Common Name: MICOTIL 300

Chemical Name: Tylosin, 4A-O-de(2,6-dideoxy-3-C-methyl-a-L-ribo-hexopyranosyl)-20-deoxo-20-[(3R,5S)-3,5-dimethyl-1-piperidinyl]-, phosphate (1:1) (salt)

Synonym(s): Tilmicosin Formulation; Tilmicosin Phosphate Formulation

Trademarks(s): Micotil; Micotil 300

Lilly Item Code(s): AH0230

NOT FOR HUMAN USE!

See attached glossary for abbreviations.

Section 2 - Composition / Information on Ingredients

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS</th>
<th>Concentration %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tilmicosin Phosphate</td>
<td>137330-13-3</td>
<td>30</td>
</tr>
<tr>
<td>Inert Ingredients</td>
<td>NA</td>
<td>70</td>
</tr>
</tbody>
</table>

Exposure Guidelines:
Tilmicosin - LEG <100 micrograms/m3 TWA for 12 hours.

Section 3 - Hazards Identification

Appearance: Clear yellow to amber-colored solution

Physical State: Liquid
Odor: Faint characteristic sweet

Emergency Overview

Emergency Overview Effective Date: 09-Dec-2003

Lilly Laboratory Labeling Codes:
Health 1 Fire 1 Reactivity 0 Special A

Primary Physical and Health Hazards: Severe Allergen. Heart Effects.

Caution Statement: MICOTIL 300 contains tilmicosin phosphate and is classified as a severe allergen because repeated unprotected exposures are likely to cause allergic reactions. Effects of exposure may include changes in heart rate/rhythm and heart tissue changes. Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Routes of Entry: Inhalation and skin contact.

Effects of Overexposure: Micotil 300 - No allergic reactions in a manufacturing setting have been reported. Compounds of similar structure have been reported to cause transient alterations in heart rate. Clinical signs from accidental human injection 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. Injection of this drug in humans has been associated with fatalities.

Tilmicosin phosphate powder - Allergic reactions in a manufacturing setting have been reported. Allergy symptoms may include skin rash, watery eyes, shortness of breath, nasal congestion, choking, coughing, and wheezing.

NOT INTENDED FOR HUMAN USE.

Medical Conditions Aggravated by Exposure: Sensitivity to tilmicosin and/or tylosin.

Carcinogenicity: No carcinogenicity data found. Not listed by IARC, NTP, ACGIH, or OSHA.

Section 4 - First Aid Measures

NOT FOR HUMAN USE!

Injection of MICOTIL in humans has been associated with fatalities. Keep out of the reach of children. 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
the injection site while avoiding direct contact with the skin. Emergency medical telephone numbers are 1-800-722-0987 or 1-317-276-2000. Avoid contact with eyes.

**Eyes:** Hold eyes open and flush with a steady, gentle stream of water for 15 minutes. See an ophthalmologist (eye doctor) or other physician immediately.

**Skin:** Remove contaminated clothing and clean before reuse. Wash all exposed areas of skin with plenty of soap and water.

**Inhalation:** Move individual to fresh air. Get medical attention if breathing difficulty occurs. If not breathing, provide artificial respiration assistance (mouth-to-mouth) and call a physician immediately.

**Ingestion:** Call a physician or poison control center immediately. If available, administer activated charcoal (6-8 heaping teaspoons) with two to three glasses of water OR give 1-2 tablespoons syrup of ipecac and drink one or two glasses of water to induce vomiting. Do not give anything by mouth to an unconscious person. Immediately transport to a medical care facility and see a physician.

**Notes 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). Dobutamine partially offset the negative inotropic effects induced by Micotil in dogs. Beta-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.

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**Section 5 - Fire Fighting Measures**

**Auto Ignition:** 418 C (784 F)
**Flash Point:** Not applicable
**UEL:** Not established
**LEL:** Not flammable at temperatures up to 100 C (212 F). No ignition up to 20.0% volume in air.

**Extinguishing Media:** Use water, carbon dioxide, dry chemical, foam, or Halon.

**Unusual Fire and Explosion Hazards:** None known.

**Hazardous Combustion Products:** May emit toxic fumes when exposed to heat or fire.

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**Section 6 - Accidental Release Measures**

**Spills:** Prevent further migration into the environment. Use absorbent/adsorbent material to solidify liquids. Sweep up or vacuum. Wear protective equipment, including eye protection, to avoid exposure (see Section 8 for specific handling precautions). Large spills due to traffic accidents, etc., should be reported immediately to CHEMTREC and Elanco Animal Health for assistance. Prevent spilled material from flowing onto adjacent land or into streams, ponds, or lakes.

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**Section 7 - Handling and Storage**
Storage Conditions: Store at 30 C (86 F) or below. Protect from direct sunlight. Product should not be used after the date printed on the container. A dating of 36 months is noted on the container.

Additional Information: Human Warnings: Not for human use. Injection of Micotil 300 in humans has been associated with fatalities. Keep out of the reach of children. Do not use in automatically powered syringes. Exercise extreme caution to avoid accidental self-injection. In case of human injection, consult a physician immediately. Emergency medical telephone numbers are 1-800-722-0987 (Rocky Mountain Poison Control Center) or (317) 276-2000 (Eli Lilly and Company). Avoid contact with eyes.

Section 8 - Exposure Controls / Personal Protection

See Section 2 for Exposure Guideline information.

Respiratory Protection: Use an approved respirator.

Eye Protection: Chemical goggles and/or face shield.

Ventilation: Laboratory fume hood or local exhaust ventilation.

Other Protective Equipment: In a manufacturing setting, wear chemical-resistant gloves and body covering to minimize skin contact. If handled in a ventilated enclosure, as in a laboratory setting, respirator and goggles or face shield may not be required. Safety glasses are always required.

Additional Exposure Precautions: Under normal use and handling conditions, wear goggles to protect eyes and wear impermeable gloves and protective equipment to avoid direct contact with skin. Wash thoroughly with soap and water after handling.

Section 9 - Physical and Chemical Properties

Appearance: Clear yellow to amber-colored solution
Odor: Faint characteristic sweet
Boiling Point: No applicable information found
Melting Point: Not applicable
Specific Gravity: No applicable information found
pH: 5.5 to 6.5 (aqueous 50/50)
Evaporation Rate: No applicable information found
Water Solubility: Soluble
Vapor Density: No applicable information found
Vapor Pressure: No applicable information found

Section 10 - Stability and Reactivity

Stability: Stable at normal temperatures and pressures.

Incompatibility: May react with strong oxidizing agents (e.g., peroxides, permanganates, nitric acid, etc.).
Hazardous Decomposition: May emit toxic fumes when heated to decomposition.

Hazardous Polymerization: Will not occur.

Section 11 - Toxicological Information

Acute Exposure
Data for tilmicosin phosphate and Micotil 300 are reported as indicated.

Oral:
Tilmicosin phosphate - Rat (fasted), median lethal dose 855 mg/kg, reduced activity, incoordination, drooping eyelids, soft stools, whole body thin, distended abdomen.

Skin:
Micotil 300 - Rabbit, 0.5 ml/kg, no deaths or toxicity.

Inhalation:
Micotil 300 - Rat, 2750 mg/m3 for 4 hours, no deaths, reduced activity, labored breathing, blood in urine.

Subcutaneous:
Micotil 300 - Rat, median lethal dose 318 mg/kg, reduced activity, leg weakness, hunched posture. Tilmicosin phosphate - Rat, median lethal dose 185 mg/kg, coma, lethargy, incoordination, reduced activity.

Intramuscular:
Micotil 300 - Monkey, a single dose of 10 mg/kg caused no signs of toxicity. A single dose of 20 mg/kg caused vomiting, and 30 mg/kg caused the death of the only monkey tested. Swine, intramuscular injection of 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.

Skin Contact:
Micotil 300 - Rabbit, slight irritant

Eye Contact:
Micotil 300 - Rabbit, slight irritant

Chronic Exposure
No data available for mixture or formulation. Data for ingredient(s) or related material(s) are presented.

Target Organ Effects:
Tilmicosin phosphate - The heart is the target of toxicity in laboratory and domestic animals given Micotil®300 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.

Other Effects:
Tilmicosin phosphate - Increased adrenal and kidney weights, increased cell size in adrenal cortex, mucosal edema of the gallbladder, and subretinal fluid accumulation. Decreased food consumption and body weight gains, slightly decreased urine pH, occult blood in urine, increased serum alanine transaminase.

**Reproduction:**
Tilmicosin phosphate - Slight increase in offspring mortality at maternally toxic doses.

**Sensitization:**
Tilmicosin phosphate - Guinea pig, not a contact sensitizer.

**Mutagenicity:**
Tilmicosin - Not mutagenic in bacterial or mammalian cells.

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**Section 12 - Ecological Information**

No environmental data for the mixture or formulation. The environmental information for ingredient(s) or related material(s) are presented.

**Ecotoxicity Data:**
Tilmicosin
Rainbow trout 96-hour median lethal concentration: 851 mg/L
Bluegill 96-hour median lethal concentration: 716 mg/L
Daphnia magna 48-hour median effective concentration: 57.3 mg/L
Bobwhite 5-day dietary median lethal concentration: > 4820 ppm
Mallard 5-day dietary median lethal concentration: > 4710 ppm
Earthworm 28-day median lethal concentration: > 918 mg/Kg
Green algae (S. capricornutum) median effective concentration: 0.354 mg/L (average specific growth rate)
Plant growth in soil for most species unaffected at 100 mg/L
Microorganisms:
- fungus (Chaetomium globosum): MIC > 1000 mg/L
- mold (Aspergillus flavus): MIC > 1000 mg/L
- soil bacteria (Comamonas acidovorans): MIC = 250 mg/L
- N-fixing bact. (Azotobacter chroococcum): MIC = 5 mg/L
- blue-green algae (Nostoc sp.): MIC = 0.5 mg/L

**Environmental Fate:**
Tilmicosin
Log Kow: <1, <1, 2.6 (pH 5, 7, 9)
Adsorption coefficients (K): 129, 181, 318 (sandy loam, loam, clay loam)
Water solubility (g/L): 566, 7.7 (pH 7, 9)
Photolysis half-life (hours): 0.84, 0.82, 0.82 (pH 5, 7, 9)
Photolysis rate constant (1/hours): 0.83, 0.84, 0.84 (pH 5, 7, 9)
Hydrolysis half-life (days): >= 365, >= 365, 156 (pH 5, 7, 9)
Hydrolysis rate constant (1/hours): 0.0001853 (pH 9)
Aerobic biodegradation: none measured after 64 days (sandy loam, loam, clay loam)
Anaerobic biodegradation: none measured after 73 days
Decline in loam soil: 45.9% after 52 weeks
Decline in clay loam soil: none after 52 weeks

Environmental Summary:
Tilmicosin - Practically nontoxic to fish, birds, earthworms, fungus, molds, soil bacteria, and most plants. Slightly toxic to aquatic invertebrates. Moderately toxic to nitrogen-fixing bacteria. Highly toxic to green algae and blue-green algae. No volatility expected. Low potential to bioconcentrate in aquatic organisms. Low mobility in soil. Persistent in the soil environment. Persistence in the aquatic environment not expected due to rapid photolysis.

Lilly Aquatic Exposure Guideline (LAEG):
Tilmicosin
LAEG for Drinking Water: 280 micrograms/L
LAEG for Chronic Exposure of Aquatic Organisms: 54 micrograms/L
LAEG for Acute Exposure of Aquatic Organisms: 354 micrograms/L

Section 13 - Disposal Considerations

Waste Disposal: Dispose of any cleanup materials and waste residue according to all applicable laws and regulations.

Container Disposal: No special package disposal required.

Section 14 - Transport Information

Regulatory Organizations:

DOT: Not Regulated

ICAO/IATA: Not Regulated

IMO: Not Regulated

Section 15 - Regulatory Information

Below is selected regulatory information chosen primarily for possible Elanco Animal Health usage. This section is not a complete analysis or reference to all applicable regulatory information. Please consider all applicable laws and regulations for your country/state.

U.S. Regulations
Tilmicosin phosphate
TSCA - No
CERCLA - Not on this list
SARA 302 - Not on this list
SARA 313 - Not on this list
OSHA Substance Specific - No
NADA Number: 140-929

EU Regulations

EC Classification
Xn (Harmful)
N (Dangerous for the Environment)

Risk Phrases
R 42/43 - May cause sensitization by inhalation and skin contact.
R 50 - Very toxic to aquatic organisms.

Safety Phrases
S 36/37 - Wear suitable protective clothing and gloves.
S 61 - Avoid release to the environment. Refer to special instructions/Safety data sheets.

Section 16 - Other Information

MSDS Sections Revised: Sections 3, 4, 11, and 16.

NOT FOR HUMAN USE! For accidental human exposure, call 1-800-722-0987. Refer to Human Warnings and Note to Physician on product label and Client Information Sheet dispensed with each bottle for further information.

As of the date of issuance, we are providing available information relevant to the handling of this material in the workplace. All information contained herein is offered with the good faith belief that it is accurate. THIS MATERIAL SAFETY DATA SHEET SHALL NOT BE DEEMED TO CREATE ANY WARRANTY OF ANY KIND (INCLUDING WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE). In the event of an adverse incident associated with this material, this safety data sheet is not intended to be a substitute for consultation with appropriately trained personnel. Nor is this safety data sheet intended to be a substitute for product literature which may accompany the finished product.

For additional information contact:
ELANCO Animal Health
1-800-428-4441
1-317-276-2000

GLOSSARY:
ACGIH = American Conference of Governmental Industrial Hygienists
AIHA = American Industrial Hygiene Association
BEI = Biological Exposure Index
CAS Number = Chemical Abstract Service Registry Number
CERCLA = Comprehensive Environmental Response Compensation and Liability Act (of 1980)
CHAN = Chemical Hazard Alert Notice
CHEMTREC = Chemical Transportation Emergency Center
DOT = Department of Transportation
EC = European Community
EINECS = European Inventory of Existing Chemical Substances
ELINCS = European List of New Chemical Substances
EPA = Environmental Protection Agency
HEPA = High Efficiency Particulate Air (Filter)
IARC = International Agency for Research on Cancer
ICAO/IATA = International Civil Aviation Organization/International Air Transport Association
IEG = Lilly Interim Exposure Guideline
IMO = International Maritime Organization
Kow = Octanol/Water Partition Coefficient
LEG = Lilly Exposure Guideline
LEL = Lower Explosive Limit
MSDS = Material Safety Data Sheet
MSHA = Mine Safety and Health Administration
NA = Not Applicable, except in Section 14 where NA = North America
NADA = New Animal Drug Application
NAIF = No Applicable Information Found
NCI = National Cancer Institute
NIOSH = National Institute for Occupational Safety and Health
NOS = Not Otherwise Specified
NTP = National Toxicology Program
OSHA = Occupational Safety and Health Administration
PEL = Permissible Exposure Limit (OSHA)
RCRA = Resource Conservation and Recovery Act
RQ = Reportable Quantity
RTECS = Registry of Toxic Effects of Chemical Substances
SARA = Superfund Amendments and Reauthorization Act
STEG = Lilly Short Term Exposure Guideline
STEL = Short Term Exposure Limit
TLV = Threshold Limit Value (ACGIH)
TPQ = Threshold Planning Quantity
TSCA = Toxic Substances Control Act
TWA = Time Weighted Average/8 Hours Unless Otherwise Noted
UEL = Upper Explosive Limit
UN = United Nations
WEEL = Workplace Environmental Exposure Level (AIHA)