ANIMAL TREATMENT ONLY.

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

- This product should be administered only 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 human injection SEEK IMMEDIATE MEDICAL ATTENTION and take the vial or the package leaflet with you. Apply a cold pack (no tice directly) to the injection site.

***NOTE TO THE PHYSICIAN*: INJECTION OF THIS DRUG IN MAN 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 man.
- Administration of dobutamine should also be considered for 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 892 0111.

Keep out of the reach of children. Avoid contact with the eyes. May cause sensitisation by skin contact. Wash hands after use.

Do not administer Apotil intravenously. Do not administer it to pigs, horses, goats or monkeys. Occasionally, a soft diffuse swelling may occur at the injection site, but this disappears within five to eight days.

Withdrawal periods

Cattle meat and offal:	70 days
Cattle milk:	36 days

Sheep meat and offal: 42 days
Sheep milk: 18 days

If Apotil 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. The dry period begins when a dry-cow tube is administered[1]. If Apotil is administered after the last milking but before the administration of a dry-cow tube, the withdrawal period of 36 days begins on the date of drying off.

If it 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.

Pharmaceutical precautions Do not store above 30°C. Protect from light. After first broaching the vial, use its contents within 28 days and discard unused material at the end of this period. Ensure there is no contamination of the contents of the vial when using it. Discard the product if it ceases to be perfectly clear or discolouration appears in it. Any unused product should be disposed of in accordance with local requirements.

Legal category POM-V.

Package quantities Amber vial containing 50 ml.

Further information Apotil is effective following a single subcutaneous injection. The concentration of tilmicosin achieved in the lung is substantially higher than that in serum. In calves, the concentration of tilmicosin in the lung has been found to remain above the MIC_{90} for *Mannheimia haemolytica* for at least 72 hours following a single subcutaneous injection at the recommended dose.

Tilmicosin is eliminated from the udder without the need for milking. Injecting cows with tilmicosin at the beginning of the dry period resulted in an initial concentration of tilmicosin in dry-udder secretion of 8000 µg/ml. By day 11 of the dry period, it had decreased to 100 µg/ml. By day 30, tilmicosin was not detected in dry-udder secretions.

Marketing-authorization number Vm 36308/4000

Marketing-authorization holder Nimrod Veterinary Products Ltd

nimrod@nimrodvet.co.uk
Telephone 01608 652593

[1] Committee for Veterinary Medicinal Products (2000). Tilmicosin (Extension to milk) Summary Report (4).