Submit completed form via E-mail to: micotil_certification@elancoah.com

**Micotil® (tilmicosin injection) Safe Handling and Use Certification Signature Page**

Please check and sign next to the appropriate business type.

_____ **I am a Veterinarian or Distributor who has a license to receive and sell animal prescription products.**

I acknowledge that I completed Micotil Safe Handling and Use certification training on _____ (Date completed).

I am confident in my ability to safely handle and administer Micotil to cattle. If not provided by Elanco, I understand it is my responsibility to provide Micotil Safe Handling and Use certification training to my staff and clients, thus ensuring they are able to safely handle and administer Micotil to cattle. The training should fit the client, their facilities and their experience with Micotil. I and my staff understand that we may NOT and will NOT sell Micotil to any customer who has not received Micotil Safe Handling and Use certification training.

By signing this form, I acknowledge that Elanco may share my information with its employees, agents, contractors or partners in connection with services that these individuals or entities perform for or with Elanco to aid in the purchase and/or sale of Micotil.

ACCEPTED:

Signature: _____

Printed Name: _____

Title: _____

Business Name: _____

Business Address: _____

Date: _____

Business E-mail: _____

☐ **Producer**

I acknowledge that I completed Micotil Safe Handling and Use certification training on _____ (Date completed).

I am confident in my ability to safely handle and administer Micotil to cattle. If not provided by Elanco, I understand it is my responsibility to provide Micotil Safe Handling and Use certification training to my staff, thus ensuring they are able to safely handle and administer Micotil to cattle. The training should fit my staff, my facilities and their experience with Micotil.

By signing this form, I acknowledge that Elanco may share my information with its employees, agents, contractors or partners in connection with services that these individuals or entities perform for or with Elanco to aid in the purchase and/or sale of Micotil.

ACCEPTED:

Signature: _____

Printed Name: _____

Title: _____

Business Name: _____

Business Address: _____

Date: _____

Business E-mail: _____

*If you have any questions or concerns about this document, the Micotil Safe Handling and Use certification process, or the handling of your information, please contact Elanco Animal Health at 800-428-4441.

Micotil 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 *Mannheimia haemolytica*.

**IMPORTANT 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.

Elanco™

# Micotil™ 300

250 mL™

## (tilmicosin injection)

**300 mg tilmicosin, USP as tilmicosin phosphate per mL**

**For Subcutaneous Use in Cattle and Sheep Only**

**Solo Para Uso Subcutáneo en Ganado Vacuno y Ovino**

**Approved by FDA under NADA # 140-929**

**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.**
**Administrar únicamente con una jeringa de seguridad con tubo. No administrar con jeringas accionadas automáticamente, jeringas de un solo uso u otros dispositivos de aplicación. Contactar a Elanco al 1-800-428-4441, o al distribuidor, para obtener una jeringa de seguridad con tubo para usar con este producto.**

**Caution:** Federal law restricts this drug to use by or on the order of a licensed veterinarian.

**Description:** Micotil (tilmicosin injection) is a solution of the antibiotic tilmicosin. Each mL contains 300 mg of tilmicosin, USP as tilmicosin phosphate in 25% propylene glycol, phosphoric acid as needed to adjust pH and water for injection, Q.S. Tilmicosin, USP is produced semi-synthetically and is in the macrolide class of antibiotics.

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

**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.**

**Micotil debe usarse con un conector de ajuste rápido hecho específicamente para su uso. Contacte a Elanco o al distribuidor para obtener este equipo. Lea la ficha técnica, incluidas las Prácticas De Manejo Seguro, antes de usar.**

**Dosage and Administration: Follow instructions for activation of the shroud before first usage.**

**Inject Subcutaneously in Cattle and Sheep Only. See Safe Handling Practices, Contraindications, and Warnings prior to use. In cattle,** administer a single subcutaneous dose of 10 to 20 mg/kg of body weight (1 to 2 mL/30 kg or 1.5 to 3 mL per 100 lbs). **In sheep** greater than 15 kg, administer a single subcutaneous dose of 10 mg/kg of body weight (1 mL/30 kg or 1.5 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 and sheep, 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.

**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 or sheep.**
**Intravenous injection in cattle or sheep will be fatal. Do not use in lambs less than 15 kg body weight. Do not administer to animals other than cattle or sheep. 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.**

**Warnings:**

**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. ß-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.**

**ADVERTENCIAS PARA EL SER HUMANO: Este producto no es para uso humano. La inyección de este medicamento al ser humano se ha asociado con muertes. Mantenga fuera del alcance de los niños. Utilice únicamente con una jeringa de seguridad con tubo. No use en jeringas operadas automáticamente, jeringas de un solo uso u otros dispositivos de aplicación. Proceda con extrema cautela para evitar la autoinyección accidental. En caso de inyección en seres humanos, consulte inmediatamente a un médico y aplique hielo o una compresa fría en el lugar de la inyección, evitando el contacto directo con la piel. Los números de teléfono para emergencias médicas son 1-800-722-0987 o 1-800-428-4441. Evite el contacto con la piel, los ojos o las membranas mucosas.**

**NOTA PARA EL MÉDICO: El sistema cardiovascular es el blanco de la toxicidad y debe vigilarse estrechamente. La toxicidad cardiovascular puede deberse al bloqueo de los canales de calcio.**
**En los perros, la administración intravenosa de calcio compensó la taquicardia y los efectos inotrópicos negativos (reducción de la contractilidad) inducidos por Micotil (tilmicosina inyectable). La dobutamina compensó parcialmente los efectos inotrópicos negativos inducidos por Micotil en perros. Los antagonistas ß-adrenérgicos, como propranolol, exacerbaron el inotropismo negativo de Micotil en los perros. La epinefrina potenció la letalidad de Micotil en cerdos. Este antibiótico persiste en los tejidos por varios días.**

**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. Not for use in lactating ewes producing milk for human consumption.**

**Precautions:** The effects of tilmicosin on bovine and ovine 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.

**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.

In sheep: dyspnea 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

**Clinical Pharmacology:** A single subcutaneous injection of Micotil (tilmicosin injection) at 10 mg/kg of body weight dose in cattle resulted in peak tilmicosin levels within one hour and detectable levels (0.07 µg/mL) in serum beyond 3 days. However, lung concentrations of tilmicosin remained above the tilmicosin MIC 95% of 3.12 µg/mL for *Mannheimia haemolytica* for at least 3 days following the single injection. Serum tilmicosin levels are a poor indicator of total body tilmicosin. The lung/serum tilmicosin ratio in favor of lung tissue appeared to equilibrate by 3 days post-injection at approximately 60. In a study with radioactive tilmicosin, 24% and 68% of the dose was recovered from urine and feces respectively over 21 days. After a single subcutaneous injection of Micotil at 10 mg/kg of body weight, tilmicosin concentrations in excess of 4 µg/mL were maintained in the alveolar macrophages and neutrophils of most cattle for at least 10 days. The clinical relevance of these findings has not been determined.

**Microbiology:** Tilmicosin has an *in vitro* antibacterial spectrum that is predominantly Gram-positive with activity against certain Gram-negative microorganisms. *In vitro* activity against several *Mycoplasma* species has also been observed.

**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.

**Animal Safety:** A safety study was conducted in feeder calves receiving subcutaneous doses of 20, 30, 40, or 60 mg/kg of body weight, injected 3 times at 72-hour intervals. Death was not seen in any of the treatment groups. Injection site swelling and mild hemorrhage at the injection site were seen in animals in all dosage groups. Lesions were described as being generally more severe and occurred at higher frequency rates in the animals treated with higher doses of tilmicosin. Lameness associated with the injection site was noted in two of twenty-four animals (one animal in the 30 mg/kg body weight treatment group and one animal in the 60 mg/kg treatment group). No other drug related lesions were observed macroscopically or microscopically. Decreases in food and water consumption were noted in all treatment groups compared to the control group.

A separate safety study conducted in feeder calves, subcutaneous doses of 10, 30, or 50 mg/kg of body weight, injected 3 times at 72-hour intervals did not cause any deaths. Edema at the site of injection was noted. The only lesion observed at necropsy was minimal myocardial necrosis in some animals dosed at 50 mg/kg.

In an additional safety study, subcutaneous doses of 150 mg/kg body weight injected at 72-hour intervals resulted in death of two of the four treated animals. Edema was marked at the site of injection. Minimal myocardial necrosis was the only lesion observed at necropsy. Deaths of cattle have been observed with a single intravenous dose of 5 mg/kg of body weight.

In sheep, single subcutaneous injections of 10 mg/kg body weight dose did not cause any deaths and no adverse effects of tilmicosin were observed on blood pressure, heart rate, or respiratory rate.

**Toxicology:** The heart is the target of toxicity in laboratory and domestic animals given Micotil (tilmicosin injection) by oral or parenteral routes. The primary cardiac effects are increased heart rate (tachycardia) and decreased contractility (negative inotropy). Cardiovascular toxicity may be due to calcium channel blockade.

Upon subcutaneous injection, the acute median lethal dose of tilmicosin in mice is 97 mg/kg, and in rats is 185 mg/kg of body weight. Given orally, the median lethal dose is 800 mg/kg and 2250 mg/kg body weight in fasted and nonfasted rats, respectively.

No compound-related lesions were found at necropsy.

In dogs, intravenous calcium offset Micotil-induced tachycardia and negative inotropy, restoring arterial pulse pressure. Dobutamine partially offset the negative inotropic effects induced by Micotil in dogs. ß- adrenergic antagonists, such as propranolol, exacerbated the negative inotropy of Micotil in dogs.

In monkeys, a single intramuscular dose of 10 mg/kg body weight caused no signs of toxicity. A single dose of 20 mg/kg body weight caused vomiting and 30 mg/kg body weight caused the death of the only monkey tested.

In swine, intramuscular injection of 10 mg/kg body weight caused increased respiration, emesis, and a convulsion, 20 mg/kg body weight resulted in mortality in 3 of 4 pigs, and 30 mg/kg body weight caused the death of all 4 pigs tested. Injection of 4.5 and 5.6 mg/kg body weight intravenously followed by epinephrine, 1mL (1:1000) intravenously 2 to 6 times, resulted in death of all pigs injected. Pigs given 4.5 mg/kg and 5.6 mg/kg body weight intravenously with no epinephrine all survived.

These results suggest intravenous epinephrine may be contraindicated.

Results of genetic toxicology studies were all negative. Results of teratology and reproduction studies in rats were negative.

The no effect level in dogs after daily oral doses for up to one year is 4 mg/kg of body weight.

**Storage Conditions:** Store at or below 86°F (30°C). Protect from direct sunlight. Use within 84 days of first puncture. Store upright between product dispensing. Disconnect and clean dosing equipment for storing as per manufacturer's instructions.
Conservar a 86 °F (30 °C). Proteger de la luz solar directa. Usar dentro de los 84 días de la primera punción. Guardar en posición vertical entre cada suministro del producto. Desconectar y limpiar el dispositivo de dosificación para el almacenamiento según las instrucciones del fabricante.

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

**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**

**Revised: 09/2021**



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