

Status: Currently Official on 14-Feb-2025
 Official Date: Official as of 01-Aug-2022
 Document Type: USP Monographs
 DocId: GUID-83B51F93-0131-48BB-A029-EA9A3C189C83_5_en-US
 DOI: https://doi.org/10.31003/USPNF_M17986_05_01
 DOI Ref: 2mu2o

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Cladribine Injection

DEFINITION

Cladribine Injection is a clear, colorless, sterile, preservative-free, isotonic solution. It contains NLT 90.0% and NMT 110.0% of the labeled amount of cladribine ($C_{10}H_{12}ClN_5O_3$).

IDENTIFICATION

- **A. [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Ultraviolet-Visible Spectroscopy: 197U](#)**

Sample solution: 0.05 mg/mL of cladribine in water

Acceptance criteria: Meets the requirements

- **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, accurately weighed, in 500 mL of water, and add another 500 mL of water. Adjust with potassium hydroxide to a pH of 6.1. [NOTE—Alternatively, dissolve 13.5 mL of triethylamine in 1 L of water, and adjust with phosphoric acid to a pH of 6.1.]

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

Diluent: Methanol and water (10:90)

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: Nominally, equivalent to 0.5 mg/mL of cladribine in *Diluent* from Injection

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 265 nm

Column: 4.6-mm × 15-cm; 5-μm packing L1

Flow rate: 1 mL/min

Injection volume: 10 μL

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between cladribine and cladribine related compound A, *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 the labeled amount of cladribine ($C_{10}H_{12}ClN_5O_3$) in the portion of Injection 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 = nominal concentration of cladribine in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• ORGANIC IMPURITIES

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

Standard solution: 0.01 mg/mL of [USP Cladribine RS](#) in *Diluent*

Chromatographic system: Proceed as directed in the Assay. In addition, the run time is NLT 2.5 times of the retention time of the cladribine peak for the *Sample solution*.

System suitability

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

Suitability requirements

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

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

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

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

C_S = concentration of [USP Cladribine RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: See [Table 1](#). Disregard any impurity peaks less than 0.1%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
2,6-Diaminopurine-2'-deoxyriboside	0.41	0.2
2'-Deoxyadenosine	0.47	0.2
2-Chloroadenine	0.60	0.5
Cladribine related compound A ^a	0.91	0.2
Cladribine	1.0	—
Any individual, unspecified impurity	—	0.2
Total impurities	—	2.0

^a 2-Methoxy-2'-deoxyadenosine.

SPECIFIC TESTS

• **BACTERIAL ENDOTOXINS TEST (85):** NMT 55 USP Endotoxin Units/mg of cladribine

• **STERILITY TESTS (71):** It meets the requirements when tested as directed for *Test for Sterility of the Product to Be Examined by Membrane Filtration*.

• **pH (791):** 5.5–8.0