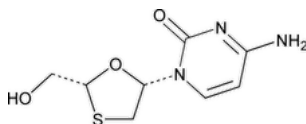


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Lamivudine



$C_8H_{11}N_3O_3S$ 229.26

$C_8H_{11}N_3O_3S \cdot 0.2 CH_3OH$ 235.66

$C_8H_{11}N_3O_3S \cdot 0.2 H_2O$ 232.86

2(1*H*)-Pyrimidinone, 4-amino-1-[2-(hydroxymethyl)-1,3-oxathiolan-5-yl]-, (2*R*-*cis*)-;

(-)-1-[(2*R*,5*S*)-2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine CAS RN®: 134678-17-4; UNII: 2T8Q726O95.

DEFINITION

Lamivudine contains NLT 98.0% and NMT 102.0% of lamivudine ($C_8H_{11}N_3O_3S$), calculated on the anhydrous and solvent-free basis. If labeled as a methanol solvate, it contains NLT 98.0% and NMT 102.0% of lamivudine ($C_8H_{11}N_3O_3S$), calculated on the anhydrous, methanol-free, and solvent-free basis.

IDENTIFICATION

Change to read:

- **A.** [▲ SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Infrared Spectroscopy: 197M ▲](#) (CN 1-MAY-2020)
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *System suitability solution*, as obtained in the test for *Limit of Lamivudine Enantiomer*.

ASSAY

• PROCEDURE

Buffer: Transfer about 1.9 g of ammonium acetate to a 1000-mL volumetric flask, dissolve in about 900 mL of water, adjust with acetic acid to a pH of 3.8 ± 0.2 , and dilute with water to volume.

Mobile phase: Methanol and *Buffer* (5:95)

System suitability solution: 0.25 mg/mL of [USP Lamivudine Resolution Mixture B RS](#) in *Mobile phase*

Standard solution: 0.25 mg/mL of [USP Lamivudine RS](#) in *Mobile phase*

Sample solution: 0.25 mg/mL of Lamivudine in *Mobile phase*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 277 nm

Column: 4.6-mm × 25-cm; packing L1

Column temperature: 35°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for lamivudine diastereomer and lamivudine are 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between lamivudine and lamivudine diastereomer, *System suitability solution*

Relative standard deviation: NMT 2.0% for lamivudine, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of lamivudine ($C_8H_{11}N_3O_3S$) in the portion of Lamivudine 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 Lamivudine RS](#) in the *Standard solution* (mg/mL)

C_u = concentration of Lamivudine in the *Sample solution* (mg/mL)

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

If labeled as a methanol solvate: 98.0%–102.0% on the anhydrous, methanol-free, and solvent-free basis

OTHER COMPONENTS

• **CONTENT OF METHANOL** (if labeled as lamivudine methanol solvate)

Diluent: *N,N*-Dimethylformamide and *t*-butanol (500:1)

Standard solution: 0.625 mg/mL of methanol in diluent. Transfer 2.0 mL of this solution into a headspace vial, and immediately seal the vial.

Sample solution: Transfer 50 mg of Lamivudine to a headspace vial, add 2.0 mL of *Diluent*, and immediately seal the vial.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: GC headspace

Detector: Flame ionization

Column: 0.53-mm × 75-m, coated with a 3-μm film of phase G43

Temperatures

Injector: 180°

Detector: 250°

Column: See [Table 1](#).

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
40	—	40	13
40	40	240	12

Injection volume: 1.0 mL

Injection type: Split ratio, 15:1

Carrier gas: Helium

Flow rate: 6 mL/min

Headspace samplers

Oven: 95°

Loop: 175°

Transfer line: 175°

Equilibrium time: 10 min

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for methanol and *t*-butanol are 1.0 and 1.9, respectively.]

Suitability requirements

Tailing factor: NMT 2.0 for methanol

Column efficiency: NLT 25,000 for methanol

Relative standard deviation: NMT 5.0% for methanol

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of methanol in the portion of lamivudine methanol solvate taken:

$$\text{Result} = (R_u/R_s) \times (C_s/C_u) \times 100$$

R_u = peak response ratio of methanol to *t*-butanol from the *Sample solution*

R_s = peak response ratio of methanol to *t*-butanol from the *Standard solution*

C_s = concentration of methanol in the *Standard solution* (mg/mL)

C_u = concentration of Lamivudine (as methanol solvate) in the *Sample solution* (mg/mL)

Acceptance criteria: 2.0%–3.0%