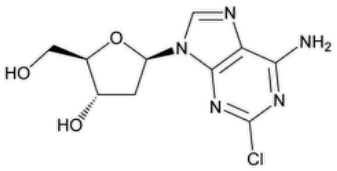
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-B96D47A0-D18A-41E1-8EEC-DE4C898E7A0F_4_en-US
DOI: https://doi.org/10.31003/USPNF_M17984_04_01
DOI Ref: p50o9

Cladribine



$C_{10}H_{12}ClN_5O_3$ 285.69

Adenosine, 2-chloro-2'-deoxy-;

2-Chloro-2'-deoxyadenosine CAS RN®: 4291-63-8; UNII: 47M74X9YT5.

DEFINITION

Cladribine contains NLT 98.0% and NMT 102.0% of cladribine ($C_{10}H_{12}ClN_5O_3$), 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 of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: Dissolve 9.96 g of triethylamine phosphate in 500 mL of water. Add another 500 mL of water, and adjust with potassium hydroxide to a pH of 6.1.

Diluent: Methanol and water (10:90)

Mobile phase: Methanol and *Buffer* (22:78)

System suitability solution: 0.02 mg/mL each of USP Cladribine RS and USP Cladribine Related Compound A RS in *Diluent*

Standard solution: 0.5 mg/mL of USP Cladribine RS in *Diluent*

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

Chromatographic system

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

Mode: LC

Detector: UV 265 nm

Column: 4.6-mm × 15-cm; packing L1

Flow rate: 1.0 mL/min

Injection volume: 10 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between the cladribine and cladribine related compound A peaks, *System suitability solution*

Tailing factor: NMT 2.0 for the cladribine peak, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of cladribine ($C_{10}H_{12}ClN_5O_3$) in the portion of Cladribine 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 Cladribine RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

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

• **Organic Impurities**

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

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 1.5 between cladribine and cladribine related compound A

Tailing factor: NMT 2.0 for the cladribine peak

Analysis

Sample: *Sample solution*

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

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

r_U = peak response of each individual impurity

r_T = sum of the responses of all the peaks

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
2,6-Diaminopurine-2'-deoxyriboside	0.41	0.20
2'-Deoxyadenosine	0.47	0.20
2-Chloroadenine	0.60	0.20
Cladribine related compound A	0.91	0.20
Any individual unspecified impurity	—	0.10
Total impurities	—	1.0

SPECIFIC TESTS

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

Sample solution: 10 mg/mL in dimethylformamide

Acceptance criteria: −17.0° to −21.0°

• **Water Determination,** *Method I* ⟨921⟩**:** NMT 4.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, and protect from light. Store between 2° and 8°.

• **USP Reference Standards** ⟨11⟩

USP Cladribine RS

USP Cladribine Related Compound A RS

2-Methoxy-2′-deoxyadenosine.

$C_{11}H_{15}N_5O_4$ 281.27

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 33(1)

Current DocID: GUID-B96D47A0-D18A-41E1-8EEC-DE4C898E7A0F_4_en-US

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