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Add the following:

▲Abacavir, Lamivudine, and Zidovudine Tablets

DEFINITION

Abacavir, Lamivudine, and Zidovudine Tablets contain an amount of abacavir sulfate, lamivudine, and zidovudine equivalent to NLT 90.0% and NMT 110.0% each of the labeled amounts of abacavir ($C_{14}H_{18}N_6O$), lamivudine ($C_8H_{11}N_3O_3S$), and zidovudine ($C_{10}H_{13}N_5O_4$), respectively.

IDENTIFICATION

• **A.** The retention times of the major peaks of the *Sample solution* correspond to those of abacavir sulfate, lamivudine, and zidovudine from the *Standard solution*, as obtained in the *Assay*.

• **B.** The UV absorption spectra of the major peaks of the *Sample solution* correspond to those of abacavir sulfate, lamivudine, and zidovudine from the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Solution A: 1.9 g/L of ammonium acetate in water. Adjust with glacial acetic acid to a pH of 3.9.

Solution B: Methanol

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	97	3
8	97	3
19	76	24
27	76	24
33	40	60
45	40	60

System suitability solution: Dissolve the contents of 1 vial of USP Lamivudine Resolution Mixture C RS in 2.5 mL of *Solution A*. [Note—One vial of USP Lamivudine Resolution Mixture C RS contains 0.8 mg of USP Lamivudine Resolution Mixture C RS.]

Standard solution: 0.35 mg/mL of USP Abacavir Sulfate RS, 0.15 mg/mL of USP Lamivudine RS, and 0.30 mg/mL of USP Zidovudine RS in *Solution A*. Sonicate to dissolve prior to final dilution.

Sample stock solution: Nominally 3 mg/mL of abacavir, 1.5 mg/mL of lamivudine, and 3 mg/mL of zidovudine in *Solution A* prepared as follows. Transfer NLT 5 Tablets to a suitable volumetric flask. Add *Solution A* to about 50% of the final flask volume and shake for NLT 30 min to disperse the Tablets. Dilute with *Solution A* to volume. Pass through a suitable filter.

Sample solution: Nominally 0.30 mg/mL of abacavir, 0.15 mg/mL of lamivudine, and 0.30 mg/mL of zidovudine in *Solution A* from *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 270 nm. For *Identification B*, use a diode array detector in the range of 220–400 nm.

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

Column temperature: 30°

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-*S*-oxide and lamivudine-*R*-oxide, in relation to the lamivudine peak, are 0.36 and 0.40, respectively; the relative retention times for lamivudine diastereomer and lamivudine are 0.96 and 1.0, respectively, *System suitability solution*.]

Suitability requirements

Resolution: NLT 1.2 between lamivudine carboxylic acid and lamivudine-*S*-oxide; NLT 1.2 between lamivudine diastereomer and lamivudine, *System suitability solution*

Relative standard deviation: NMT 2.0% each for abacavir, lamivudine, and zidovudine, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of abacavir ($C_{14}H_{18}N_6O$) in the portion of Tablets taken:

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

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

r_S = peak response of abacavir from the *Standard solution*

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

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

M_{r1} = molecular weight of abacavir multiplied by 2, 572.66

M_{r2} = molecular weight of abacavir sulfate, 670.74

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 of lamivudine from 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)

Calculate the percentage of the labeled amount of zidovudine ($C_{10}H_{13}N_5O_4$) in the portion of Tablets taken:

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

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

r_S = peak response of zidovudine from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0% each of the labeled amounts of abacavir, lamivudine, and zidovudine

PERFORMANCE TESTS

• **DISSOLUTION** ⟨711⟩

Medium: 0.1 N hydrochloric acid, degassed; 900 mL

Apparatus 2: 75 rpm

Time: 30 min

Standard solution 1: 0.35 mg/mL of USP Abacavir Sulfate RS in *Medium*. Sonicate to dissolve prior to final dilution.

Standard solution 2: 0.15 mg/mL of USP Lamivudine RS in *Medium*. Sonicate to dissolve prior to final dilution.

Standard solution 3: 0.30 mg/mL of USP Zidovudine RS in *Medium*. Sonicate to dissolve prior to final dilution.

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

Instrumental conditions

Mode: UV

Wavelength range: 240–320 nm

Cell: 0.05 cm

Blank: *Medium*

Analysis: The calculations of the percentages dissolved are performed using multi-component analysis software.

Samples: *Standard solution 1*, *Standard solution 2*, *Standard solution 3*, and *Sample solution*

Calculate the percentage of the labeled amount each of abacavir, lamivudine, and zidovudine dissolved.

Tolerances: NLT 80% (*Q*) each of the labeled amount of abacavir, lamivudine, and zidovudine is dissolved.

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

IMPURITIES

• **Organic Impurities**

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

Analysis

Sample: *Sample solution*

Calculate the percentage of any individual abacavir related impurity and any unspecified impurity in the portion of Tablets taken:

$$\text{Result} = r_U/\{\Sigma[r_U \times (1/F)] + r_T\} \times (1/F) \times 100$$

r_U = peak response of each individual abacavir related impurity or any unspecified impurity

F = relative response factor for each individual impurity (see *Table 2*)

r_T = sum of the peak responses of abacavir, all abacavir related impurities, and all unspecified impurities

Calculate the percentage of any individual lamivudine related impurity in the portion of Tablets taken:

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

r_U = peak response of each individual lamivudine related impurity

r_T = sum of the peak responses of lamivudine and all lamivudine related impurities

Calculate the percentage of any individual zidovudine related impurity in the portion of Tablets taken:

$$\text{Result} = r_U/\{\Sigma[r_U \times (1/F)] + r_T\} \times (1/F) \times 100$$

r_U = peak response of each individual zidovudine related impurity

F = relative response factor for each individual zidovudine impurity (see *Table 2*)

r_T = sum of the peak responses of zidovudine and all zidovudine related impurities

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Cytosine[a,b]	0.17	1.0	—
Uracil[a,b]	0.23	1.0	—
Lamivudine carboxylic acid[a,b,c]	0.31	1.0	—
Lamivudine-*S*-sulfoxide[a,b,d]	0.36	1.0	—
Lamivudine-*R*-sulfoxide[a,b,e]	0.40	1.0	—
3'-Amino-3'-deoxythymidine[f]	0.44	1.0	0.4
Thymine[b,f]	0.48	1.7	—
Lamivudine diastereomer (lamivudine-*trans*)[a,b,g]	0.96	1.0	—
Lamivudine	1.0	—	—

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Thymidine[b,f]	1.1	1.0	—
Lamivudine–uracil derivative[a,b,h]	1.2	1.0	—
Cyclopropyldiaminopurine[b,i,j]	1.37	1.4	—
Salicylic acid[a,b]	1.40	1.0	—
Descyclopropyl abacavir[b,i,k]	1.6	1.0	—
Zidovudine	1.8	—	—
Zidovudine related compound B[b,f,l]	1.9	1.0	—
Abacavir	2.3	—	—
Any unspecified impurity[m]	—	1.0	0.2
Total abacavir related impurities[n]	—	—	1.0
Total lamivudine related impurities[n]	—	—	0.6
Total zidovudine related impurities[n]	—	—	2.0

[a] Lamivudine related impurity.

[b] This is a process impurity and included for peak identification purposes.

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

[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] Zidovudine related impurity.

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

[h] 1-[(2*RS*,5*SR*)-2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]uracil.

[i] Abacavir related impurity.

[j] N^6-Cyclopropyl-9*H*-purine-2,6-diamine.

[k] [(1*S*,4*R*)-4-(2,6-Diamino-9*H*-purin-9-yl)cyclopent-2-enyl]methanol.

[l] 3'–Chloro-3'-deoxythymidine.

[m] For any unspecified impurity, report the largest impurity observed, excluding descyclopropyl abacavir, thymine, and other process impurities. Percent for any unknown is based on total abacavir related peak areas.

[n] Drug process impurities are not included in the total impurities content, except thymine and descyclopropyl abacavir, which are included in the total zidovudine related impurities and total abacavir related impurities, respectively.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Abacavir Sulfate RS

USP Lamivudine RS

USP Lamivudine Resolution Mixture C RS

This is a mixture of lamivudine and the following impurities (other impurities may also be present):
Uracil;
Pyrimidine-2,4(1*H*,3*H*)-dione.

$C_4H_4N_2O_2$ 112.09

Lamivudine-uracil derivative;
1-[(2*RS*,5*SR*)-2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]uracil. $C_8H_{10}N_2O_4S$ 230.24

Cytosine;
4-Aminopyrimidin-2(1*H*)-one. $C_4H_5N_3O$ 111.10

Lamivudine-*S*-sulfoxide;
1-[(2*R*,3*S*,5*S*)-2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine *S*-oxide. $C_8H_{11}N_3O_4S$ 245.26

Lamivudine-*R*-sulfoxide;
1-[(2*R*,3*R*,5*S*)-2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine *S*-oxide. $C_8H_{11}N_3O_4S$ 245.26

Lamivudine carboxylic acid;
(2*RS*,5*SR*)-5-(Cytosine-1-yl)-1,3-oxathiolane-2-carboxylic acid. $C_8H_9N_3O_4S$ 243.24

Lamivudine diastereomer;
1-[(2*RS*,5*RS*)-2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine. $C_8H_{11}N_3O_3S$ 229.26

Salicylic acid;
2-Hydroxybenzoic acid. $C_7H_6O_3$ 138.12

USP Zidovudine RS▲ (USP 1-May-2021)

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

Topic/Question	Contact	Expert Committee
ABACAVIR, LAMIVUDINE AND ZIDOVUDINE TABLETS	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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