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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, Membrane Filtration*.

• **pH ⟨791⟩:** 5.5–8.0

Change to read:

• ▲**Osmolality and Osmolarity** ⟨785⟩

Osmolality:▲ (Official 1-Aug-2022) 250–370 mOsmol/kg

• **Particulate Matter in Injections** ⟨788⟩**:** It meets the requirements for small-volume injections.

• **Other Requirements:** It meets the requirements under *Injections and Implanted Drug Products* ⟨1⟩.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-use clear flint glass vials. Store refrigerated at 2°–8°C. Protect from light.

• **Labeling:** Label it to indicate that it is to be diluted with 0.9% Sodium Chloride Injection USP for the single daily dose and to be diluted with bacteriostatic 0.9% Sodium Chloride Injection USP (0.9% benzyl alcohol preserved) to prepare the 7-day infusion solution.

• **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 INJECTION	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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