Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-May-2018
Document Type: USP Monographs
DocId: GUID-BA385E09-8A20-4045-B0AB-A2166A8FA6D1_3_en-US
DOI: https://doi.org/10.31003/USPNF_M83620_03_01
DOI Ref: tm7cw

Tilmicosin Injection

» Tilmicosin Injection is a sterile solution of Tilmicosin in a mixture of Propylene Glycol and Water for Injection, and is solubilized with the aid of Phosphoric Acid. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of tilmicosin ($C_{46}H_{80}N_2O_{13}$).

Packaging and storage—Preserve as described in *Packaging and Storage Requirements ⟨659⟩, Injection Packaging*; protect from light. Store at or below 30°.

Labeling—Label the Injection to indicate that it is for veterinary use only.

USP Reference standards ⟨11⟩—

USP Tilmicosin RS

Identification—The chromatogram of the *Assay preparation* obtained as directed in the *Assay* exhibits major peaks for the tilmicosin *trans*-isomers and the tilmicosin *cis*-isomers, the retention times of which correspond to those exhibited in the chromatogram of the *Standard preparation* obtained as directed in the *Assay*.

Bacterial Endotoxins Test ⟨85⟩—It contains not more than 0.5 USP Endotoxin Unit per mg of tilmicosin.

Sterility Tests ⟨71⟩—It meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined*, except that the test mixture is prepared as follows. Transfer aseptically 1 mL from each of 20 containers to a vessel containing 200 mL of a mixture containing 2 mL of polysorbate 20 in *Buffer B.16* (see *Antibiotics—Microbial Assays ⟨81⟩, Media and Solutions, Solutions, Buffers*). After that solution has been filtered, wash the filter with three 100-mL portions of the same solution, instead of *Diluting Fluid A*.

pH ⟨791⟩: between 5.5 and 6.5.

Particulate Matter in Injections ⟨788⟩—Use the procedure under *Microscopic Particle Count Test:* not more than 50 particles per mL that are equal to or greater than 10 µm in effective spherical diameter, and not more than 5 particles per mL that are equal to or greater than 25 µm in effective spherical diameter are found.

Content of propylene glycol—

Internal standard solution—Prepare a solution of pentadecane in acetone containing about 0.5 mg per mL.

Standard solution—Transfer about 125 mg of propylene glycol, accurately weighed, to a 100-mL volumetric flask, dilute with acetone to volume, and mix. Mix equal, accurately measured volumes of this solution and the *Internal standard solution*. This solution contains about 0.625 mg of propylene glycol per mL.

Test solution—Transfer an accurately measured volume of Injection, equivalent to about 250 mg of propylene glycol, to a 200-mL volumetric flask, dilute with acetone to volume, and mix. Mix equal, accurately measured volumes of this solution and the *Internal standard solution*.

Chromatographic system (see *Chromatography ⟨621⟩*)—The gas chromatograph is equipped with a flame-ionization detector and a 0.53-mm × 15-m fused silica column that has liquid phase G16 bonded to the inner surface at a thickness of 1 µm. The injection port and the detector block are maintained at about 250°, and the column is maintained at a temperature of about 100°. Helium is used as the carrier gas at a flow rate of about 15 mL per minute. Chromatograph the *Standard solution*, and record the peak responses as directed for *Procedure:* the relative retention times are about 0.6 for pentadecane and 1.0 for propylene glycol, the resolution, *R,* between the pentadecane peak and the propylene glycol peak is not less than 7.0, and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 1 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the area responses for the major peaks. Calculate the quantity, in mg, of propylene glycol in each mL of the Injection taken by the formula:

$$400(C/V)(R_U/R_S)$$

in which C is the concentration, in mg per mL, of propylene glycol in the *Standard solution*, V is the volume, in mL, of Injection taken, and R_U and R_S are the ratios of the propylene glycol peak area response to the pentadecane peak area response obtained from the *Test solution* and the *Standard solution*, respectively. Between 80.0% and 120.0% of the labeled amount of propylene glycol is found.

Assay—

Dibutylammonium phosphate buffer—To 700 mL of water, add 168 mL of dibutylamine. Add phosphoric acid slowly until the dibutylamine is just dissolved, stirring vigorously during the addition. Allow to cool, and adjust with phosphoric acid to a pH of 2.55 ± 0.05. Dilute with water

to 1000 mL, mix, and filter under vacuum.

Mobile phase—To 700 mL of water, add 115 mL of acetonitrile, 55 mL of tetrahydrofuran, and 25 mL of *Dibutylammonium phosphate buffer*. Dilute with water to 1000 mL, and mix. Each component may be filtered before mixing, or the *Mobile phase* may be filtered, minimizing solvent evaporation. Store the *Mobile phase* in a sealed container when not in use. Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Diluent—To 700 mL of water add 200 mL of acetonitrile and 25 mL of *Dibutylammonium phosphate buffer*, dilute with water to 1000 mL, and mix.

Standard preparation—Quantitatively dissolve an accurately weighed quantity of USP Tilmicosin RS in acetonitrile to obtain a solution having a known concentration of about 2.5 mg per mL. Transfer 4.0 mL of this solution to a 20-mL volumetric flask, add 10 mL of water, and 0.5 mL of *Dibutylammonium phosphate buffer*, dilute with water to volume, and mix.

Assay preparation—Transfer an accurately measured volume of Injection, equivalent to about 300 mg of tilmicosin, to a 30-mL volumetric flask, dilute with *Diluent* to volume, and mix. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, dilute with *Diluent* to volume, and mix.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 280-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 1.1 mL per minute. Chromatograph the *Standard preparation*, and record the responses as directed for *Procedure:* the relative retention times are about 0.8 for the tilmicosin *trans*-isomers and 1.0 for the tilmicosin *cis*-isomers, the resolution, *R,* between the tilmicosin *trans*-isomers peak and the tilmicosin *cis*-isomers peak is not less than 1.25, the tailing factors for the peaks are not less than 0.7 and not more than 2, and the relative standard deviation for replicate injections is not more than 1.5%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the area responses for the major peaks. Calculate the quantity, in mg, of each of the tilmicosin isomers in each mL of the Injection taken by the formula:

$$0.6(CP/V)(r_I/r_S)$$

in which C is the concentration, in mg per mL, of USP Tilmicosin RS in the *Standard preparation*, P is the potency, in µg per mg, of the relevant (*trans* or *cis*) tilmicosin isomers in the USP Tilmicosin RS, V is the volume of Injection taken to prepare the *Assay preparation*, r_I is the peak response of the relevant tilmicosin isomers obtained from the *Assay preparation*, and r_S is the peak area response for the relevant (*trans* or *cis*) tilmicosin isomers obtained from the *Standard preparation*. Calculate the quantity, in mg, of $C_{46}H_{80}N_2O_{13}$ in each mL of the Injection taken by adding the quantities, in mg per mL, of *cis*- and *trans*-isomers found.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
TILMICOSIN INJECTION	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. Information currently unavailable

Current DocID: GUID-BA385E09-8A20-4045-B0AB-A2166A8FA6D1_3_en-US
Previous DocID: GUID-BA385E09-8A20-4045-B0AB-A2166A8FA6D1_1_en-US
DOI: https://doi.org/10.31003/USPNF_M83620_03_01
DOI ref: tm7cw