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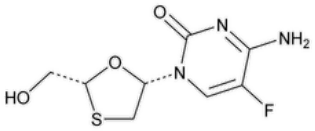
Add the following:

▲Emtricitabine



$C_8H_{10}FN_3O_3S$ 247.24

(2*R*-*cis*)-4-Amino-5-fluoro-1-[2-(hydroxymethyl)-1,3-oxathiolan-5-yl]-2(1*H*)-pyrimidinone;

5-Fluoro-1-[(2*R*,5*S*)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine CAS RN®: 143491-57-0; UNII: G70B4ETF4S.

DEFINITION

Emtricitabine contains NLT 98.0% and NMT 102.0% of emtricitabine ($C_8H_{10}FN_3O_3S$), calculated on the dried basis.

IDENTIFICATION

• **A.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

• **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**

Solution A: 2.72 g/L of potassium phosphate monobasic in water

Solution B: Methanol and *Solution A* (80:20)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
35	89	11
47	0	100
59	0	100
60	100	0
65	100	0

Standard solution: 1 mg/mL of USP Emtricitabine RS in water. Sonicate, if necessary, to dissolve prior to final dilution.

Sample solution: 1 mg/mL of Emtricitabine in water. Sonicate, if necessary, to dissolve prior to final dilution.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

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

Column temperature: 40°

Flow rate: 1.2 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of emtricitabine ($C_8H_{10}FN_3O_3S$) in the portion of Emtricitabine taken:

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

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

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

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

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%

- **Organic Impurities**

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

System suitability solution: 1 mg/mL of USP Emtricitabine System Suitability Mixture B RS in water. Sonicate, if necessary, to dissolve prior to final dilution.

Standard solution: 1 µg/mL of USP Emtricitabine RS in water prepared from the *Standard solution* in the *Assay*

Sensitivity solution: 0.5 µg/mL of USP Emtricitabine RS in water prepared from the *Standard solution*

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between emtricitabine and emtricitabine 5-fluorouracil analog, *System suitability solution*

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

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any impurity in the portion of Emtricitabine taken:

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

r_U = peak response of any impurity from the *Sample solution*

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

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

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

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

Acceptance criteria: See *Table 2*. Disregard the peak due to the emtricitabine diastereomer with a relative retention time of 1.04, if present, as it is monitored in a separate method.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Fluorocytosine[a]	0.16	1.2	0.15
Emtricitabine acid[b]	0.35	0.86	0.50
Emtricitabine *S*-sulfoxide[c]	0.44	0.75	0.15
Emtricitabine *R*-sulfoxide[d]	0.46	0.68	0.15
Lamivudine[e]	0.78	1.0	0.20
Emtricitabine	1.00	—	—
Emtricitabine 5-fluorouracil analog[f]	1.10	0.83	0.15
Any unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

[a] 4-Amino-5-fluoropyrimidin-2(1*H*)-one.

[b] *cis*-5-[4-Amino-5-fluoro-2-oxopyrimidin-1(2*H*)-yl]-1,3-oxathiolane-2-carboxylic acid.

[c] 4-Amino-5-fluoro-1-[(2*R*,3*S*,5*S*)-2-(hydroxymethyl)-3-oxo-1,3-oxathiolan-5-yl]pyrimidin-2(1*H*)-one.

[d] 4-Amino-5-fluoro-1-[(2*R*,3*R*,5*S*)-2-(hydroxymethyl)-3-oxo-1,3-oxathiolan-5-yl]pyrimidin-2(1*H*)-one.

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

[f] 5-Fluoro-1-[(2*R*,5*S*)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]uracil.

- **Enantiomeric and Diastereomeric Purity**

Mobile phase: *n*-Hexane, ethanol, methanol, trifluoroacetic acid, and diethylamine (800:150:50:1:1)

Diluent: Methanol and *Mobile phase* (10:90)

System suitability solution: 1 mg/mL of USP Emtricitabine System Suitability Mixture A RS prepared as follows. Transfer a suitable amount of USP Emtricitabine System Suitability Mixture A RS to a suitable volumetric flask. Add about 10% volume of methanol to dissolve. Dilute with *Mobile phase* to volume.

Standard stock solution: 0.3 mg/mL of USP Emtricitabine RS prepared as follows. Transfer a suitable amount of USP Emtricitabine RS to a suitable volumetric flask. Add about 10% volume of methanol to dissolve. Dilute with *Mobile phase* to volume.

Standard solution: 3 µg/mL of USP Emtricitabine RS in *Diluent* prepared from the *Standard stock solution*

Sample solution: 1 mg/mL of Emtricitabine prepared as follows. Transfer a suitable amount of emtricitabine to a suitable volumetric flask. Add about 10% volume of methanol to dissolve. Dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 25-cm; 5-µm packing L51

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of emtricitabine

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between emtricitabine and emtricitabine 5-epimer, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the enantiomer and diastereomers in the portion of Emtricitabine taken:

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

r_U = peak response of the enantiomer and diastereomers from the *Sample solution*

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

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

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

F = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Emtricitabine enantiomer[a]	0.52	1.0	0.3
Emtricitabine	1.00	—	—
Emtricitabine 5-epimer[b,c]	1.22	0.88	0.2
Emtricitabine 2-epimer[c,d]	1.29	0.88	

[a] 5-Fluoro-1-[(2*S*,5*R*)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine.

[b] 5-Fluoro-1-[(2*R*,5*R*)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine.

[c] Use the sum of the areas of both emtricitabine 5-epimer and emtricitabine 2-epimer in the calculation.

[d] 5-Fluoro-1-[(2*S*,5*S*)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine.

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 3 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Emtricitabine RS

USP Emtricitabine System Suitability Mixture A RS

This is a mixture containing the following components:

Emtricitabine.

Emtricitabine 5-epimer: 5-Fluoro-1-[(2*R*,5*R*)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine.

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USP Emtricitabine System Suitability Mixture B RS

This is a mixture containing the following components:

Emtricitabine.

Emtricitabine 5-fluorouracil analog: 5-Fluoro-1-[(2*R*,5*S*)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]uracil.

$C_8H_9FN_2O_4S$ 248.22▲ (USP 1-May-2023)

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

Chromatographic Database Information: Chromatographic Database

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