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Gemcitabine for Injection

DEFINITION

Gemcitabine for Injection contains an amount of gemcitabine hydrochloride equivalent to NLT 95% and NMT 105% of the labeled amount of gemcitabine ($C_9H_{11}F_2N_3O_4$).

[CAUTION—Gemcitabine Hydrochloride is a potent cytotoxic agent. Great care should be taken to prevent inhaling particles and exposing the skin to it.]

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Ultraviolet-Visible Spectroscopy: 197U**

Medium: 0.14 M phosphate buffer with a pH of 2.5 prepared as follows. Add 13.8 g of monobasic sodium phosphate and 2.5 mL of phosphoric acid to 1 L of water.

Sample solution: 16 µg/mL of gemcitabine in *Medium*

- **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

Mobile phase: 13.8 g of monobasic sodium phosphate and 2.5 mL of phosphoric acid in 1 L of water. [NOTE—The pH of this solution is 2.4–2.6.]

System suitability solution: Transfer 10 mg of gemcitabine hydrochloride to a small vial, add 4 mL of 168 mg/mL of potassium hydroxide in methanol, cap tightly, and sonicate. Heat at 55° for 6–16 h, allow to cool, and transfer the contents to a 100-mL volumetric flask with successive washes of 1% phosphoric acid. Dilute with 1% (v/v) phosphoric acid to volume. [NOTE—This solution contains about 0.02 mg/mL of gemcitabine α-anomer.]

Standard solution: 0.1 mg/mL of [USP Gemcitabine Hydrochloride RS](#) in water

Sample solution: Equivalent to 0.1 mg/mL of gemcitabine in water from Gemcitabine for Injection prepared as follows. Reconstitute a suitable number of vials with an appropriate amount of water, based on the labeled amount of gemcitabine.

Chromatographic system

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

Mode: LC

Detector: UV 275 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Flow rate: 1.2 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for gemcitabine α-anomer and gemcitabine are about 0.5 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 8.0 between gemcitabine α-anomer and gemcitabine, *System suitability solution*

Tailing factor: NMT 1.5 for the gemcitabine peak, *System suitability solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of gemcitabine ($C_9H_{11}F_2N_3O_4$) in the portion of Gemcitabine for Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_s = peak response from the *Standard solution*

C_s = concentration of [USP Gemcitabine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

C_u = nominal concentration of gemcitabine in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of gemcitabine, 263.20

M_{r2} = molecular weight of gemcitabine hydrochloride, 299.66

Acceptance criteria: 95%–105%

PERFORMANCE TESTS

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

IMPURITIES

Change to read:

• ORGANIC IMPURITIES

System suitability solution and **Chromatographic system:** Proceed as directed in the Assay.

Solution A: Use the *Mobile phase* as directed in the Assay.

Solution B: Methanol

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

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	97	3
8	97	3
13	50	50
20	50	50
25	97	3

Standard solution: 2 µg/mL each of [USP Gemcitabine Hydrochloride RS](#) and [USP Cytosine RS](#) in water

Sample solution: Equivalent to 2 mg/mL of gemcitabine in water prepared by reconstituting the vial with an appropriate amount of water, based on the labeled amount of gemcitabine

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 8.0 between gemcitabine α -anomer and gemcitabine, *System suitability solution*

Tailing factor: NMT 1.5 for the gemcitabine peak, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of cytosine, expressed as a percentage of gemcitabine hydrochloride ($C_9H_{11}F_2N_3O_4 \cdot HCl$), in the portion of Gemcitabine for Injection taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times (M_{r1}/M_{r2}) \times 100$$

r_u = peak response of cytosine from the *Sample solution*

r_s = peak response of cytosine from the *Standard solution*

C_s = concentration of [USP Cytosine RS](#) in the *Standard solution* (mg/mL)