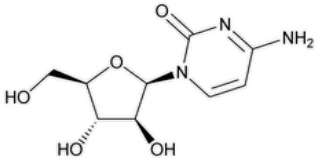


Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-AE23EDFB-4FDA-489E-8F9B-C26C800B5237_5_en-US
DOI: https://doi.org/10.31003/USPNF_M21810_05_01
DOI Ref: 8kza6

Cytarabine



$C_9H_{13}N_3O_5$ 243.22

2(1*H*)-Pyrimidinone, 4-amino-1-β-D-arabinofuranosyl-;

1-β-D-Arabinofuranosylcytosine CAS RN®: 147-94-4.

DEFINITION

Cytarabine contains NLT 98.0% and NMT 102.0% of cytarabine ($C_9H_{13}N_3O_5$), calculated on the dried basis.

Change to read:

IDENTIFICATION

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

• **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: 0.73 g/L of monobasic sodium phosphate and 1.4 g/L of dibasic sodium phosphate in water

Mobile phase: Methanol and *Solution A* (5:95)

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

System suitability solution: 0.1 mg/mL each of USP Uracil Arabinoside RS and USP Cytarabine RS in water, prepared as follows. Dissolve USP Uracil Arabinoside RS in *Standard solution*.

Sample solution: 0.1 mg/mL of Cytarabine in water

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; packing L1

Flow rate: 1.0 mL/min

Injection volume: 10 µL

[Note—After chromatography has been completed, flush the column with a mixture of water and methanol (7:3).]

System suitability

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

[Note—The relative retention times for cytarabine and uracil arabinoside are about 1.0 and 1.3, respectively.]

Suitability requirements

Resolution: NLT 2.5 between cytarabine and uracil arabinoside, *System suitability solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of cytarabine ($C_9H_{13}N_3O_5$) in the portion of Cytarabine 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 USP Cytarabine RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.5%
- **Organic Impurities**

Buffer A: 0.02 M monobasic sodium phosphate in water

Buffer B: 0.02 M dibasic sodium phosphate in water

Buffer: *Buffer A* and *Buffer B* (1:1). Adjust with 0.1 M sodium hydroxide or 0.1 M phosphoric acid to a pH of 7.0.

Solution A: Methanol and *Buffer* (2:98)

Solution B: Methanol and *Buffer* (30:70)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
10	100	0
20	0	100
25	0	100
30	100	0
50	100	0

System suitability solution: 0.02 mg/mL of USP Uridine RS, 0.02 mg/mL of USP Uracil Arabinoside RS, and 5.0 mg/mL of USP Cytarabine RS in water

Standard solution: 4 µg/mL of USP Cytarabine RS in water

Sample solution: 5 mg/mL of Cytarabine in water. Prepare this solution fresh daily.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.25 between cytarabine and uridine, *System suitability solution*

Relative standard deviation: NMT 3.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Cytarabine taken:

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

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

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

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

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Cyclocytidine[a]	0.38	1.5	0.10
Cytosine[b]	0.43	1.5	0.10
Uracil[c]	0.55	2.5	0.10
Uridine[d]	1.14	1.5	0.10
Uracil arabinoside	1.62	1.34	0.30
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.30

[a] (2*R*,3*R*,3a*S*,9a*R*)-2-(Hydroxymethyl)-6-imino-2,3,3a,9a-tetrahydro-6*H*-furo[2',3':4,5]oxazolo[3,2-a]pyrimidin-3-ol.

[b] 6-Amino-2(1*H*)-pyramidinone.

[c] Pyrimidine-2,4(1*H*,3*H*)-dione.

[d] 1-β-D-Ribofuranosylpyrimidine-2,4(1*H*,3*H*)-dione.

SPECIFIC TESTS

• **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*

Sample solution: 10 mg/mL in water

Acceptance criteria: +154° to +160°

• **Loss on Drying** ⟨731⟩

Analysis: Dry under vacuum at a pressure not exceeding 5 mm of mercury at 60° for 3 h.

Acceptance criteria: NMT 1.0%

• **Sterility Tests** ⟨71⟩**:** Where the label states that Cytarabine is sterile, it meets the requirements.

• **Bacterial Endotoxins Test** ⟨85⟩**:** Where the label states that Cytarabine is sterile or must be subjected to further processing during the preparation of injectable dosage forms, it contains NMT 0.07 USP Endotoxin Units/mg of cytarabine.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers.

• **Labeling:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

• **USP Reference Standards** ⟨11⟩

USP Cytarabine RS

USP Uracil Arabinoside RS

2,4(1*H*,3*H*)-Pyrimidinedione, 1-β-D-arabinofuranosyl-.

$C_9H_{12}N_2O_6$ 244.20

USP Uridine RS

1-β-D-Ribofuranosylpyrimidine-2,4(1*H*,3*H*)-dione.

$C_9H_{12}N_2O_6$ 244.20

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

Topic/Question	Contact	Expert Committee
CYTARABINE	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 43(6)

Current DocID: GUID-AE23EDFB-4FDA-489E-8F9B-C26C800B5237_5_en-US

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