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# Cidofovir Injection

## DEFINITION

Cidofovir Injection is a sterile aqueous solution. It contains an amount of cidofovir equivalent to NLT 95.0% and NMT 105.0% of the labeled amount of anhydrous cidofovir ($C_8H_{14}N_3O_6P$).

## IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*:** 197U

  **Standard solution:** 7.5 µg/mL of USP Cidofovir RS in water. Adjust with 0.1 N sodium hydroxide to a pH of 7.5.

  **Sample solution:** Nominally 7.5 µg/mL of cidofovir from Injection in water

  **Acceptance criteria:** Meets 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**

  **Solution A:** Acetonitrile and water (40:60)

  **Buffer:** Dissolve 1.2 g of dibasic ammonium phosphate and 2.0 g of tetrabutylammonium phosphate in 1 L of water. Adjust with ammonium hydroxide to a pH of 9.2.

  **Mobile phase:** *Solution A* and *Buffer* (20:80)

  **Standard solution:** 0.17 mg/mL of USP Cidofovir RS in water. [Note—0.17 mg/mL of USP Cidofovir RS is equivalent to 0.15 mg/mL of cidofovir on the anhydrous basis.]

  **Sample solution:** Nominally 0.15 mg/mL of cidofovir from Injection in water

  **Chromatographic system**

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

  **Mode:** LC

  **Detector:** UV 274 nm

  **Column:** 4.6-mm × 25-cm; 5-µm packing L1

  **Temperatures**

  **Autosampler:** 10°

  **Column:** 30°

  **Flow rate:** 1 mL/min

  **Injection volume:** 20 µL

  **System suitability**

  **Sample:** *Standard solution*

  **Suitability requirements**

  **Tailing factor:** NMT 1.5

  **Relative standard deviation:** NMT 2.0%

  **Analysis**

  **Samples:** *Standard solution* and *Sample solution*

  Calculate the percentage of the labeled amount of anhydrous cidofovir ($C_8H_{14}N_3O_6P$) in the portion of Injection taken:

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

  $r_U$ = peak response of cidofovir from the *Sample solution*

  $r_S$ = peak response of cidofovir from the *Standard solution*

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

$C_U$ = nominal concentration of anhydrous cidofovir in the *Sample solution* (mg/mL)

**Acceptance criteria:** 95.0%–105.0% on the anhydrous basis

## IMPURITIES

• **Organic Impurities**

**Mobile phase** and **Chromatographic system:** Proceed as directed in the *Assay* with a run time NLT 4.5 times the retention time of cidofovir.

**Standard solution:** 0.0015 mg/mL of USP Cidofovir RS in water

**Sample solution:** Nominally 1.5 mg/mL of anhydrous cidofovir from Injection in water

**System suitability**

**Sample:** *Standard solution*

**Suitability requirements**

**Relative standard deviation:** NMT 5.0%

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Injection taken:

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

$r_U$ = peak response of each individual impurity from the *Sample solution*

$r_S$ = peak response of cidofovir from the *Standard solution*

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

$C_U$ = nominal concentration of anhydrous cidofovir in the *Sample solution* (mg/mL)

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

**Acceptance criteria:** See *Table 1*.

**Table 1**

| Name | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|---|---|---|---|
| Cidofovir diol analog[a,b] | 0.30 | — | — |
| Cidofovir related compound A[b] | 0.54 | — | — |
| Cidofovir related compound B[b] | 0.63 | — | — |
| Cidofovir | 1.0 | — | — |
| Cidofovir uracil analog[c] | 1.4 | 0.59 | 6.0 |
| Bromocidofovir[b,d] | 2.0 | — | — |
| Any individual unspecified impurity | — | — | 0.2 |
| Total impurities | — | — | 6.0 |

[a] 1-[(*S*)-2,3-Dihydroxypropyl]cytosine.

[b] These are included in the table for identification only. These are process impurities controlled in the drug substance. They are not to be included in the total impurities.

[c] 1-[(*S*)-3-Hydroxy-2-(phosphonomethoxy)propyl]uracil.

[d] 1-[(*S*)-3-Bromo-2-(phosphonomethoxy)propyl]cytosine.

**SPECIFIC TESTS**

- **pH ⟨791⟩:** 7.1–7.7
- **Particulate Matter in Injections ⟨788⟩:** Meets the requirements
- **Bacterial Endotoxins Test ⟨85⟩:** NMT 1 USP Endotoxin Unit/mg of anhydrous cidofovir
- **Sterility Tests ⟨71⟩:** Meets the requirements

***Change to read:***

- **▲Osmolality and Osmolarity ⟨785⟩**

**Osmolarity:** ▲ (Official 1-Aug-2022) 550–650 mOsmol/L

- **Other Requirements:** Meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*

**ADDITIONAL REQUIREMENTS**

- **Packaging and Storage:** Preserve in single-dose containers. Store at controlled room temperature.
- **USP Reference Standards ⟨11⟩**

USP Cidofovir RS
USP Endotoxin RS

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| CIDOFOVIR INJECTION | Documentary Standards Support | SM12020 Small Molecules 1 |

**Chromatographic Database Information:** Chromatographic Database

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