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Add the following:

▲Entecavir Oral Solution

DEFINITION

Entecavir Oral Solution contains NLT 90.0% and NMT 105.0% of the labeled amount of entecavir ($C_{12}H_{15}N_5O_3$).

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Solution A: 19.1 g/L of sodium tetraborate, decahydrate in water. Add 35 mL of methanol per liter of the solution. Pass through a suitable filter of 0.45-µm pore size.

Solution B: Methanol

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
12	100	0
30	68.5	31.5
31	50	50
34	50	50
35	100	0
43	100	0

Diluent: Methanol and water (20:80)

System suitability solution: 0.05 mg/mL of USP Entecavir Monohydrate RS and 1.5 mg/mL of methylparaben prepared as follows. Transfer an amount of USP Entecavir Monohydrate RS and methylparaben to a suitable volumetric flask and add about 5% of the flask volume of methanol. Sonicate to dissolve. Dilute with *Diluent* to volume.

Standard stock solution: 0.2 mg/mL of USP Entecavir Monohydrate RS prepared as follows. Transfer an amount of USP Entecavir Monohydrate RS to a suitable volumetric flask and add about 4% of the flask volume of methanol. Sonicate to dissolve. Dilute with *Diluent* to volume.

Standard solution: 0.05 mg/mL of USP Entecavir Monohydrate RS in *Diluent* from *Standard stock solution*

Sample solution: Nominally 0.05 mg/mL of entecavir from a measured volume of Oral Solution

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Column temperature: 30°

Flow rate: 0.8 mL/min

Injection volume: 20 µL

System suitability

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

[NOTE—The relative retention times for entecavir and methylparaben are 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 2.0 between entecavir and methylparaben, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of entecavir ($C_{12}H_{15}N_5O_3$) in the portion of Oral Solution taken:

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

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

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

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

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

Acceptance criteria: 90.0%–105.0%

PERFORMANCE TESTS

• **DELIVERABLE VOLUME** ⟨698⟩

For multiple-unit containers: Meets the requirements

IMPURITIES

• **ORGANIC IMPURITIES**

Solution A, Solution B, Mobile phase, Diluent, System suitability solution, Standard stock 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 impurity in the portion of Oral Solution taken:

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

r_U = peak response of each individual impurity from the *Sample solution*

r_T = sum of all the peak responses from the *Sample solution*

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Entecavir	1.0	—
Epimer-1[a]	1.5	1.0
Epimer-2[a]	1.6	1.0

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Individual unspecified impurity	—	0.5
Total impurities	—	2.2

[a] 2-({9-[(1*S*,3*R*,4*S*)-4-Hydroxy-3-(hydroxymethyl)-2-methylenecyclopentyl]-6-oxo-6,9-dihydro-1*H*-purin-2-yl}amino)propanoic acid. Configuration of epimers may be interchangeable.

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count does not exceed 10^2 cfu/mL. The total yeasts and molds count is NMT 10^1 cfu/mL. It meets the requirements of the test for absence of *Escherichia coli*.

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards ⟨11⟩**

USP Entecavir Monohydrate RS▲2S *(USP41)*

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

Topic/Question	Contact	Expert Committee
ENTECAVIR ORAL SOLUTION	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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