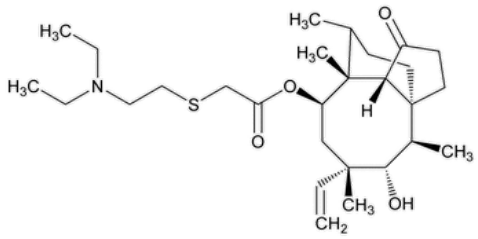
Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-Dec-2020
Document Type: USP Monographs
DocId: GUID-6B4AEFC0-25EC-4FFF-BC6A-20235446D16F_6_en-US
DOI: https://doi.org/10.31003/USPNF_M1136_06_01
DOI Ref: wnz8m

Tiamulin



$C_{28}H_{47}NO_4S$ 493.74

Acetic acid, [[2-(diethylamino)ethyl]thio]-, 6-ethenyldecahydro-5-hydroxy-4,6,9,10-tetramethyl-1-oxo-3a,9-propano-3a*H*-cyclopentacycloocten-8-yl ester [3a*S*-(3aα,4β,5α,6α,8β,9α,9aβ,10*S**)]-;

[[2-(Diethylamino)ethyl]thio]acetic acid 8-ester with (3a*S*,4*R*,5*S*,6*S*,8*R*,9*R*,9a*R*,10*R*)-octahydro-5,8-dihydroxy-4,6,9,10)-tetramethyl-6-vinyl-3a,9-propano-3a*H*-cyclopentacycloocten-1(4*H*)-one CAS RN®: 55297-95-5; UNII: E38WZ4U54R.

DEFINITION

Tiamulin contains NLT 96.5% and NMT 102.0% of tiamulin ($C_{28}H_{47}NO_4S$), calculated on the dried basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K.
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution,* as obtained in the *Assay*.

ASSAY

- **Procedure**

Buffer: Dissolve 10.0 g of ammonium carbonate in water, add 22 mL of perchloric acid TS, and dilute with water to 1000 mL. Adjust with ammonium hydroxide to a pH of 10.0.

Mobile phase: Methanol, acetonitrile, and *Buffer* (490:210:300)

Diluent: Acetonitrile and *Buffer* (1:1)

Standard solution: 5.0 mg/mL of USP Tiamulin Fumarate RS in *Diluent*

Sample solution: 4.0 mg/mL of Tiamulin in *Diluent*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 212 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2 between tiamulin and its subsequent peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of tiamulin ($C_{28}H_{47}NO_4S$) in the portion of Tiamulin taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

C_S = concentration of USP Tiamulin Fumarate RS in the *Standard solution* (mg/mL)

C_U = concentration Tiamulin in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of tiamulin, 493.74

M_{r2} = molecular weight of tiamulin fumarate, 609.82

Acceptance criteria: 96.5%–102.0% on the dried basis

IMPURITIES

• **Limit of Alcohol and Toluene**

Proceed as directed in *Residual Solvents ⟨467⟩*.

Acceptance criteria

Alcohol: NMT 1.0%

Toluene: NMT 0.08%

Sum of alcohol and toluene: NMT 1.0%

Change to read:

• **Organic Impurities**

Buffer, Mobile phase, Diluent, Standard solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Toluene solution: Transfer 0.1 mL of toluene to a 100-mL volumetric flask, and dilute with acetonitrile to volume. Transfer 0.1 mL of this solution to another 100-mL volumetric flask, and dilute with *Diluent* to volume.

Diluted sample solution: 0.04 mg/mL of Tiamulin from the *Sample solution* in *Diluent*

Analysis

Samples: *Standard solution*, *Sample solution*, *Toluene solution*, and *Diluted sample solution*

Calculate the area percentage of each impurity, relative to tiamulin, in the portion of Tiamulin taken:

$$\text{Result} = (r_U/r_T) \times {}^{\blacktriangle}D \times {}^{\blacktriangle}_{\text{(ERR 1-Dec-2020)}}\,100$$

r_U = peak area of each individual impurity from the *Sample solution*

r_T = peak area of tiamulin from the *Diluted sample solution*

${}^{\blacktriangle}D$ = dilution factor for the *Sample solution*, $0.01{}^{\blacktriangle}_{\text{(ERR 1-Dec-2020)}}$

Acceptance criteria: See *Table 1*. Disregard the toluene peak and any peak from the *Sample solution* less than 0.1 times the area of the principal peak from the *Diluted sample solution*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Mutilin	0.22	1.0
2-(Benzylsulfanyl)-*N*,*N*-diethylethanamine	0.50	1.0
2,2'-(Disulfane-1,2-diyl)bis(*N*,*N*-diethylethanamine)	0.66	1.0
Tiamulin	1.0	—
Hydroxy-11-oxotiamulin	1.1	1.0

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
1-Hydroxy-11-oxotiamulin	1.6	1.0
11-Oxotiamulin	2.4	1.0
Any individual unspecified impurity	—	0.2
Total impurities	—	3.0

SPECIFIC TESTS

- **Bacterial Endotoxins Test ⟨85⟩:** It contains NMT 0.4 USP Endotoxin Units/mg.
- **Loss on Drying ⟨731⟩**

  Analysis: Dry at 80° to constant weight.

  Acceptance criteria: NMT 1.0%
- **Clarity and Color of Solution**

  Sample: 2.5 g

  Instrumental conditions

  (See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

  Analytical wavelength: 420 nm

  Analysis: Dissolve the *Sample* in methanol, and dilute with methanol to 50.0 mL.

  Acceptance criteria: The solution is clear, and its absorbance is NMT 0.050.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed, light-resistant containers, and store at room temperature.
- **Labeling:** Label it to indicate that it is for veterinary use only.
- **USP Reference Standards ⟨11⟩**

  USP Tiamulin RS

  USP Tiamulin Fumarate RS

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

Topic/Question	Contact	Expert Committee
TIAMULIN	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. PF 43(3)

Current DocID: GUID-6B4AEFC0-25EC-4FFF-BC6A-20235446D16F_6_en-US

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