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Lomustine Capsules

DEFINITION

Lomustine Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of lomustine ($C_9H_{16}ClN_3O_2$).

[CAUTION—Great care should be taken to prevent inhalation of particles of lomustine and to prevent exposure to the skin.]

IDENTIFICATION

• **A. [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy: 197K](#)**

Sample: Transfer the contents of 2 Capsules to a stoppered Erlenmeyer flask containing 25 mL of methylene chloride. Shake vigorously, and filter. Evaporate the methylene chloride from the filtrate under a stream of dry nitrogen. Prepare a potassium bromide pellet of the residue.

Acceptance criteria: Meet 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**

[NOTE—Protect the solutions from light. Use freshly prepared solutions.]

Mobile phase: Acetonitrile and water (7:13)

Standard solution: 0.2 mg/mL of [USP Lomustine RS](#) in acetonitrile

Sample solution: 0.2 mg/mL of lomustine in acetonitrile prepared as follows. Transfer a portion of the Capsule fill (from NLT 20 Capsules) to a suitable volumetric flask, and add acetonitrile equivalent to 75% of the volume. Shake for 15 min, and dilute with acetonitrile to volume. Pass through a suitable filter, and discard the first few mL of filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 7.5-cm; 3-μm packing L1

Flow rate: 1.5 mL/min

Injection volume: 10 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Tailing factor: NMT 1.3

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lomustine ($C_9H_{16}ClN_3O_2$) in the portion of Capsules 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 lomustine in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **ORGANIC IMPURITIES**

[NOTE—Protect the solutions from light. Use freshly prepared solutions.]

Solution A: Water

Solution B: Acetonitrile

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
3	90	10
40	65	35
47	65	35
52	50	50
55	50	50
55.1	5	95
60	5	95
60.1	90	10
65	90	10

Standard solution A: 0.032 mg/mL each of [USP Carmustine Related Compound A RS](#), [USP Lomustine Related Compound B RS](#), and [USP Lomustine Related Compound C RS](#), and 0.04 mg/mL of [USP Lomustine Related Compound D RS](#) and 2 mg/mL of [USP Lomustine RS](#) in acetonitrile

Standard solution B: 8 µg/mL of [USP Lomustine RS](#) in acetonitrile

Sample solution: 8 mg/mL of lomustine in acetonitrile prepared as follows. Transfer a portion of the Capsule fill (from NLT 20 Capsules) to a suitable volumetric flask, and dilute with acetonitrile to volume. Sonicate for 30 min, and then stir for 30 min. Pass a portion of the solution through a suitable filter of 0.2-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 195 and 230 nm

Column: 4.6-mm × 10-cm; 2.6-µm packing L43

Temperatures

Column: 35°

Sample: 15°

Flow rate: 0.8 mL/min

Injection volume: 4 µL

System suitability

Samples: *Standard solution A* and *Standard solution B*

Suitability requirements

Resolution: NLT 1.2 between the lomustine and lomustine related compound D peaks determined at 230 nm, *Standard solution A*

Relative standard deviation: NMT 10% for carmustine related compound A, lomustine related compounds B and C determined at 195 nm, *Standard solution A*; NMT 10% for lomustine determined at 230 nm, *Standard solution B*

Tailing factor: Between 0.7 and 1.3 for the lomustine peak determined at 230 nm, *Standard solution A*

Analysis

Samples: *Standard solution A*, *Standard solution B*, and *Sample solution*

Calculate the percentage of carmustine related compound A and lomustine related compounds B and C in the portion of Capsules taken:

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

r_U = peak area of each impurity from the *Sample solution*, determined at 195 nm

r_S = peak area of the corresponding related compound from *Standard solution A*, determined at 195 nm

C_S = concentration of the corresponding [USP Carmustine Related Compound A RS](#), [USP Lomustine Related Compound B RS](#), or [USP Lomustine Related Compound C RS](#) in *Standard solution A* (mg/mL)

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