

BRIEFING

Lamivudine Oral Solution. This monograph was posted on the USP website as a Draft USP Pending Monograph in September 2009 for review and public comments. No comments were received. The Monograph Development–Antivirals and Antimicrobials Expert Committee approved the monograph as an Authorized USP Pending Monograph.

The proposed liquid chromatographic procedures in the *Assay* and in the test for *Organic Impurities* are based on analyses performed with the Hypersil BDS brand of L1 column. The typical retention time for lamivudine is 3.4 min in the *Assay* and 8.5 min in the test for *Organic Impurities*.

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Lamivudine Oral Solution

v.1 Authorized April 1, 2010

DEFINITION

Lamivudine Oral Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of lamivudine (C₈H₁₁N₃O₃S).

IDENTIFICATION

- 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: 1.9 g/L of ammonium acetate in water. Adjust with acetic acid to a pH of 3.8.

Solution A: Methanol and *Buffer* (1:19)

Solution B: Methanol

Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	100	0
5	100	0
6	0	100
12	0	100
13	100	0
20	100	0

Standard solution: 20 µg/mL of USP Lamivudine RS in *Solution A*. [NOTE—Sonicate to dissolve.]

Sample solution: 20 µg/mL of lamivudine from Oral Solution in *Solution A*. [NOTE—Sonicate to dissolve.]

Chromatographic system

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

Mode: LC

Detector: UV 277 nm

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

Column temperature: 35°

Flow rate: 1.5 mL/min

Injection size: 10 µL

Run time: 1.7 times the retention time of lamivudine for the *Standard solution*

Data acquisition time: 3 times the retention time of lamivudine

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 2000 theoretical plates

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of lamivudine in the portion of Oral Solution 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 = nominal concentration of lamivudine in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **DELIVERABLE VOLUME** (698)

For Oral Solution packaged in multiple-unit containers:

Meets the requirements

IMPURITIES

Organic Impurities

• **PROCEDURE**

Buffer, Solution A, and Solution B: Proceed as directed in the *Assay*.

Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	100	0
60	100	0
70	0	100
80	0	100
90	100	0
110	100	0

System suitability solution: 0.25 mg/mL of USP Lamivudine Resolution Mixture B RS in *Solution A*. [NOTE—Lamivudine resolution mixture B contains lamivudine and lamivudine diastereomer.]

Standard solution: 0.3 µg/mL of USP Lamivudine RS in *Solution A*. [NOTE—Sonicate to dissolve.]

Sample solution: 0.3 mg/mL of lamivudine in *Solution A*. [NOTE—Sonicate for 10 min.]

Chromatographic system

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

Mode: LC

Detector: UV 277 nm

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

Column temperature: 35°

Flow rate: 1.0 mL/min

Injection size: 10 µL

Run time: 2 times the retention time of lamivudine for the *Standard solution*

Data acquisition time: 6.5 times the retention time of lamivudine

System suitability

Samples: *System suitability solution* and *Standard solution* [NOTE—The relative retention times for lamivudine and lamivudine diastereomer are 1.0 and 0.9, respectively.]

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

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual degradation product in the portion of Oral Solution taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times (1/F) \times 100$$

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- r_U = peak response of each individual impurity in the *Sample solution*
- r_S = peak response of lamivudine from the *Standard solution*
- C_S = concentration of USP Lamivudine RS in the *Standard solution* (mg/mL)
- C_U = nominal concentration of lamivudine in the *Sample solution* (mg/mL)
- F = relative response factor (see *Impurity Table 1*)

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 6.5%

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Cytosine ^a	0.32	1.67	0.50
Specified impurity A [#]	0.40	1.0	0.30
Lamivudine- <i>S</i> -sulfoxide ^b	0.43	1.0	0.85
Lamivudine- <i>R</i> -sulfoxide ^c	0.45	1.0	1.8
Lamivudine diastereomer [*]	0.90	—	—

^a 4-Aminopyrimidin-2(1*H*)-one.

^b 1-[(2*R*,3*S*,5*S*)-2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine *S*-oxide.

^c 1-[(2*R*,3*R*,5*S*)-2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine *S*-oxide.

^d 1-[(2*R*,5*S*)-2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]uracil.

^{*} For system suitability and identification purposes only.

[#] Unidentified impurities.

Impurity Table 1 (continued)

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Specified impurity B [#]	0.90	1.0	0.20
Lamivudine	1.0	—	—
Lamivudine uracil derivative ^d	1.5	0.45	3.5
Any individual unspecified degradation product	—	—	0.10

^a 4-Aminopyrimidin-2(1*H*)-one.

^b 1-[(2*R*,3*S*,5*S*)-2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine *S*-oxide.

^c 1-[(2*R*,3*R*,5*S*)-2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine *S*-oxide.

^d 1-[(2*R*,5*S*)-2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]uracil.

^{*} For system suitability and identification purposes only.

[#] Unidentified impurities.

SPECIFIC TESTS

- **PH (791):** Between 5.7 and 6.3

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers supplied with drying agent. Store at controlled room temperature.
- **USP REFERENCE STANDARDS (11)**
USP Lamivudine RS
USP Lamivudine Resolution Mixture B RS