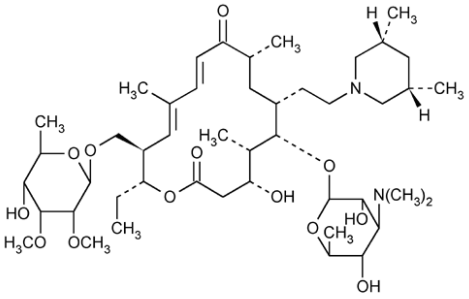
1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY /UNDERTAKING

1.1. PRODUCT IDENTIFIER

Trade name:	TILMOVET® 250 mg/ml Concentrate for Oral Solution
Common name:	Tilmicosin.
International non- proprietary name:	Tilmicosin
Chemical name:	Tylosin, 4^{A}-*O*-de(2,6-dideoxy-3-*C*-methyl-α–L-*ribo*-hexopyranosyl)-20-deoxo-20-(3,5-dimethyl-1-piperidinyl)-, 20(*cis*)-. 4^{A}-*O*-de(2,6-Dideoxy-3-*C*-methyl-α–L-*ribo*-hexopyranosyl)-20-deoxo-20-(*cis*-3,5-dimethylpiperidino)-tylosin.
Chemical group:	Antimicrobials for systemic use, macrolides
Molecular formula:	$C_{46}H_{80}N_2O_{13}$
Structural formula	
Molecular weight:	869.13.

1.2. RELEVANT IDENTIFIED USES OF THE SUBSTANCE OR MIXTURE AND USES ADVISED AGAINST

Identified uses:	Veterinary medicinal product.
Uses advised against:	None known.

1.3. DETAILS OF THE SUPPLIER OF THE SAFETY DATA SHEET

Holder of Authorisation for EU:
Huvepharma N.V.
Uitbreidingstraat 80
2600 Antwerp
Belgium, www.huvepharma.com
Tel +32-3-288-1849
Fax +32-3-289-7845
E-mail: customerservice@huvepharma.com

Manufacturer:
BIOVET Joint Stock Company
39, Petar Rakov St.
4550 Peshtera - Bulgaria
Tel.: +359 350 65619
Fax: +359 350 65636
E-mail: **biovet@biovet.com**

1.4. EMERGENCY TELEPHONE NUMBERS

+359 887 939420.

2. HAZARDS IDENTIFICATION

2.1. CLASSIFICATION OF THE SUBSTANCE

This preparation has been assessed and/or tested for its physical, health and environmental hazards and the following classification applies.

Health hazards

Skin corrosion/irritation	Category 2	H315: Causes skin irritation.
Serious eye damage/eye irritation	Category 2	H319: Causes serious eye irritation.

2.2. LABEL ELEMENTS

Labeling according to Regulation (EC) No 1272/2008 of December 2008 as amended

Signal words

Warning

Hazard statements:
H315: Causes skin irritation.
H319: Causes serious eye irritation.

Precautionary Statements – Prevention
P264 Wash hands thoroughly after handling.
P280 Wear protective gloves/protective clothing/eye protection/face protection.

Precautionary Statements - Response
P302 + P352 IF ON SKIN: Wash with plenty of soap and water.
P321 Specific treatment (see heading "After contact with skin" in item 4).
P332 + P313 If skin irritation occurs: Get medical advice/attention.
P362 + P364 Take off contaminated clothing and wash it before reuse.
P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P337 + P313 If eye irritation persists: Get medical advice/attention.

2.3. OTHER HAZARDS

None.

3. COMPOSITION/INFORMATION ON INGREDIENTS

3.2. MIXTURES

General information :

Chemical Name	% content	CAS No/EC no	REACH registration No	INDEX No	CLP classification
Tilmicosin	25	108050-54-0	-	-	H317 H319 H334 H400
Phosphoric acid (concentrated)	confidential	7664-38-2	-	-	H290 H314
Disodium edetate	< 10	6381-92-6	-	-	H302 H315 H319 H335
Propyl gallate	< 10	121-79-9	-	-	H302 H317

Composition comments:
The full text for H-phrases is displayed in section 16.
Excipients may include: Purified water.

4. FIRST AID MEASURES

4.1. DESCRIPTION OF FIRST AID MEASURES

General: People with known hypersensitivity to macrolides should avoid contact with the veterinary medicinal product.
Contaminated clothing must be taken off.
The person must receive immediate medical attention.

Ingestion: If swallowed, wash out mouth with water. Never give anything by mouth to an unconscious person. Get medical attention.

Inhalation: Safely remove victim to fresh air. If not breathing, institute cardiopulmonary resuscitation (CPR). If breathing is difficult, ensure clear airway and give oxygen. Get medical attention.

Eyes exposure:	Flush immediately with large amounts of water for at least 15 minutes. Eyelids should be held away from the eyeball to ensure thorough rinsing. Get medical attention if irritation persists.
Skin exposure:	Wash area thoroughly with soap and water. Remove and wash contaminated clothing. Get medical attention if irritation persists.
Precautions to be considered:	In case of hypersensitivity to the substance, avoid direct contact.

4.2. MOST IMPORTANT SYMPTOMS AND EFFECTS, BOTH ACUTE AND DELAYED

NDA.

4.3. INDICATION OF ANY IMMEDIATE MEDICAL ATTENTION AND SPECIAL TREATMENT NEEDED

NDA.

5. FIREFIGHTING MEASURES

5.1. EXTINGUISHING MEDIA

Water spray, carbon dioxide, dry chemical powder or appropriate foam. Use extinguishing media suitable for surrounding fire.

5.2. SPECIAL HAZARDS ARISING FROM THE SUBSTANCE OR MIXTURE

May emit toxic fumes under fire conditions. They are: carbon monoxide, carbon dioxide, nitrogen oxides, and sulphur oxides.

5.3. ADVICE FOR FIREFIGHTERS

As with all fires, evacuate personnel to save area. Fire fighters should use self-contained breathing equipment and protective clothing.

6. ACCIDENTAL RELEASE MEASURES

6.1. PERSONAL PRECAUTIONS, PROTECTIVE EQUIPMENT AND EMERGENCY PROCEDURES

Persons with a history of allergies, contact dermatitis, chronic rashes or respiratory problems should use special precautions to avoid skin contact or exposure to dust.
Wear suitable protective equipment and a self-contained breathing apparatus.

6.2. ENVIRONMENTAL PRECAUTIONS

Prevent spilled material from flowing onto adjacent land or into streams, ponds or lakes.

6.3. METHODS AND MATERIAL FOR CONTAINMENT AND CLEANING UP

Carefully wipe the spillage and discard. Place material in a dry container and cover. Remove from the area. Flush spill area with water.

6.4. REFERENCE TO OTHER SECTIONS

Information regarding exposure controls/personal protection and disposal considerations can be found in section 8 and 13.

7. HANDLING AND STORAGE

7.1. PRECAUTIONS FOR SAFE HANDLING

Use personal protective device while handling the product (see heading 8.2). The use of local exhaust hood and general exchange in the facility is recommended (see heading 8.2).

7.2. CONDITIONS FOR SAFE STORAGE INCLUDING ANY INCOMPATIBILITIES

Do not store above 30°C.
Store in the original container.
Store in a dry place.

7.3. SPECIFIC END USE(S)

As concentrate for oral solution for use in drinkign water or milk replacer.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. CONTROL PARAMETERS

Recommended monitoring procedures:	None.
Occupational Exposure Limits:	None.
Biological Limit Values:	No biological exposure limits noted for the ingredients.
Derived no-effect level (DNEL):	Not available.
Predicted no-effect concentrations (PNECs):	Not available.

8.2. EXPOSURE CONTROLS

Ventilation:	Local exhaust hood:	Recommended.
	General exchange:	Recommended.

Occupational exposure controls
People with known hypersensitivity to tilmicosin should avoid contact with the product.
The veterinary medicinal product may cause irritation or sensitisation by skin contact.
Avoid skin and ocular contact.
Wear protective gloves and protective clothes when handling the veterinary medicinal product.
In case of contact with skin or eyes, rinse abundantly with fresh water.
If irritation persists and in case of incidental ingestion, seek immediately medical advice or call a poison center (dangers linked to disturbances in cardiac conduction).
Wash hands after use.

9. PHYSICAL AND CHEMICAL PROPERTIES

9.1. INFORMATION ON BASIC PHYSICAL AND CHEMICAL PROPERTIES

a) Appearance:	A clear yellow to amber solution.
b) Odour:	Characteristic.
c) Odour threshold:	NDA
d) pH:	4.0 - 5.0
e) Melting point/freezing point:	NDA
f) Initial boiling point and boiling range:	NDA
g) Flash point:	NDA
h) Evaporation rate:	NDA
i) Flammability (solid, gas):	NDA
j) Upper/lower flammability or explosive limits:	NDA
k) Vapour pressure:	NDA
l) Vapour density:	NDA
m) Relative density:	NDA
n) Solubility:	Tilmicosin - slightly soluble in water; slightly soluble in n-hexane; soluble in dilute solutions of mineral acids.
o) Partition coefficient n-octanol/water:	Tilmicosin - from -2.5 (pH 5) to 2.6 (pH 9).
p) Auto-ignition temperature:	Tilmicosin - 280°C (dust layer).
q) Decomposition temperature:	NDA
r) Viscosity:	NDA
s) Explosive properties:	NDA
t) Oxidising properties:	NDA

9.2. OTHER INFORMATION

pK_a: pK_a' (66 % DMF):	Tilmicosin - 7.4, 8.5.
Optical rotation:	Tilmicosin - $[\alpha]_D^{23}$ +12.75° (c = 0.010004 in $CHCl_3$, 5 cm).
Density, g/cm^3	1.078 - 1.084

10. STABILITY AND REACTIVITY

10.1. REACTIVITY

TILMOVET® 250 mg/ml Concentrate for Oral Solution is a non-reactive product.

10.2. CHEMICAL STABILITY

TILMOVET® 250 mg/ml Concentrate for Oral Solution is a stable product.

10.3. POSSIBILITY OF HAZARDOUS REACTIONS

NDA.

10.4. CONDITIONS TO AVOID

Moisture.

10.5. INCOMPATIBLE MATERIALS

Strong oxidising agents.

10.6. HAZARDOUS DECOMPOSITION PRODUCTS

Carbon monoxide, carbon dioxide, nitrogen oxides, sulphur oxides.

11. TOXICOLOGICAL INFORMATION

11.1. INFORMATION ON TOXICOLOGICAL EFFECTS

a) acute toxicity:

Mixture		**Species**	**Test results**
Tilmovet 250 mg/ml Oral Solution (CAS N.A.)	Acute LD_{50} p.o.	Rat	832.5 mg/kg b.w.
Components		**Species**	**Test results**
Tilmicosin (CAS 108050-54-0)	Acute LD_{50} p.o.	Rat	2200 mg/kg b.w.
	Acute LD_{50} s.c.	Rat	212 mg/kg b.w.
	Acute LD_{50} s.c.	Mouse	97 mg/kg b.w. (male) 109 mg/kg b.w. (female)
	Acute LC_{50} inhalation	Rat	560 mg/m^3 (1 hour)
	Acute LD_{50} dermal	Rabbit	> 5000 mg/kg b.w.
Phosphoric acid, concentrated (CAS 7664-38-2)	Acute, Oral LD_{50}	Rat	1.53 g/kg b.w.
	Acute LD_{50} dermal	Rabbit	2.74 g/kg
Propyl Gallate (CAS 121-79-9)	Acute, Oral LD_{50}	Cat	0.4 g/kg b.w.
	Acute, Oral LD_{50}	Mouse	1.7 g/kg b.w.
	Acute, Oral LD_{50}	Rat	2.1 g/kg b.w.
	Acute, i.p. LD_{50}	Rat	0.38 g/kg b.w.
Disodium Edetate (CAS 6381-92-6)	Acute, i.p. LD_{50}	Mouse	0.26 g/kg b.w.
	Acute, i.v. LD_{50}	Mouse	0.056 g/kg b.w.
	Acute, o.p. LD_{50}	Mouse	2.05 g/kg b.w.
	Acute, i.v. LD_{50}	Rabbit	0.047 g/kg b.w.
	Acute, o.p. LD_{50}	Rabbit	2.3 g/kg b.w.
	Acute, o.p. LD_{50}	Rat	2.0 g/kg b.w.

b) skin corrosion/irritation: Tilmicosin - Rabbit – slight irritant effect

c) serious eye damage/irritation: Tilmicosin - Rabbit – causes serious eye irritation

d) respiratory or skin sensitization: Tilmicosin - May cause allergy or asthma symptoms or breathing difficulties if inhaled.
Tilmicosin - Guinea pig – does not cause skin sensitisation.

e) germ cell mutagenicity (Tilmicosin)

Reverse mutation	*Salmonella*	Negative
Reverse mutation	*Escherichia coli*	Negative
Forward mutation	Mouse lymphoma cells	Negative
Forward mutation	Chinese hamster ovary cells	Negative
Unscheduled DNA synthesis assay	Primary cultures of rat hepatocytes	Negative
Sister chromatid exchange assay	Chinese hamster bone marrow	Negative
Chromosome abberations	Rat bone marrow	Negative

f) carcinogenicity (Tilmicosin):

1 Year	Rat	Oral	Effects on heart (tachycardia and dilatation) and kidneys (nephrosis) and relative weight of organs (heart, liver, kidney)
1 Year	Dog	Oral	4 mg/kg b.w., NOEL

g) reproductive toxicity (Tilmicosin):

Reproductive toxicity

Rat, oral	2-generation	10 mg/kg b.w., NOEL	No treatment related effects observed

Teratogenicity

Rat, Oral	10 mg/kg b.w., NOEL	No effects observed

h) STOT-single exposure: NDA

i) STOT-repeated exposure: NDA

j) aspiration hazard: NDA

12. ECOLOGICAL INFORMATION

12.1. TOXICITY

- 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.

Conclusion: 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.

12.2. PERSISTENCE AND DEGRADABILITY

- 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.

Conclusion: 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. Therefore, Tilmicosin does not meet the criteria for a “persistent” compound.

12.3. BIOACCUMULATIVE POTENTIAL

Tilmicosin does not meet the criteria for a "bioaccumulative" compound.

12.4. MOBILITY IN SOIL

Tilmicosin has low mobility in soil.

12.5. RESULTS OF PBT AND VPVB ASSESSMENT

Tilmicosin is not classified as a PBT or vPvB substance.

12.6. OTHER ADVERSE EFFECTS

No other adverse environmental effects (e.g. ozone depletion, photochemical ozone creation potential, endocrine disruption, global warming potential) are expected from this component.

13. DISPOSAL CONSIDERATIONS

13.1. WASTE TREATMENT METHODS

Dispose of contents/container in accordance with local/regional/national/international regulations.

14. TRANSPORT INFORMATION

14.1. UN NUMBER

Not applicable as this product is not regulated by IMDG/IMO, ADR/RID, IATA/ICAO.

14.2. UN PROPER SHIPPING NAME

Not applicable as this product is not regulated by IMDG/IMO, ADR/RID, IATA/ICAO.

14.3. TRANSPORT HAZARD CLASS(ES)

Not applicable as this product is not regulated by IMDG/IMO, ADR/RID, IATA/ICAO.

14.4. PACKING GROUP

Not applicable as this product is not regulated by IMDG/IMO, ADR/RID, IATA/ICAO.

14.5. ENVIRONMENTAL HAZARDS

Not applicable as this product is not regulated by IMDG/IMO, ADR/RID, IATA/ICAO.

14.6. SPECIAL PRECAUTIONS FOR USER

Not applicable as this product is not regulated by IMDG/IMO, ADR/RID, IATA/ICAO.

14.7. TRANSPORT IN BULK ACCORDING TO ANNEX II OF MARPOL73/78 AND THE IBC CODE

Not applicable as this product is not regulated by IMDG/IMO, ADR/RID, IATA/ICAO.

15. REGULATORY INFORMATION

15.1. SAFETY, HEALTH AND ENVIRONMENTAL REGULATIONS/LEGISLATION SPECIFIC FOR THE SUBSTANCE

EU regulations

- **Regulation (EC) No. 1005/2009 on substances that deplete the ozone layer, Annex I**
  Not listed.
- **Regulation (EC) No. 1005/2009 on substances that deplete the ozone layer, Annex II**
  Not listed.
- **Regulation (EC) No. 850/2004 On persistent organic pollutants, Annex I as amended**
  Not listed.
- **Regulation (EC) No. 1907/2006, REACH Article 59(1) Candidate List as currently published by ECHA**
  Not listed.

Authorisations

- **Regulation (EC) No. 1907/2006, REACH Annex XIV Substances subject to authorization, as amended**
  Not listed.

Restrictions on use

- **Regulation (EC) No. 1907/2006, REACH Annex XVII Substances subject to restriction on marketing and use as amended**
  Not listed.
- **Directive 2004/37/EC: on the protection of workers from the risks related to exposure to carcinogens and mutagens at work**
  Not listed.

Other EU regulations

- **Directive 96/82/EC (Seveso II) on the control of major-accident hazards involving dangerous substances**
  Not listed.
- **Directive 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work**
  Not listed.

Other regulations

- The product is classified and labelled in accordance with EC directives or respective national laws.
- This Safety Data Sheet complies with the requirements of Regulation (EC) No 1907/2006.

National regulations

- Young people under 18 years old are not allowed to work with this product according to the EU Directive 94/33/EC on the protection of young people at work.

15.2. CHEMICAL SAFETY ASSESSMENT

A chemical safety assessment according to REACH-regulation has not been carried out.

16. OTHER INFORMATION

The data and information reported in this Safety Data Sheet are based on information and studies made with TILMOVET® 250 mg/ml Concentrate for Oral Solution and Tilmicosin, and are only a guide for the user. They respect the actual level of the scientific and technical state of the art. In any case they cannot involve a responsibility of HUVEPHARMA if they are not respected, in particular for the aspects not considered.

LIST OF ABBREVIATIONS IN THE MSDS

ACGIH	American Conference of Governmental Industrial Hygienists;
ADR	International Carriage of Dangerous Goods by Road;
CAS Number	Chemical Abstract Service Registry Number;
EU	European Union;
IARC	International Agency for Research on Cancer;
ICAO/IATA	International Civil Aviation Organization/International Air Transport Association;
IMDG	International Maritime Dangerous Goods;
LD_{50}	Lethal dose 50;
NA	Not applicable;
NDA	No Data Available;
NTP	National Toxicology Program;
OSHA	Occupational Safety and Health Administration;
RID	International Carriage of Dangerous Goods by Rail.

FULL TEXT OF H STATEMENTS UNDER SECTION 3

H290:	May be corrosive to metals.
H302:	Harmful if swallowed.
H314:	Causes severe skin burns and eye damage.
H315:	Causes skin irritation.
H317:	May cause an allergic skin reaction.
H319:	Causes serious eye irritation.
H335:	May cause respiratory irritation.
H400:	Very toxic to aquatic life.