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Didanosine Delayed-Release Capsules

DEFINITION
Didanosine Delayed-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of didanosine ($C_{10}H_{12}N_4O_3$).

IDENTIFICATION

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

Change to read:

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

Sample: Empty the contents of a suitable number of Capsules, and grind to a fine powder.

ASSAY

• **Procedure**

Buffer: 0.77 g/L of ammonium acetate in water and pass through a suitable membrane filter of 0.45-µm pore size

Mobile phase: Acetonitrile and *Buffer* (35:965)

Diluent: 34.8 g/L of dibasic potassium phosphate and adjust with phosphoric acid to a pH of 7.5. Use within two weeks of preparation.

Standard solution: 0.1 mg/mL of USP Didanosine RS in water

Sample stock solution: Nominally prepare a solution at 0.6 mg/mL to 2.0 mg/mL of didanosine as follows. Mix a composite of the Capsule contents from NLT 20 Capsules in a suitable container, weigh 1 Capsule fill weight, transfer to a suitable size volumetric flask, and add 50% of the final volume of *Diluent*. Stir, shake or sonicate to dissolve. Cool to room temperature, and dilute with *Diluent* to final volume.

Sample solution: Nominally 0.1 mg/mL of didanosine in *Diluent* from the *Sample stock solution* and use within 24 h

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

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

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of didanosine ($C_{10}H_{12}N_4O_3$) in the portion of Capsules taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩:** Proceed as directed for *Method B* under *Procedure*, *Apparatus 1*, *Apparatus 2*, and *Delayed-Release Dosage Forms*.

Acid stage medium: 0.1 N hydrochloric acid; 1000 mL

Buffer 1: 76 g/L of tribasic sodium phosphate in water

Buffer stage medium: 0.1 N hydrochloric acid and 0.2 M tribasic sodium phosphate (3:1). Adjust with phosphoric acid or 10 N sodium hydroxide to a pH of 6.8; 1000 mL

Buffer 2: 1.36 g/L of monobasic potassium phosphate in water

Apparatus 1: 100 rpm

Times

Acid stage: 2 h

Buffer stage: 45 min

Mobile phase: Acetonitrile and *Buffer 2* (2:98)

Sample solution: Run the *Acid stage*. After the time specified, withdraw a portion of the solution under test, and pass it through a suitable filter. To the filtrate, add a volume of 10 N sodium hydroxide equivalent to 1% of the filtrate volume. Raise the basket. Discard the *Acid stage medium* from the vessels. Rinse the vessel with water. Add the *Buffer stage medium* pre-warmed to the vessel. After the time specified, withdraw a portion of the solution under test and pass it through a suitable filter. Store the acid stage and buffer stage filtrates at 5°.

Standard stock solution: 0.8 mg/mL of USP Didanosine RS in water

Didanosine related compound A standard stock solution: 0.1 mg/mL of USP Didanosine Related Compound A RS in water

Standard solution: Accurately transfer portions of the *Standard stock solution* and the *Didanosine related compound A standard stock solution* to a volumetric flask, and dilute with water to volume to obtain a didanosine final concentration of (*L*/1000) mg/mL where *L* is the Capsule label claim in mg and 0.01 mg/mL of didanosine related compound A.

Chromatographic system

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

Mode: LC

Detector: UV 270 nm

Column: 3.9-mm × 5-cm; 5-µm packing L7

Flow rate: 1 mL/min

Sample temperature: 5°

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for both the didanosine and didanosine related compound A peaks

Relative standard deviation: NMT 2.0% for the didanosine peak and NMT 5.0% for the didanosine related compound A peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of didanosine as calculated based on response of didanosine related compound A released in the *Acid stage*:

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

Calculate the percentage of didanosine released in the *Buffer stage*:

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

r_U = peak response from the *Sample solution*. [NOTE—During the *Acid stage*, didanosine is converted to didanosine related compound A so the peak response is the hypoxanthine peak.]

r_S = peak response from the *Standard solution*. [NOTE—During the *Acid stage*, didanosine is converted to didanosine related compound A so the peak response is the hypoxanthine peak.]

C_S = concentration of USP Didanosine Related Compound A RS in the *Standard solution* for the *Acid stage* or concentration of USP Didanosine RS in the *Standard solution* for the *Buffer stage* (mg/mL)

L = label claim (mg/Capsule)

D = dilution factor of the *Sample solution*, if applicable

M_{r1} = molecular weight of didanosine, 236.2

M_{r2} = molecular weight of didanosine related compound A, 136.11

V = volume of medium, 1000 mL

Tolerances

Acid stage: NMT 10% (*Q*) of the labeled amount of didanosine ($C_{10}H_{12}N_4O_3$) is dissolved in 2 h.

Buffer stage: NLT 80% (*Q*) of the labeled amount of didanosine ($C_{10}H_{12}N_4O_3$) is dissolved in 45 min.

- **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Buffer, Mobile phase, Diluent, Sample stock solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 0.1 mg/mL of USP Didanosine RS and 5 µg/mL of USP Didanosine Related Compound A RS in water

Standard solution: 5 µg/mL of USP Didanosine Related Compound A RS in water

System suitability

Sample: *System suitability solution*

Suitability requirements

Tailing factor: NMT 1.5 for the didanosine peak

Relative standard deviation: NMT 2.0% for the didanosine peak and NMT 5.0% for the didanosine related compound A peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of didanosine related compound A in the portion of Capsules taken:

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

r_U = peak response of didanosine related compound A from the *Sample solution*

r_S = peak response of didanosine related compound A from the *Standard solution*

C_S = concentration of USP Didanosine Related Compound A RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any unspecified impurities in the portion of Capsules taken:

$$\text{Result} = (r_X/r_{SUM}) \times 100$$

r_X = peak response of each impurity from the *Sample solution*

r_{SUM} = peak response of all peaks from the *Sample solution*

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Didanosine related compound A[a]	0.21	2
Didanosine	1.0	—
Any unspecified impurities	—	0.2
Total unspecified impurities	—	0.5
Total impurities	—	2.5

[a] Hypoxanthine.

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count is not more than 10^2 cfu/g. The total yeasts and molds count is not more than 10^2 cfu/g.

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards ⟨11⟩**

USP Didanosine RS

USP Didanosine Related Compound A RS

6-Hydroxypurine (Hypoxanthine).

$C_5H_4N_4O$ 136.11

Topic/Question	Contact	Expert Committee
DIDANOSINE DELAYED-RELEASE CAPSULES	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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