

MICOTIL® (TILMICOSIN INJECTION)

MICOTIL® (TILMICOSIN INJECTION) METAPHYLAXIS EFFECTS ON REDUCING BOVINE RESPIRATORY DISEASE (BRD) MORBIDITY IN CATTLE



This report summarizes data from



STUDIES

conducted on the use of Micotil metaphylaxis in stressed cattle to determine the effect of administration timing on reducing BRD morbidity. The studies compared treatments administered pre-shipment, on-arrival, post-arrival and post-arrival based on temperature.

KEY TAKEAWAYS

- Research supports the use of antibiotic metaphylaxis in high-risk cattle as a proactive tool for reducing impact of BRD in cattle populations.
- On-arrival administration of Micotil metaphylaxis consistently proved most effective at reducing respiratory morbidity.
- Treating high-risk cattle early with Micotil metaphylaxis is cost-effective and increases ROI due to feed efficiency and reduced retreats.
- Micotil metaphylaxis is proven to reduce morbidity in cattle.

SUMMARY OF MICOTIL METAPHYLAXIS TIMING STUDIES¹⁻⁴

Investigator	Animal Origin	Number in Study (hd)	Study Length (days)	Average Weight (lbs.)	Treatment Groups	Morbidity Reduction, %	Average Daily Gain (lbs.)	Results
Klemesrud	Nebraska	952	24	495	Untreated control	22.30%	1.62	Mass treatment on-arrival or on day six administration proved most effective at reducing BRD morbidity. No advantages found in delayed administration where the temperature based method was used.
					Micotil treatment on-arrival	12.90%	1.80	
					Micotil treatment 6 days post-arrival	14.03%	1.81	
					Micotil treatment 6 days post-arrival (temperature-based)	35.56%	1.62	
McClary & Vogel	Multiple Southeastern Auction Barns	400	28	473	Untreated control	20.00%	2.24	Metaphylaxis on-arrival proved more effective at reducing BRD morbidity, although morbidity was reduced in all groups where Micotil was used.
					Micotil treatment on-arrival	2.00%	2.64	
					Micotil treatment 3 days post-arrival	1.00%	2.64	
Guthrie	Colorado & Wyoming	799	206	578	Untreated control	66.10%	3.41	BRD morbidity in the on-arrival metaphylaxis group was significantly lower than controls and tended to be lower than the delayed metaphylaxis group.
					Micotil treatment on-arrival	27.60%	3.43	
					Micotil treatment 5 days post-arrival	47.60%	3.46	
					Micotil treatment 5 days post-arrival (temperature-based)	46.70%	3.45	
Duff	Mississippi	96	35	491	Untreated control	71.90%	2.60	The percentage of cattle treated for BRD was decreased in all Micotil treated groups compared to controls.
					Micotil treatment pre-shipment	45.20%	2.73	
					Micotil treatment on-arrival	46.90%	2.79	
Duff	Mississippi	240	28	390	Untreated control	40.00%	2.93	The percentage of cattle treated for BRD was decreased in all Micotil treated groups compared to controls.
					Micotil treatment pre-shipment	18.70%	3.13	
					Micotil treatment on-arrival	7.50%	2.95	

ELANCO'S BRD PORTFOLIO

Micotil is part of Elanco's industry-leading BRD portfolio of vaccines, antibiotics and immunostimulants to help producers prevent, control and treat the most pervasive disease in the industry.



Micotil® (tilmicosin injection) is indicated for the treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni*, and for the control of respiratory disease in cattle at high risk of developing BRD associated with *M. haemolytica*.

IMPORTANT MICOTIL SAFETY INFORMATION

Before using this product, it is important to read the entire product insert, including the boxed human warning. Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian. Not for human use. Injection of this drug in humans has been associated with fatalities. Keep out of reach of children. Administer only with a tube-fed safety syringe. Do not use in automatically powered syringes, single-use syringes, or other delivery devices. Exercise extreme caution to avoid accidental self-injection. In case of human injection, consult a physician immediately and apply ice or cold pack to injection site while avoiding direct contact with the skin. Avoid contact with eyes. Always use proper drug handling procedures to avoid accidental self-injection. Consult your veterinarian on the safe handling and use of all injectable products prior to administration. For use in cattle or sheep only. Inject subcutaneously. Injection of this antibiotic has been shown to be fatal in swine and non-human primates, and may be fatal in horses and goats. Do not use in lambs less than 15 kg body weight. Do not use in female dairy cattle 20 months of age or older. Use in lactating dairy cattle or sheep may cause milk residues. The following adverse reactions have been reported: in cattle: injection site swelling and inflammation, lameness, collapse, anaphylaxis/anaphylactoid reactions, decreased food and water consumption, and death; in sheep: dyspnea and death. Micotil has a pre-slaughter withdrawal time of 42 days.

¹Duff, G., Walker, D. et al. 2000. "Effects of pre-shipment versus arrival medication with tilmicosin phosphate and feeding chlortetracycline on health and performance of newly received beef cattle." J. Anim. Sci. 78:267-274.

²Elanco Animal Health. Data on File.

³Klemesrud, M., Apfel, M. et al. 1997. "Synchronizing Micotil treatment with time of sickness in newly received calves." Nebraska Beef Rep.

⁴McClary, D. and Vogel, G. 1999. "Effect of timing of tilmicosin metaphylaxis on control of bovine respiratory disease and performance in feeder cattle." Bov. Pract. 33(2):155-161.

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FULL PRESCRIPTION INFORMATION FOR USE IN CATTLE ONLY. SEE PRODUCT INSERT FOR COMPLETE DOSING AND ADMINISTRATION INFORMATION.



300 mg tilmicosin, USP as tilmicosin phosphate per mL
For Subcutaneous Use in Cattle Only

Administer only with a tube-fed safety syringe. Do not use in automatically powered syringes, single-use syringes, or other delivery devices. Contact Elanco at 1-800-428-4441, or your distributor, for a tube-fed safety syringe for use with this product.

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian. Before using Micotil, please consult the product insert, a summary of which follows:

Indications: For the treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni*. For the control of respiratory disease in cattle at high risk of developing BRD associated with *Mannheimia haemolytica*.

Approved by FDA under NADA # 140-929

Micotil must be used with the quick-fit connector made specifically for its use. Contact Elanco or your distributor for this equipment. Read product labeling, including Safe Handling Practices, before use.

Dosage and Administration: Follow instructions for activation of the shroud before first usage. Inject subcutaneously in Cattle Only. See Safe Handling Practices, Contraindications, and Warnings prior to use. In cattle, administer a single subcutaneous dose of 10 to 20 mg/kg body weight (1 to 2 mL/30 kg or 1.5 to 3 mL per 100 lbs).

Do not inject more than 10 mL per injection site. If no improvement is noted within 48-hours, the diagnosis should be reevaluated. For cattle injection under the skin in the neck is suggested. If not accessible, inject under the skin behind the shoulders and over the ribs.

Note: Swelling at the subcutaneous site of injection may be observed. See product insert for complete dosing and administration information.

CONTRAINDICATIONS: Do not use in automatically powered syringes, single-use syringes, or other delivery devices not specified in the labeling. Do not administer intravenously to cattle. Intravenous injection in cattle will be fatal. Do not administer to animals other than cattle. Injection of tilmicosin has been shown to be fatal in swine and non-human primates. Death following exposure to tilmicosin injection has been reported to FDA/CVM in goats, rabbits, pheasants, pigs, dogs, deer, cats, alpacas, and horses.

Residue Warnings: Animals intended for human consumption must not be slaughtered within 42 days of the last treatment. Not for use in lactating dairy cattle 20 months of age or older. Use of tilmicosin in this class of cattle may cause milk residues.

Precautions: The effects of tilmicosin on bovine reproductive performance, pregnancy and lactation have not been determined. Intramuscular injection will cause a local reaction which may result in trim loss of edible tissue at slaughter.

Storage Conditions: Store at or below 86 °F (30 °C). Protect from direct sunlight. Use within 84 days of first puncture. Date of first puncture: _____

To report adverse effects, access medical information, or obtain additional product information, call 1-800-428-4441.

HUMAN WARNINGS: Not for human use. Injection of this drug in humans has been associated with fatalities. Keep out of reach of children. Administer only with a tube-fed safety syringe. Do not use in automatically powered syringes, single-use syringes, or other delivery devices. Exercise extreme caution to avoid accidental self-injection. In case of human injection, consult a physician immediately and apply ice or cold pack to injection site while avoiding direct contact with the skin. Emergency medical telephone numbers are 1-800-722-0987 or 1-800-428-4441. Avoid contact with skin, eyes or mucous membranes.

NOTE TO THE PHYSICIAN: The cardiovascular system is the target of toxicity and should be monitored closely. Cardiovascular toxicity may be due to calcium channel blockade. In dogs, administration of intravenous calcium offset Micotil-induced tachycardia and negative inotropy (decreased contractility). Dobutamine partially offset the negative inotropic effects induced by Micotil in dogs. β-adrenergic antagonists, such as propranolol, exacerbated the negative inotropy of Micotil in dogs. Epinephrine potentiated lethality of Micotil in pigs. This antibiotic persists in tissues for several days.

Adverse Reactions: The following adverse reactions have been reported post-approval: In cattle: injection site swelling and inflammation, lameness, collapse, anaphylaxis/anaphylactoid reactions, decreased food and water consumption, and death.

For additional information about reporting adverse drug experiences for animal drugs, contact FDA at 1-888-FDA-VETS or <http://www.fda.gov/reportanimalae>

Effectiveness: In a multi-location field study, 1508 calves with naturally occurring BRD were treated with Micotil. Responses to treatment were compared to saline-treated controls. A cure was defined as a calf with normal attitude and activity, normal respiration, and a rectal temperature of <104°F on Day 13. The cure rate was significantly higher (P=0.004) in Micotil-treated calves (63.1%) compared to saline-treated calves (29.2%). During the treatment phase of the study, there were 10 BRD-related deaths in the Micotil-treated calves compared to 47 in the saline-treated calves.

How Supplied: Micotil (tilmicosin injection) is supplied in 250 mL multi-dose amber glass bottles in a non-removable polymer protector.

Manufactured for:
Elanco US, Inc. Greenfield, IN 46140, USA

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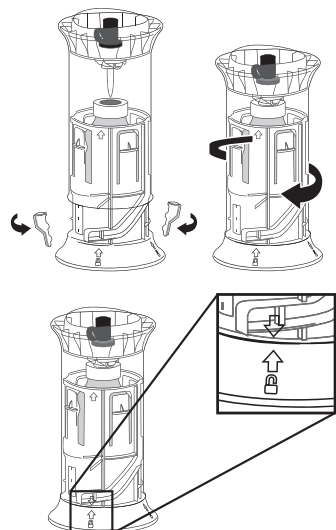
Instructions for Activation of the Shroud

Before first usage activate the shroud-vial-system as shown in the pictures. Administer only with a tube-fed safety syringe. Do not use in automatically powered syringes, single-use syringes, or other delivery devices. This product must be used with the quick-fit connector made specifically for use with Micotil (tilmicosin injection) that attaches to the shroud fitting. To obtain a tube-fed safety syringe and quick-fit connector, contact Elanco at 1-800-428-4441, or your distributor

Step 1. Twist the two tamper-evident tabs to break them off the Shroud Base.

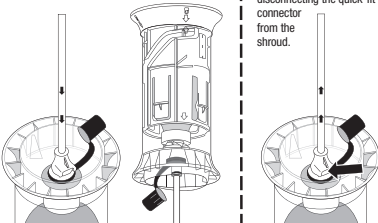
Step 2. Rotate the Shroud Top through a quarter-turn clockwise. The spike will pierce the vial closure, and the Shroud Top will lock into its final position at an audible "click".

Step 3. The correct final position can be confirmed by the alignment of the 2 arrows as shown in the picture.



Step 4. Remove the flexible cap from the fluid connection. Attach the quick-fit connector to tubing if not already attached. Push the quick-fit connector downwards onto the shroud fitting until it clicks into place.

Step 5. Invert the Micotil Shroud, then prime the tube-fed safety syringe following manufacturer's instructions.



Micotil should not be stored in dosing equipment. Dosing equipment should be disconnected from the shroud after each use. Store product upright. The dosing equipment should be cleaned according to the manufacturer's instructions. Avoid contact with skin, eyes, or mucous membranes.

1. WHAT ARE THE POSSIBLE EFFECTS OF ACCIDENTAL HUMAN INJECTION?

Human injections of Micotil have been associated with fatalities. Clinical signs from human exposure include off taste in the mouth, nausea, headache, dizziness, rapid heart rate, chest pain, anxiety, or lightheadedness. Local reactions such as injection site pain, bleeding, swelling or inflammation have been reported.

2. WHAT SHOULD I DO IN THE CASE OF ACCIDENTAL HUMAN INJECTION?

- Immediately seek medical attention.
- Apply ice or cold pack to injection site, while avoiding direct contact with the skin, and transport immediately to a hospital.
- Call 1-800-722-0987 or 1-800-428-4441 for further emergency information.

3. WHAT SHOULD MY PHYSICIAN KNOW IN THE CASE OF ACCIDENTAL HUMAN INJECTION?

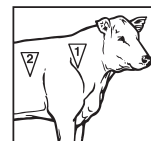
- The cardiovascular system is the target of toxicity and should be monitored closely.
- Cardiovascular toxicity may be due to calcium channel blockade.
- Intravenous calcium administration reversed the cardiovascular effects of Micotil in dogs and may provide benefit in patients exhibiting low blood pressure (hypotension) or rapid heart rate (tachycardia).
- Dobutamine improved some of the cardiac function in dogs given Micotil.
- Epinephrine increased the toxicity of Micotil in pigs, resulting in death.
- Propranolol (a beta-adrenergic antagonist) further decreased cardiac function in dogs given Micotil.
- The active ingredient in Micotil is tilmicosin phosphate and persists in tissue for several days.
- Call 1-800-722-0987 or 1-800-428-4441 for further emergency information.

4. WHAT ARE THE PROPER WAYS TO HANDLE AND STORE MICOTIL?

- Store at or below 86°F (30°C), out of direct sunlight, in a safe location, not easily accessible to the general public. Use within 84 days of first puncture. Store upright between product dispensing. Disconnect and clean dosing equipment for storing as per manufacturer's instructions.
- Avoid contact with skin, eyes, or mucous membranes.
- Read, understand, and follow all label use directions.
- Wash hands thoroughly with soap and water after handling.

5. WHAT ARE THE PROPER METHODS FOR ADMINISTERING MICOTIL?

- Properly restrain animals prior to administration.
- Work in a team, or if alone, advise someone of your location and how long you plan to be there.
- For subcutaneous use: Administer only with a tube-fed safety syringe. Do not use in automatically powered syringes, single-use syringes, or other delivery devices. Contact Elanco at 1-800-428-4441, or your distributor, for a tube-fed safety syringe for use with this product.
- Use a 1/2-inch to 5/8-inch, 18- to 16-gauge needle.
- With a single hand on the safety syringe insert the needle subcutaneously, at a top-down angle, while avoiding penetration of underlying muscle.
- For cattle, injection under the skin in the neck is suggested. If not accessible, inject under the skin behind the shoulders and over the ribs.
- In cattle, administer a single subcutaneous dose of 1.5 to 3.0 mL of Micotil (tilmicosin injection) per 100 lbs of body weight, in either of the two areas noted in the adjacent drawing.
- For beef cattle, Beef Quality Assurance recommends injection site 1, unless this site is inaccessible or places the operator in a potentially dangerous situation.
- Wash hands thoroughly with soap and water after administration.
- Do not administer intravenously (IV) as IV administration will be fatal.
- Intramuscular injection will cause a local reaction, which may result in trim loss.
- Do not inject more than 10 mL per injection site.
- Do not use in lambs less than 15 kg body weight.



6. WHAT ARE SAFE WAYS TO REMOVE AND CHANGE NEEDLES?

- Always follow the manufacturer's instruction of how to safely remove and change needles from the safety syringe.
- Plan for the safe handling and disposal of needles before use.
- Keep the needle capped until ready to use.
- Avoid recapping a used needle.
- To safely remove used needles, use tools appropriate for the specific type of safety syringe. Do not remove a used needle with your fingers.
- Dispose used needles in an appropriate sharps disposal container. Do not overfill sharps containers and do not put your fingers into a sharps container.
- Never place loose needles in household or public trash cans.