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Lamivudine Tablets

DEFINITION
Lamivudine Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of lamivudine ($C_8H_{11}N_3O_3S$).

IDENTIFICATION

Change to read:

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

Sample: Crush 1 Tablet and transfer it to a suitable container. Add 5 mL of methanol and shake for 15 min. Pass through a suitable filter, collecting about 2 mL of the filtrate. Evaporate the filtrate to dryness under a gentle stream of nitrogen, and use the residue.

Standard: Dissolve a suitable amount of USP Lamivudine RS in a small amount of methanol, shaking until completely dissolved. Evaporate to dryness under a gentle stream of nitrogen, and use the residue.

Acceptance criteria: Meet the requirements

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

Mobile phase: Methanol and *Buffer* (50:950)

System suitability solution: 0.2 mg/mL of USP Lamivudine Resolution Mixture B RS in *Mobile phase*

Standard solution: 0.2 mg/mL of USP Lamivudine RS in *Mobile phase*

Sample stock solution: Nominally about 3–4 mg/mL of lamivudine in water prepared as follows. Transfer the required number of Tablets, based on the labeled amount, to a suitable volumetric flask, and soak or shake for at least 15 min in water to disperse the sample. Dilute with water to volume, mix, and pass through a suitable filter or centrifuge.

Sample solution: Nominally 0.2 mg/mL of lamivudine in *Mobile phase* from the *Sample stock solution*

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: 30 ± 5°

Flow rate: 1 mL/min

Injection volume: 20 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%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lamivudine ($C_8H_{11}N_3O_3S$) in the portion of Tablets 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

• **Dissolution** ⟨711⟩

Test 1

Procedure for products labeled as Lamivudine Tablets 100-mg or 150-mg

Medium: Water, degassed; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: (*L*/900) mg/mL of USP Lamivudine RS in *Medium*, where *L* is the Tablet label claim in mg

Sample solution: Pass a portion of the solution under test through a suitable filter to obtain a concentration similar to that of the *Standard solution*.

Instrumental conditions

Mode: UV

Analytical wavelength: 270 nm

Cell: 1 mm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lamivudine ($C_8H_{11}N_3O_3S$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of lamivudine ($C_8H_{11}N_3O_3S$) is dissolved.

Procedure for products labeled as Lamivudine Tablets 300-mg

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 75 rpm

Time: 15 min

Standard solution: (*L*/900) mg/mL of USP Lamivudine RS in *Medium*, where *L* is the Tablet label claim in mg

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

Mode: UV

Analytical wavelength: 280 nm

Cell: 0.5 mm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lamivudine ($C_8H_{11}N_3O_3S$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of lamivudine ($C_8H_{11}N_3O_3S$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 15 min

Buffer: 1.93 g/L of ammonium acetate in water. Adjust with glacial acetic acid to a pH of 3.8.

Mobile phase: Methanol and *Buffer* (40:60)

Standard solution: (*L*/900) mg/mL of USP Lamivudine RS in *Medium*, where *L* is the Tablet label claim in mg

Sample solution: Pass a portion of the solution under test through a suitable filter to obtain a concentration similar to that of the *Standard solution*.

Chromatographic system

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

Mode: LC

Detector: 285 nm

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

Flow rate: 1 mL/min

Injection volume: 5 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Tailing factor: NMT 1.5

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lamivudine ($C_8H_{11}N_3O_3S$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times 100$$

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)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of lamivudine ($C_8H_{11}N_3O_3S$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

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

Analysis

Sample: *Sample solution*

Calculate the percentage of each individual impurity in the portion of Tablets taken:

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

r_U = peak response of each individual impurity

r_T = sum of all the peak responses

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Cytosine[a]	0.32	0.2
Lamivudine-carboxylic acid[b]	0.39	—[c]
Lamivudine-*S*-sulfoxide[d]	0.43	0.2
Lamivudine-*R*-sulfoxide[e]	0.45	0.2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Lamivudine diastereomer (Lamivudine-*trans*)[f]	0.92	—[c]
Lamivudine	1.0	—
Salicylic acid	2.2	—[c]
Any other individual impurity	—	0.2
Total impurities	—	0.6

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

[b] (2*RS*,5*SR*)-5-(Cytosine-1-yl)-1,3-oxathiolane-2-carboxylic acid.

[c] Process impurity included in the table for identification only. Process impurities are controlled in the drug substance and are not to be reported or included in the total impurities for the drug product.

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

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

[f] 1-[(2*RS*,5*RS*)-2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩
  USP Lamivudine RS
  USP Lamivudine Resolution Mixture B RS

[Note—The resolution mixture contains lamivudine and lamivudine diastereomer. Other impurities may also be present.]

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

Topic/Question	Contact	Expert Committee
LAMIVUDINE TABLETS	Documentary Standards Support	SM12020 Small Molecules 1

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