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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 ($C_5H_9Cl_2N_3O_2$).

[**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-nitrosourea.
$C_5H_9Cl_2N_3O_2$ 214.05

USP Carmustine Related Compound A RS

1,3-Bis(2-chloroethyl) urea.
$C_5H_{10}Cl_2N_2O$ 185.05

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

Topic/Question	Contact	Expert Committee
CARMUSTINE FOR INJECTION	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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