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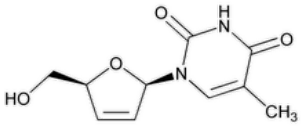
Stavudine



$C_{10}H_{12}N_2O_4$ 224.21

Thymidine, 2',3'-didehydro-3'-deoxy-;

1-(2,3-Dideoxy-β-D-*glycero*-pent-2-enofuranosyl)thymine CAS RN®: 3056-17-5; UNII: BO9LE4QFZF.

DEFINITION

Stavudine contains NLT 98.0% and NMT 102.0% of stavudine ($C_{10}H_{12}N_2O_4$), calculated on an anhydrous and solvent-free basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

• **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**

All solutions containing stavudine must be prepared immediately before use and remain refrigerated until use.

Solution A: 0.77 g/L of ammonium acetate

Mobile phase: Acetonitrile and *Solution A* (5:95)

Standard solution: 0.02 mg/mL of USP Stavudine RS in water

Sample solution: 0.02 mg/mL of Stavudine in water

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 3.3-cm; 3-µm packing L1

Flow rate: 0.7 mL/min

Injection volume: 25 µL

System suitability

Sample: *Standard solution*

[Note—The retention time of the stavudine peak is between 2.8 and 5.0 min.]

Suitability requirements

Column efficiency: NLT 800 theoretical plates

Tailing factor: NMT 1.6

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of stavudine ($C_{10}H_{12}N_2O_4$) in the portion of Stavudine taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 98.0%–102.0% on the anhydrous, solvent-free basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.3%

• **Organic Impurities**

All solutions containing stavudine must be prepared immediately before use and remain refrigerated until use.

Solution A: 0.77 g/L of ammonium acetate in water

Solution B: Acetonitrile and *Solution A* (3.5:96.5)

Solution C: Acetonitrile and *Solution A* (25:75)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution B (%)	Solution C (%)
0	100	0
10	100	0
20	0	100
30	0	100
35	100	0
40	100	0

System suitability solution: 0.50 mg/mL of USP Stavudine System Suitability Mixture RS in water

Sample solution: 0.5 mg/mL of Stavudine in water

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 2.1 mL/min

Injection volume: 10 µL

Run time: 2 times the retention time of the stavudine peak, or at least until the last impurity has eluted

System suitability

Sample: *System suitability solution*

[Note—The retention time of the main stavudine peak is 10.5 ± 2 min. The relative retention times for stavudine and thymine are listed in *Table 2*.]

Suitability requirements

Resolution: NLT 1.15 between the thymidine epimer and thymidine; NLT 1.0 between stavudine and α-stavudine

Column efficiency: NLT 9500 theoretical plates

Capacity factor, *k*': NLT 4

Analysis

Samples: *System suitability solution* and *Sample solution*

Calculate the percentage of thymine in the portion of Stavudine taken:

$$\text{Result} = (r_U/r_T) \times F \times 100$$

r_U = peak response of thymine from the *Sample solution*

r_T = sum of all the peak responses from the *Sample solution*

F = relative response factor (see *Table 2*)

Calculate the percentage of all other impurities in the portion of Stavudine taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response for each impurity from the *Sample solution*

r_T = sum of all the peak responses from the *Sample solution*

Acceptance criteria: See *Table 2*. Disregard threshold is 0.03%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Thymine	0.28	0.69	0.5
Stavudine	1.0	—	—
Any other individual impurity	—	1.0	0.1
Total impurities[a]	—	—	1.0

[a] Including thymine.

SPECIFIC TESTS

- **Optical Rotation,** *Specific Rotation* ⟨781S⟩

  Sample solution: 10 mg/mL

  Acceptance criteria: −40° to −45°, calculated on the anhydrous basis

- **Water Determination,** *Method I* ⟨921⟩**:** NMT 0.5%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, protected from light and humidity. Store at 25°, excursions permitted between 15° and 30°.
- **USP Reference Standards** ⟨11⟩

  USP Stavudine RS

  USP Stavudine System Suitability Mixture RS

It is a mixture of stavudine and the following related compounds: thymidine, thymine, alpha-stavudine, and *xylo*-thymidine.

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

Topic/Question	Contact	Expert Committee
STAVUDINE	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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