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Ganciclovir for Injection

DEFINITION

Ganciclovir for Injection is a freeze-dried powder prepared by the neutralization of Ganciclovir with the aid of Sodium Hydroxide. It contains NLT 90.0% and NMT 110.0% of the labeled amount of ganciclovir ($C_9H_{13}N_5O_4$), calculated on the anhydrous basis.

[**Caution—**Handle Ganciclovir for Injection with great care because it is a potent cytotoxic agent and suspected carcinogen.]

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*.

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Aug-2024)

ASSAY

Change to read:

• **Procedure**

Mobile phase: ▲Dissolve 1.4 g of monobasic ammonium phosphate in 500 mL of water. Add 1.2 mL of 85% phosphoric acid and dilute with water to 1000 mL.▲ (USP 1-Aug-2024)

Internal standard solution: 0.15 mg/mL of hypoxanthine in water

Standard stock solution: 0.25 mg/mL of USP Ganciclovir RS in water

Standard solution: 0.05 mg/mL of USP Ganciclovir RS prepared as follows. Transfer a suitable volume of the *Standard stock solution*, add 10% of the flask volume of the *Internal standard solution*, and dilute with *Mobile phase* to volume.

Sample stock solution: Nominally 1 mg/mL of ganciclovir, from Ganciclovir for Injection in water

Sample solution: Nominally 0.05 mg/mL of ganciclovir prepared as follows. Transfer a suitable volume of the *Sample stock solution*, add 10% of the flask volume of the *Internal standard solution*, and dilute with *Mobile phase* to volume.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 254 nm. ▲For *Identification B*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-Aug-2024)

Column: ▲4.6-mm × 25-cm; 5-µm packing L1▲ (USP 1-Aug-2024)

Flow rate: 1.2 mL/min

Injection volume: 10 µL

▲**Run time:** NLT 1.5 times the retention time of ganciclovir▲ (USP 1-Aug-2024)

System suitability

Sample: *Standard solution*

[Note—The relative retention times for hypoxanthine and ganciclovir are about ▲0.55▲ (USP 1-Aug-2024) and 1.0, respectively.]

Suitability requirements

▲▲ (USP 1-Aug-2024)

Tailing factor: NMT 2.0 ▲for ganciclovir▲ (USP 1-Aug-2024)

Relative standard deviation: NMT 2.0% ▲for the peak response ratio of ganciclovir to hypoxanthine▲ (USP 1-Aug-2024)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ganciclovir ($C_9H_{13}N_5O_4$) in the portion of Ganciclovir for Injection taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak response ratio of ganciclovir to the internal standard from the *Sample solution*

R_S = peak response ratio of ganciclovir to the internal standard from the *Standard solution*

C_S = concentration of USP Ganciclovir RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0% on the anhydrous basis

Add the following:

▲IMPURITIES

• **Organic Impurities**

Mobile phase, Internal standard solution, Standard stock solution, Standard solution, Sample stock solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Guanine stock solution: 0.05 mg/mL of USP Guanine RS prepared as follows. Weigh and transfer a suitable quantity of USP Guanine RS to a suitable volumetric flask. Add water to 50% of the flask volume and 1.5% of the flask volume of hydrochloric acid, and sonicate to dissolve. Dilute with water to volume.

Guanine solution: 0.005 mg/mL of USP Guanine RS in *Mobile phase* from *Guanine stock solution*

Sensitivity solution: 0.05 µg/mL each of USP Ganciclovir RS and USP Guanine RS in *Mobile phase*, prepared from the *Standard stock solution* and *Guanine solution*

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Relative standard deviation: NMT 2.0% for the peak response ratio of ganciclovir to hypoxanthine, *Standard solution*

Tailing factor: NMT 2.0 for ganciclovir, *Standard solution*

Signal-to-noise ratio: NLT 10 for each guanine and ganciclovir, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each degradation product in the portion of Ganciclovir for Injection taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times (1/F) \times 100$$

R_U = peak response ratio of each degradation product to the internal standard from the *Sample solution*

R_S = peak response ratio of ganciclovir to the internal standard from the *Standard solution*

C_S = concentration of USP Ganciclovir RS in the *Standard solution* (mg/mL)

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

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. The reporting threshold is 0.1%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Guanine	0.36	1.4	1.0
Ganciclovir	1.0	—	—
Any unspecified degradation product	—	1.0	0.2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Total degradation products	—	—	1.0▲ (USP 1-Aug-2024)

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample: Constituted as directed in the labeling.

Acceptance criteria: 10.8–11.4

• **Water Determination** ⟨921⟩, *Method I*

Analysis: Proceed as directed in the chapter, except for the following modifications. Use a mixture of anhydrous formamide and methanol (1:1) instead of methanol as the titration vessel solvent. The reagent volume required to condition the titration vessel solvent is NMT 10% of the initial volume of solvent. The concentration of Ganciclovir for Injection in the titration vessel is NMT 7 mg/mL.

Acceptance criteria: NMT 3.0%

Change to read:

• **Bacterial Endotoxins Test** ⟨85⟩**:** ▲Meets the requirements▲ (USP 1-Aug-2024)

• **Particulate Matter in Injections** ⟨788⟩**:** Meets the requirements for small-volume injections

Change to read:

• **Sterility Tests** ⟨71⟩**:** Meets the requirements ▲▲ (USP 1-Aug-2024)

• **Injections and Implanted Drug Products** ⟨1⟩**:** At the time of use, it meets the requirements for *Constituted Solutions*.

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** ▲Preserve in tightly closed containers. Store at controlled room temperature.▲ (USP 1-Aug-2024)

• **Labeling:** Label it to state that it is to be handled with great care because it is a potent cytotoxic agent and suspected carcinogen.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Ganciclovir RS

▲ USP Guanine RS

2-Amino-1,7-dihydro-6*H*-purin-6-one.

$C_5H_5N_5O$ 151.13▲ (USP 1-Aug-2024)

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

Topic/Question	Contact	Expert Committee
GANCICLOVIR FOR INJECTION	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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