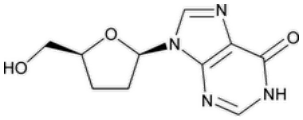
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-50705BC8-4E24-4F0F-B042-19753146E50A_5_en-US
DOI: https://doi.org/10.31003/USPNF_M25200_05_01
DOI Ref: nx6dp

Didanosine



$C_{10}H_{12}N_4O_3$ 236.23

Inosine, 2',3'-dideoxy-;

2',3'-Dideoxyinosine CAS RN®: 69655-05-6; UNII: K3GDH6OH08.

DEFINITION

Didanosine contains NLT 98.0% and NMT 102.0% of $C_{10}H_{12}N_4O_3$, calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

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

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

ASSAY

• **Procedure**

Buffer: 0.77 g/L of ammonium acetate in water

Mobile phase: Acetonitrile and *Buffer* (1:21)

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

Sample solution: 0.1 mg/mL of Didanosine in water

[Note—Mix for 1 h to dissolve completely before use.]

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; packing L1

Flow rate: 2 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

[Note—The retention time of didanosine is between 7 and 11 min.]

Suitability requirements

Column efficiency: NLT 6000 theoretical plates

Tailing factor: NMT 2.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of didanosine ($C_{10}H_{12}N_4O_3$) in the portion of Didanosine 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 the *Standard solution* (mg/mL)

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

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

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.2%

Change to read:

• **Related Compounds**

Buffer: Prepare as directed in the *Assay*.

Diluent: Adjust the pH of the *Buffer* with sodium hydroxide to 9. Prepare a mixture of acetonitrile and *Buffer* (1:19).

Solution A: Acetonitrile and *Buffer* (1:19)

Solution B: Acetonitrile and *Buffer* (1:3)

System suitability solution: 0.5 mg/mL of ▲▲ (ERR 1-Jun-2019) USP Didanosine System Suitability Mixture RS in *Diluent*

Standard stock solution A: 0.05 mg/mL of USP Didanosine Related Compound A RS in *Diluent*

Standard stock solution B: 0.025 mg/mL of USP Didanosine RS in *Diluent*

Standard stock solution C: 0.025 mg/mL of USP Didanosine Related Compound B RS in *Diluent*

Standard solution: 5 µg/mL of USP Didanosine Related Compound A RS, 1.5 µg/mL of USP Didanosine RS, and 1.5 µg/mL of USP Didanosine Related Compound B RS from a mixture of *Standard stock solution A*, *Standard stock solution B*, and *Standard stock solution C*, respectively, diluted with *Diluent*

Sample solution: 0.5 mg/mL of Didanosine in *Diluent*

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
15	100	0
20	0	100
30	0	100
35	100	0
45	100	0

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 size: 10 µL

System suitability

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

[Note—Didanosine elutes between 6 and 7.5 min; the relative retention times for didanosine, didanosine related compound A, and didanosine related compound B are 1.0, 0.28, and 2.11, respectively.]

Suitability requirements

Resolution: NLT 3.0 between didanosine and dideoxydidehydroinosine, *System suitability solution*

Column efficiency: NLT 6000 theoretical plates for dideoxydidehydroinosine, *System suitability solution*

Relative standard deviation: NMT 2.0% for didanosine related compound A, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of didanosine related compound A in the portion of Didanosine 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 = concentration of didanosine in the *Sample solution* (mg/mL)

Calculate the percentage of all other impurities in the portion of Didanosine taken:

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

r_U = peak response of each impurity in the *Sample solution*

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

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Didanosine related compound A	0.28	0.5
Inosine	0.39	0.2
2'-Deoxyinosine	0.45	0.3
3'-Deoxyinosine	0.51	0.2
2',3'-Anhydroinosine	0.59	0.2
Dideoxydidehydroinosine	0.81	0.2
Didanosine	1.0	—
Didanosine related compound B	2.1	0.2
5'-Deoxydideoxyadenosine	3.1	0.2
Any other individual, unidentified impurity	—	0.1
Total impurities	—	1.0

SPECIFIC TESTS

- **Optical Rotation,** *Specific Rotation* ⟨781S⟩
  Sample solution: 10 mg/mL in water
  Acceptance criteria: −28° to −24°, anhydrous
- **Water Determination,** *Method I* ⟨921⟩**:** NMT 2.0%

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
  Hypoxanthine.
  USP Didanosine Related Compound B RS
  2',3'-Dideoxyadenosine.
  USP Didanosine System Suitability Mixture RS

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 34(1)

Current DocID: GUID-50705BC8-4E24-4F0F-B042-19753146E50A_5_en-US

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