

Elanco

Micotil[®]

TM

Micotil[®] Safe Handling & Use Training

Training Objectives

- Educate users on the importance of Micotil[®] (tilmicosin injection) Safe Handling & Use practices
- Reinforce that Micotil and other injectable products can be used safely when appropriate cautionary measures are followed



Expectations of Micotil Users

- Take time to read the Booklet Label contained in packaging
- Display Dose & Administration Poster in all treatment facilities
- Communicate regularly with staff to reinforce good safety practices when working with animals
 - Review Micotil Safe Handling & Use annually with all employees
 - Train all new staff prior to allowing the use of any injectable product, including Micotil
- Store Micotil in a secure location



Micotil Booklet Label

- Contains:
 1. Complete label
 2. Human warnings and note to physician
 3. What to do in case of accidental human exposure
 - consult a physician immediately
 - apply ice or cold pack to injection site
 - Call 1-800-722-0987

Micotil Booklet Label, continued

PRODUCT LABEL PROFILE - AH0230
MICOTIL INJECTION

1

FRONT PANEL BOOKLET LABEL - BOTTLE - 100 mL

Pull here/Tirez ici.
AH 0230

DIN 00857602
Net 100 mL

Pr **Micotil**TM

**Tilmicosin Injection USP
VETERINARY USE ONLY**

Sterile

**Each mL contains 300 mg of tilmicosin
For subcutaneous use in cattle and lambs
only (see pull-out label for important
safety information).**

**Tilmicosine injectable USP
USAGE VÉTÉRINAIRE SEULEMENT**

Sterile

**Chaque mL renferme 300 mg de
tilmicosine
Pour usage par voie sous-cutanée
exclusivement chez le bovin et l'agneau
(voir l'étiquette rabattable pour les
renseignements importants d'innocuité).**

**HUMAN WARNINGS: Not for human use.
Human injection has been associated
with fatalities. Do not use in
automatically powered syringes.
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. Do not apply ice directly to
skin. For emergency medical information
call 1-800-722-0987.**

**SEE NOTE TO PHYSICIAN FOR
ADDITIONAL INFORMATION.**

**MISES EN GARDE – HUMAINS : Ne pas
utiliser chez l'humain. Des décès chez
l'humain ont déjà été associés à l'injection
de Micotil. Ne pas utiliser de seringues
automatiques pour l'administration.
Utiliser avec beaucoup de précaution afin
d'éviter toute auto-injection accidentelle
chez l'humain. En cas d'injection chez
l'humain, consulter immédiatement un
médecin et appliquer de la glace ou une
compresse froide au site d'injection. Ne
pas appliquer de glace directement sur la
peau. Pour les renseignements d'urgence,
composer le 1-800-722-0987.**

**POUR DES RENSEIGNEMENTS
SUPPLÉMENTAIRES, CONSULTER L'AVIS
AU MÉDECIN.**

Expectations of Veterinarians and Suppliers

- Ensure producers are informed regarding safe handling and use recommendations
- Work with clients to define a proper, secure storage location prior to dispensing
- Dispense Micotil only when a valid Veterinarian-Client-Patient Relationship (VCPR) is in place

Proper Drug Use Principles

- Read, understand and follow all label use directions, in particular, observe all caution statements and human warnings
- Consult with your veterinarian to determine which product is most appropriate for your situation



Training Agenda



- SAFE guidelines
- About Micotil
- Administration recommendations
 - Animal restraint
 - Syringe
- Micotil storage recommendations
- Knowledge assessment

Safe Use Principles

- **S**afety for you
- **A**nimal Safety
- **F**ood Chain Safety
- **E**nvironmental Safety



Safety for you

- Keep children and bystanders out of work area
- Properly restrain all animals
- Be aware of uneven or changing walking surfaces
- Use a safety syringe
- Keep needles properly covered until use
- Never walk around with loaded syringes



Safety for you

- Work in a team-
NEVER work alone
- Clearly establish a team leader and roles
- Evaluate the experience of those around you
- Identify an exit route in case of emergency



Animal Safety

- Use adequate facilities for proper animal restraint
 - Squeeze chute
 - Head gate
- Minimize handling stress in accordance with animal behavior
- Adjust your activity to the temperament of each animal



Animal Safety

- If an animal cannot be properly restrained or there is concern about operator skill, consider using alternative treatments





Food Chain Safety

- Use only VDD-approved products
- Follow label directions
 - Dose, route, cautions, warnings, withdrawal times, etc.



Food Chain Safety

- Record all products administered
 - Animal ID, date treated, product used, dosage, route and location of administration, first marketing date to meet withdrawal requirements



Environmental Safety

- Post emergency procedures and contacts
 - Call Rocky Mountain Poison & Drug Center at 1-800-722-0987
- Remove potential hazards in work area
- Repair or remove broken equipment
- Properly dispose of used needles and bottles
- Recycle all injectable syringes and bottle packaging

About Micotil

Each mL contains 300 mg of tilmicosin

DESCRIPTION: Micotil injection is a preconstituted solution of the antibiotic tilmicosin. Each mL contains 300 mg of tilmicosin activity; 25% propylene glycol; phosphoric acid as needed to adjust pH; water for injection, q.s. Tilmicosin is produced semi-synthetically and is a member of the macrolide class of antibiotics.

INDICATIONS: For the treatment of bovine respiratory disease (BRD) associated with *Mannheimia (Pasteurella) haemolytica* and *Pasteurella multocida*.

For the reduction of morbidity associated with bovine respiratory disease (BRD) in feedlot calves, caused by *Mannheimia (Pasteurella) haemolytica* and *Pasteurella multocida*, during the first 30 days in the feedlot, when administered at the time of arrival.

For the treatment of pneumonic pasteurellosis in lambs associated with *Mannheimia (Pasteurella) haemolytica*.



Injection Guidelines

DOSAGE AND ADMINISTRATION: FOR SUBCUTANEOUS USE IN CATTLE. FOR SUBCUTANEOUS USE IN LAMBS GREATER THAN 15 KG BODY WEIGHT ONLY.

Administer a single subcutaneous injection of 10 mg tilmicosin per kg of body weight (1 mL per 30 kg/1.5 mL per 100 lbs.). Do not inject more than 10 mL per injection site.

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.



Injection Guidelines, continued

If no improvement is noted within 48 hours, the diagnosis should be reconfirmed.

NOTE: Swelling at the subcutaneous site of injection may be observed but is transient and usually mild.

CONTRAINDICATIONS: DO NOT ADMINISTER INTRAVENOUSLY. INTRAVENOUS INJECTION IN CATTLE AND LAMBS HAS BEEN FATAL.

DO NOT ADMINISTER TO ANIMALS OTHER THAN CATTLE OR SHEEP. INJECTION OF TILMICOSIN IN SWINE, GOATS AND NON-HUMAN PRIMATES HAS BEEN FATAL. TILMICOSIN MAY BE FATAL IN HORSES AND OTHER EQUIDS.

WARNINGS: Treated cattle must not be slaughtered for use in food for at least 28 days after latest treatment with this drug. Do not use in lactating dairy cattle. Treated sheep must not be slaughtered for use in food for at least 36 days after latest treatment with this drug.



Boxed Warning

HUMAN WARNINGS: Not for human use. Human injection has been associated with fatalities. Do not use in automatically powered syringes. 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. Do not apply ice directly to skin. For emergency medical information call 1-800-722-0987.

NOTE TO 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) within approximately 20 minutes. Dobutamine dose-dependently partially offset the negative inotropic effects induced by Micotil in dogs, but did not have an effect on the increased heart rate caused by Micotil. β -adrenergic antagonists, such as propranolol, exacerbated the negative inotropy of Micotil in dogs. Epinephrine potentiated lethality of Micotil in pigs. **Epinephrine is contraindicated.** This antibiotic persists in tissues for several days.

Elanco

Micotil.

Possible Effects of Accidental Human Injection

- Human injections of Micotil have been associated with fatalities
- Clinical signs of 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

Human-Exposure Actions

If accidental exposure occurs **seek immediate medical attention:**

- **REACH** for and apply ice pack
- **REFERENCE** product label “Note To The Physician” and/or product insert and provide to doctor
- **REMEMBER** to contact Rocky Mountain Poison & Drug Center at 1-800-722-0987



Exercise Caution to Avoid Accidental Self-injection

- Always keep needles properly covered until ready to use
- Carry syringe in proper manner to ensure safe handling
- Handle loaded syringes with care
- Never carry loaded syringes in coat or pockets
- If syringe is broken or damaged in any way, discontinue use immediately and replace
- Exercise caution and care when removing needle from syringe so as to not pierce skin with needle

Administration Recommendations

- Elanco recommends that Micotil be administered only by those individuals who have received safe handling and use training
- Producers should consider designating trained and responsible individual(s) on their animal health team to administer Micotil



Administration Recommendations

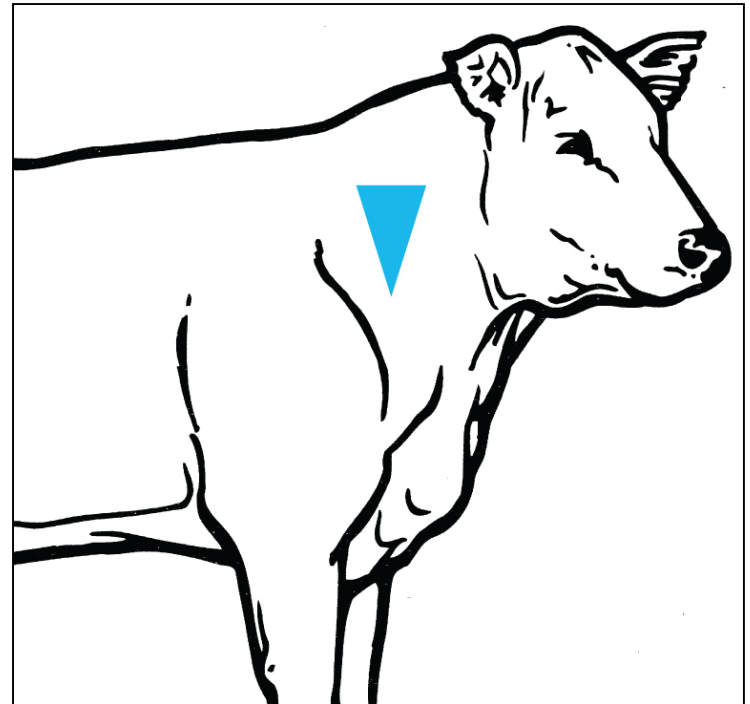
Animal Restraint

- It is recommended that Micotil only be used in situations where animals can be properly restrained
 - Producers should consult their veterinarian for specific restraint recommendations
- Generally, proper animal restraint would include restraint via a squeeze chute, headgate, headlock or similar device



Administration Technique

- Select a 1/2" to 5/8", 18- to 16- gauge needle
- With a single hand on the syringe, insert the needle subcutaneously, at a top-down angle, while avoiding penetration of underlying muscle
- Administer a single subcutaneous dose of 1.5 mL of Micotil per 100 lbs of body weight, in the area noted in the illustration



Administration Technique, continued

- Ensure proper disposal of needles, syringes and used bottles
- Discuss any concerns with your veterinarian



Simcro™ Sekurus™ Syringe

- Elanco recommends use of the Sekurus™ syringe, which features a 2-stage activation process to reduce risk of accidental injection
- Patented self-tenting technology
 - Makes sure operator's hand is not close to injection site
- Two-stage activation
 - To activate, pull the trigger & then push the syringe cone against the animal
 - Both must be performed in order to expose the needle & insert it into the animal
 - Depress the syringe handle to inject Micotil into the animal
 - DO NOT use the opposite hand to tent the skin, use only one hand (the other hand should be kept away from the injection area)



Sekurus Syringe — Use Instructions

- Fill the syringe
 - Prior to attaching the needle, pull the trigger & push the syringe cone back
 - Repeatedly depress the syringe handle until the barrel fills
- Place the needle on the syringe
 - Remove the cap from the needle cover
 - Do not remove the cover from the needle until it is attached to the syringe
 - Use the needle cover to place the needle hub into the syringe
 - Twist the needle clockwise until it locks into place
 - To remove the needle, place the needle cover over the needle and twist in the opposite direction (counterclockwise)

Storage Recommendations

- **Storage of Micotil in a secure location to prevent misuse is recommended. The risk of misuse by humans should be considered when storing, administering & disposing of Micotil**
- Recommended storage method is in a locked cabinet, storage room or a similar secure container, depending on inventory
- Keep full or empty Micotil bottles, used syringes & needles out of the reach of children and the general public



Micotil.

250 mL bottle shroud

- Offers added protection from breakage and during the handling of bottles
- Safe and convenient handling
 - With safety seals on top and bottom, and a built-in hanger
- Recyclable bottle shroud



Educational Tools Available

- Micotil Dose & Administration Poster
 - Bilingual (English & French)
- Dose & Administration Detailer
 - Bilingual (English & French)
- SAFE use guidelines sheet
 - Bilingual (English & French)

Summary

- In the event of a human exposure, **seek immediate medical attention:**
 - REACH for & apply an ice pack
 - REFERENCE product label “Note to the Physician” and/or product insert & provide to doctor
 - REMEMBER to contact Rocky Mountain Poison & Drug Center at 1-800-722-0987

Questions?

Elanco

Micotil[®]

TM

Safe Handling and Use Knowledge Assessment

Quick Test

How should Micotil be administered?

- a. Intramuscular (IM)
- b. Intravenously (IV)
- c. SubQ (SC)

Quick Test

Which action step is not recommended in the event of accidental self-injection?

- a. Seek immediate medical attention
- b. REACH for & apply an ice pack
- c. Go home and rest
- d. REFERENCE product label “Note to the Physician” and/or product insert & provide to doctor
- e. REMEMBER to contact Rocky Mountain Poison & Drug Center at 1-800-722-0987

Quick Test

What is the pre-slaughter withdrawal time for Micotil?

- a. None
- b. 7 days
- c. 28 days
- d. 42 days
- e. 60 days

Quick Test

What is the pre-slaughter withdrawal time for Micotil?

- a. None
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- c. 28 days
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- e. 60 days

Micotil Label

<https://cdmv.cvpsservice.com/product/view/1184024>

ELANCO, Division Eli Lilly Canada Inc. & ELANCO CANADA
LIMITED (successor to Novartis Animal Health Canada Inc.)
RESEARCH PARK CENTRE, 150 RESEARCH LANE, SUITE 120, GUELPH, ON, N1G 4T2
Telephone: 519-821-0277
Order Desk: 800-773-7603
Fax: 519-821-7831
Elanco Canada Limited Customer Service Telephone: 800-387-6325
Elanco Canada Limited Customer Service Fax: 800-827-5782
Website: www.Elanco.ca



Every effort has been made to ensure the accuracy of the information published. However, it remains the responsibility of the readers to familiarize themselves with the product information contained on the Canada product label or package insert.

Tilmicosin Injection USP

DIN 00857602

AH 0230

Each mL contains 300 mg of tilmicosin

VETERINARY USE ONLY

Sterile

For subcutaneous use in cattle and lambs only (see pull-out label for important safety information).

Active Ingredient: tilmicosin

Non-medicinal Ingredients: Propylene glycol 25% w/v.

DESCRIPTION: Micotil injection is a preconstituted solution of the antibiotic tilmicosin. Each mL contains 300 mg of tilmicosin activity; 25% propylene glycol; phosphoric acid as needed to adjust pH; water for injection, q.s. Tilmicosin is produced semi-synthetically and is a member of the macrolide class of antibiotics.

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NOTE: Swelling at the subcutaneous site of injection may be observed but is transient and usually mild.

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WARNINGS: Treated cattle must not be slaughtered for use in food for at least 28 days after latest treatment with this drug. Do not use in lactating dairy cattle.

Treated sheep must not be slaughtered for use in food for at least 36 days after latest treatment with this drug.

HUMAN WARNINGS: Not for human use. Human injection has been associated with fatalities. Do not use in automatically powered syringes. 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. Do not apply ice directly to skin. For emergency medical information call 1-800-722-0987.

KEEP OUT OF REACH OF CHILDREN. AVOID CONTACT WITH EYES.

NOTE TO 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) within approximately 20 minutes. Dobutamine dose-dependently partially offset the negative inotropic effects induced by Micotil in dogs, but did not have an effect on the increased heart rate caused by Micotil. β -adrenergic antagonists, such as propranolol, exacerbated the negative inotropy of Micotil in dogs. Epinephrine potentiated lethality of Micotil in pigs. **Epinephrine is contraindicated.** 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. In sheep: dyspnea and death.

For technical assistance or to report suspected adverse drug events, contact Elanco, Division Eli Lilly Canada Inc. at 1-800-265-5475.

ACTIVITY: Micotil has an *in vitro* antibacterial spectrum that is predominantly Gram positive with activity against certain Gram negative microorganisms. Activity against several mycoplasma species has also been detected.

In addition to its direct antibacterial action, tilmicosin may exert an anti-inflammatory effect in the lung by increasing neutrophil apoptosis and reducing the release of pro-inflammatory mediators. However, the clinical significance of this effect is unknown.

In clinical trials, BRD treatment success with **Micotil** was usually characterized by rapid reduction in body temperatures, less severity of clinical signs, better weight gains and reduced mortality.

TOXICOLOGY: The cardiovascular system appears to be the target of toxicity in laboratory animals and domestic livestock administered **Micotil** 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 injection subcutaneously, the acute median lethal dose (MLD) of tilmicosin in mice is 97 mg of activity per kg and in rats is 185 mg/kg of body weight. Given orally, the MLD of tilmicosin is 800 mg/kg and 2250 mg/kg 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 within approximately 20 minutes. Dobutamine dose-dependently partially offset the negative inotropic effects induced by Micotil in dogs, but did not have an effect on the increased heart rate caused by Micotil. β -adrenergic antagonists, such as propranolol, exacerbated the negative inotropy of Micotil in dogs.

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

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

In cattle, subcutaneous doses of Micotil at 10, 30 and 50 mg/kg of body weight, each injected at 72 hour intervals for three times, did not cause any deaths. As expected, edema at the site of injection was noted. In cattle, the only lesion observed at necropsy was minimal myocardial necrosis in the 50 mg/kg Micotil group. Subcutaneous doses of Micotil

at 150 mg/kg injected at 72-hour intervals resulted in deaths. 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 Micotil at 5 mg/kg of body weight.

In lambs, single subcutaneous doses of Micotil up to 150 mg/kg of body weight did not cause death. Deaths of lambs have been observed with a single intravenous dose of Micotil at 7.5 mg/kg body weight.

PHARMACOKINETICS: A single subcutaneous injection of **Micotil** at 10 mg/kg of body weight 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 (Pasteurella) haemolytica* for at least three days following the single injection. Serum tilmicosin levels are a poor indicator of total body tilmicosin. The lung/serum tilmicosin ratio in favour of lung tissue appeared to equilibrate by three 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.

STORAGE: Store at 30° C (86° F) or below. Protect from direct sunlight.

HOW SUPPLIED: Micotil is supplied in multidose amber bottles containing 300 mg of tilmicosin activity per mL.

MANUFACTURED BY: Elanco, Division Eli Lilly Canada Inc., 150 Research Lane, Suite 120, Guelph, ON N1G 4T2, Canada

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CPN: 1184024.5



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