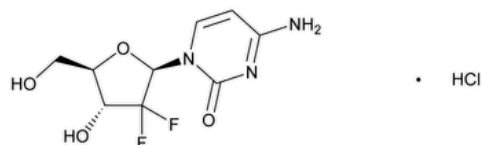


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Gemcitabine Hydrochloride



$C_9H_{11}F_2N_3O_4 \cdot HCl$ 299.66

Cytidine, 2'-deoxy-2',2'-difluoro-, monohydrochloride;

2'-Deoxy-2',2'-difluorocytidine monohydrochloride (β-isomer) CAS RN[®]: 122111-03-9; UNII: U347PV74IL.

DEFINITION

Gemcitabine Hydrochloride contains NLT 97.5% and NMT 101.5% of gemcitabine hydrochloride ($C_9H_{11}F_2N_3O_4 \cdot HCl$), calculated on the as-is basis.

[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), Infrared Spectroscopy:** 197A or 197K.

Meets the requirements

- **B. IDENTIFICATION TESTS—GENERAL (191), Chemical Identification Tests, Chloride:** Meets the requirements
- **C.** 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: 0.1 mg/mL of Gemcitabine Hydrochloride in [water](#)

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 gemcitabine hydrochloride ($C_9H_{11}F_2N_3O_4 \cdot HCl$) in the portion of Gemcitabine Hydrochloride 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 Gemcitabine Hydrochloride RS](#) in the *Standard solution* (mg/mL) C_U = concentration of Gemcitabine Hydrochloride in the *Sample solution* (mg/mL)**Acceptance criteria:** 97.5%–101.5% on the as-is basis**IMPURITIES**

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

Change to read:

- **ORGANIC IMPURITIES**

System suitability solution and **Chromatographic system:** Proceed as directed in the Assay.**Solution A:** Use the *Mobile phase*, prepared 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: 0.002 mg/mL each of [USP Gemcitabine Hydrochloride RS](#) and [USP Cytosine RS](#) in [water](#)**Sample solution:** 2 mg/mL of Gemcitabine Hydrochloride in [water](#)**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 in the portion of Gemcitabine Hydrochloride taken:

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

 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)