

# MICOTIL® (TILMICOSIN INJECTION)

## THE EFFECTS OF METAPHYLAXIS WITH MICOTIL® ON HEALTH AND PERFORMANCE OF CALF-FED HOLSTEINS AT HIGH RISK OF CONTRACTING BOVINE RESPIRATORY DISEASE

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### OBJECTIVE

Study<sup>1</sup> conducted to evaluate the effects of Micotil® (tilmicosin injection) on bovine respiratory disease (BRD) morbidity, mortality and performance when used metaphylactically at the time of on-arrival processing in newly received Holstein bull calves at the feedyard.

### TRIAL ELEMENTS



Calves derived from two California ranches.



Processed within six hours of arrival.

**960**

960 high-risk, Holstein bull calves.

**290 LBS.**

290 pounds in weight.



Calves were randomly assigned to treat/non-treat groups.



Animals harvested 339-343 days later.

### KEY FINDINGS

Calves treated metaphylactically with Micotil resulted in:

**73%**

reduction in BRD morbidity

**12 LBS.**

greater live weight gain

**9 LBS.**

greater hot carcass weight gain

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.

TABLE 1:  
EFFECTS OF MICOTIL METAPHYLAXIS AT PROCESSING ON MORBIDITY AND MORTALITY IN CALF-FED HOLSTEINS.

	Control	Micotil Metaphylaxis	SEM <sup>a</sup>	P-Value
No. animals	480	480	—	—
No. pens	6	6	—	—
BRD morbidity, %	10.8	2.9	1.54	0.01
BRD mortality, %	2.5	0.2	0.70	0.06
Total mortality, %	4.17	1.67	1.31	0.15
Removals, %	2.3	0.4	0.6	0.02

<sup>a</sup> Standard error of the mean

TABLE 2:  
EFFECTS OF MICOTIL METAPHYLAXIS AT PROCESSING ON PERFORMANCE IN CALF-FED HOLSTEINS, DEADS OUT.

	Control	Micotil Metaphylaxis	SEM <sup>a</sup>	P-Value
Initial body weight, lbs.	289	292	6.8	.08
Final weight, lbs.	1,260	1,275	7.3	.07
Weight gain, lbs.	971	983	8.0	.07
Average daily gain, lbs.	2.84	2.87	0.02	.08
DM intake, lbs.	14.1	14.7	0.2	.09
Conversion (feed : grain)	4.98	5.11	0.08	.27
HCW, lbs.	756	765	2.8	.07

<sup>a</sup> Standard error of the mean

### RESULTS

Study demonstrates that metaphylactic treatment with Micotil decreases morbidity and mortality in calf-fed Holsteins at high risk of contracting BRD. The reduction in respiratory morbidity and the associated pulmonary pathology, as well as the increased dry matter (DM) intake, are likely critical contributors to the higher weight gain in calves and increased hot carcass weights in calves.

### 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.

<sup>1</sup>Elanco Animal Health. Data on file.

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Elanco™

Micotil™ 300

250 mL

(tilmicosin injection)

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 altitude 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.**

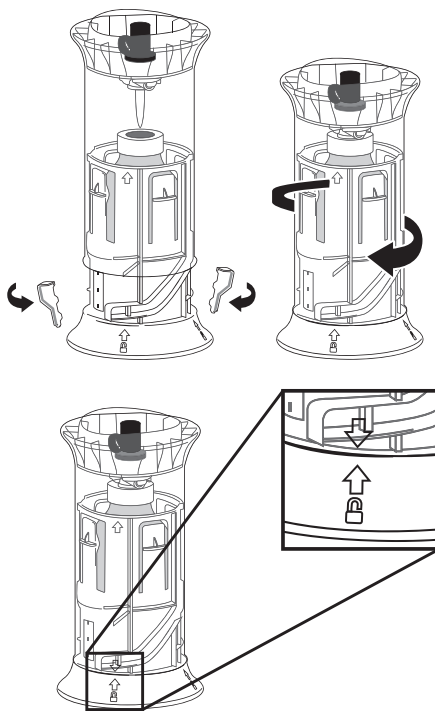
Twist the two taper-evident tabs to break them off the Shroud Base.

**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 by an audible "click".

**Step 3.**

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



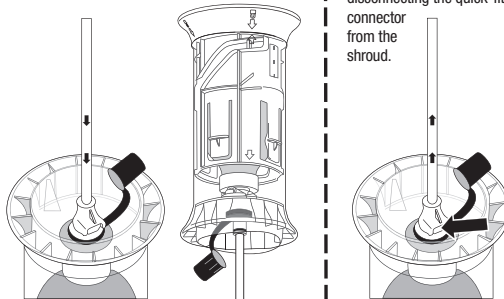
**Step 4.**

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.

Return shroud to upright position after finishing operation. Leave tubing attached to tube-fed safety syringe and quick-fit connector until dosing equipment has been removed from the shroud. Remove dosing equipment by pushing the trigger as shown in the picture, then disconnecting the quick-fit connector from the shroud.



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?**

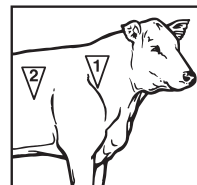
- The cardiovascular system is the target of toxicity and should be monitored closely.
- Cardiovascular toxicity may be due to calcium channel blockade.
- Intravenous calcium administration reversed the cardiovascular effects of Micotil in dogs and may provide benefit in patients exhibiting low blood 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.