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Carmustine for Injection

DEFINITION

Carmustine for Injection is a sterile lyophilized preparation of carmustine. It contains NLT 90.0% and NMT 110.0% of the labeled amount of carmustine (C₅H₉Cl₂N₃O₂).

[CAUTION—Use appropriate surgical gloves, arm covers, and a dust mask. Perform all work under a fume hood approved for testing cytotoxic agents when possible.]

IDENTIFICATION

Change to read:

- A. [▲] [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy: 197F](#) ▲ (CN 1-MAY-2020)
Sample: Melt a small portion of the sample in a suitable container in a controlled water bath or oven, and set the temperature between 33° and 40°.
Standard: A similar preparation of [USP Carmustine RS](#)
- 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**

[NOTE—Prepare solutions in low-actinic glassware, and keep them refrigerated until use.]

Mobile phase: See the gradient table below.

Time (min)	Water (%)	Acetonitrile (%)
0	90	10
2.5	90	10
7	40	60
8.5	90	10
10.5	90	10

Diluent: Acetonitrile and water (1:3)
Standard stock solution: 2.0 mg/mL of [USP Carmustine RS](#) in acetonitrile
Standard solution: 0.2 mg/mL of [USP Carmustine RS](#) in *Diluent*, from *Standard stock solution*
Impurity standard stock solution: 0.1 mg/mL of [USP Carmustine Related Compound A RS](#) in acetonitrile
System suitability solution: 0.2 mg/mL of [USP Carmustine RS](#) and 0.002 mg/mL of [USP Carmustine Related Compound A RS](#) in *Diluent*, from the *Standard stock solution* and *Impurity standard stock solution*, respectively
Sample stock solution: 2.0 mg/mL of carmustine in acetonitrile, from Carmustine for Injection. [NOTE—Allow test vials to warm to room temperature in a desiccator for 1 h.]
Sample solution: 0.2 mg/mL of carmustine in *Diluent*, from the *Sample stock solution*
Chromatographic system
(See [Chromatography \(621\)](#), [System Suitability](#).)
Mode: LC
Detector: UV 200 nm
Refrigerated autosampler temperature: 5°
Column: 4.6-mm × 7.5-cm; 3-μm packing L1
Flow rate: 1.5 mL/min
Injection size: 20 μL
System suitability
Sample: *System suitability solution*
[NOTE—The relative retention times for carmustine related compound A and carmustine are 0.5 and 1.0, respectively.]

Suitability requirements**Resolution:** NLT 2.0 between carmustine related compound A and carmustine**Tailing factor:** NMT 1.5 for the carmustine related compound A and carmustine peaks**Relative standard deviation:** NMT 2.0% for the carmustine related compound A and carmustine peaks**Analysis****Samples:** *Standard solution* and *Sample solution*Calculate the percentage of carmustine ($C_5H_9Cl_2N_3O_2$) in the portion of Carmustine for Injection taken:

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

 r_U = peak area of the *Sample solution* r_S = peak area of the *Standard solution* C_S = concentration of carmustine in the *Standard solution* (mg/mL) C_U = nominal concentration of carmustine in the *Sample solution* (mg/mL)**Acceptance criteria:** 90.0%–110.0%**PERFORMANCE TESTS**

- [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meets the requirements

IMPURITIES**ORGANIC IMPURITIES**

- **PROCEDURE: LIMIT OF CARMUSTINE RELATED COMPOUND A**

Diluent, Impurity standard stock solution, System suitability solution, Sample solution, Chromatographic system, and System suitability: Proceed as directed in the Assay.**Standard solution:** 0.002 mg/mL of [USP Carmustine Related Compound A RS](#) in *Diluent*, from the *Impurity standard stock solution***Analysis****Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of carmustine related compound A in the portion of Carmustine for Injection taken:

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

 r_U = peak response of carmustine related compound A from the *Sample solution* r_S = peak response of carmustine related compound A from the *Standard solution* C_S = concentration of carmustine related compound A in the *Standard solution* (mg/mL) C_U = nominal concentration of carmustine in the *Sample solution* (mg/mL) A = assay of Carmustine for Injection, as a percentage**Acceptance criteria****Carmustine related compound A:** NMT 1.0%**SPECIFIC TESTS**

- [BACTERIAL ENDOTOXINS TEST \(85\)](#): NMT 0.95 USP Endotoxin Unit/mg of carmustine
- [STERILITY TESTS \(71\)](#): Meets the requirements
- [pH \(791\)](#): Between 4.0 and 6.8 in a constituted solution prepared as directed in the labeling
- [WATER DETERMINATION, Method I \(921\)](#): NMT 1.0%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve as described in [Packaging and Storage Requirements \(659\)](#), [Injection Packaging](#), [Packaging for constitution](#) at a temperature between 2° and 8°.
- **LABELING:** It meets the requirements in [Labeling \(7\)](#), [Labels and Labeling for Injectable Products](#).
- **CONSTITUTED SOLUTION:** At time of use, it meets the requirements in [Injections and Implanted Drug Products \(1\)](#), [Specific Tests, Completeness and clarity of solutions](#).
- [USP REFERENCE STANDARDS \(11\)](#).

[USP Carmustine RS](#)Urea, *N,N'*-bis(2-chloroethyl)-*N*-nitroso-;

1,3-Bis(2-chloroethyl)-1-nitroso-urea.

 $C_5H_9Cl_2N_3O_2$ 214.05
[USP Carmustine Related Compound A RS](#)

1,3-Bis(2-chloroethyl) urea.

 $C_5H_{10}Cl_2N_2O$ 185.05