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Bendamustine Hydrochloride for Injection

DEFINITION

Bendamustine Hydrochloride for Injection is a sterile, lyophilized mixture of Bendamustine Hydrochloride and Mannitol. It contains NLT 90.0% and NMT 110.0% of the labeled amount of bendamustine hydrochloride ($C_{16}H_{21}Cl_2N_3O_2 \cdot HCl$).

IDENTIFICATION

- A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

Change to read:

- B.** [▲ SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Ultraviolet-Visible Spectroscopy: 197U ▲](#) (CN 1-MAY-2020)

Sample solution: Nominally equivalent to 5 µg/mL of bendamustine hydrochloride, from Bendamustine Hydrochloride for Injection, in water

Acceptance criteria: Meets the requirements

ASSAY

PROCEDURE

Solution A: 0.1% (v/v) trifluoroacetic acid in water

Solution B: 0.1% (v/v) trifluoroacetic acid in acetonitrile

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

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	93	7
5	93	7
13	73	27
16	73	27
25	43	57
26	10	90
31	10	90
40	93	7
45	93	7

Diluent: 1-Methyl-2-pyrrolidone and *Solution A* (1:1)

Standard solution: 4.2 mg/mL of [USP Bendamustine Hydrochloride RS](#) in *Diluent*

Sample solution: Nominally equivalent to 4.2 mg/mL of bendamustine hydrochloride in *Diluent*, from Bendamustine Hydrochloride for Injection

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 5-µm packing L60

Temperatures

Autosampler: 2°–8°

Column: 30°

Flow rate: 1 mL/min
Injection volume: 2 µL
Analysis time: 25 min

System suitability

Sample: *Standard solution*

Suitability requirements

[NOTE—The slower syringe draw rate and higher detector sampling rate can be applied in order to improve the precision.]

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of bendamustine hydrochloride ($C_{16}H_{21}Cl_2N_3O_2 \cdot HCl$) in the portion of Bendamustine Hydrochloride for 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 Bendamustine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of bendamustine hydrochloride 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**

Mobile phase, Diluent, Standard solution, Sample solution, and Chromatographic system: Proceed as directed in the Assay.

System suitability solution: 4.2 mg/mL of [USP Bendamustine Hydrochloride RS](#), and 0.02 mg/mL each of [USP Bendamustine Related Compound A RS](#), [USP Bendamustine Related Compound B RS](#), [USP Bendamustine Related Compound C RS](#), [USP Bendamustine Related Compound D RS](#), [USP Bendamustine Related Compound E RS](#), [USP Bendamustine Related Compound F RS](#), [USP Bendamustine Related Compound G RS](#), [USP Bendamustine Related Compound H RS](#), and [USP Bendamustine Related Compound I RS](#) in *Diluent*

Sensitivity solution: 2 µg/mL of [USP Bendamustine Hydrochloride RS](#) in *Diluent*, from the *Standard solution*

System suitability

Samples: *System suitability solution* and *Sensitivity solution*

Suitability requirements

Resolution: NLT 5 between the bendamustine related compound G and bendamustine peaks; NLT 4 between the bendamustine related compound H and bendamustine related compound I peaks, *System suitability solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Bendamustine Hydrochloride for Injection taken:

$$\text{Result} = (r_U / \{\Sigma [r_U \times (1/F)] + r_S\}) \times (1/F) \times 100$$

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

F = relative response factor for each impurity (see [Table 2](#))

r_S = peak area of bendamustine from the *Sample solution*

Acceptance criteria: See [Table 2](#). The reporting threshold is 0.1%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Bendamustine related compound A	0.25	0.76	0.3



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