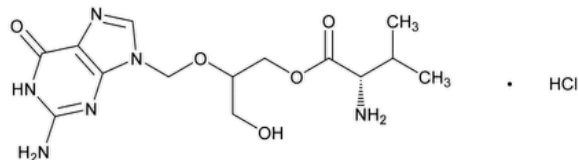


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Valganciclovir Hydrochloride



$C_{14}H_{22}N_6O_5 \cdot HCl$ 390.82

L-Valine, ester with 9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]guanine, monohydrochloride.

L-Valine, 2-[(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)methoxy]-3-hydroxypropyl ester, monohydrochloride CAS RN®: 175865-59-5; UNII: 4P3T9QF9NZ.

DEFINITION

Valganciclovir Hydrochloride contains NLT 97.0% and NMT 102.0% of valganciclovir hydrochloride ($C_{14}H_{22}N_6O_5 \cdot HCl$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K
- **B.** The retention times of valganciclovir diastereomeric peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.
- **C. IDENTIFICATION TESTS—GENERAL (191), Chloride:** Meets the requirements

ASSAY

PROCEDURE

Buffer: 11.5 g/L of [monobasic ammonium phosphate](#) in [water](#). Adjust with [phosphoric acid](#) (85%) to a pH of 2.8 ± 0.2 prior to final dilution.

Mobile phase: [Methanol](#) and *Buffer* (8:92)

System suitability solution: 0.2 mg/mL of [USP Valganciclovir Hydrochloride RS](#) and 0.01 mg/mL of [USP Methoxymethylguanine RS](#) in [0.001 N hydrochloric acid](#)

Standard solution: 0.2 mg/mL of [USP Valganciclovir Hydrochloride RS](#) in [0.001 N hydrochloric acid](#)

Sample solution: 0.2 mg/mL of Valganciclovir Hydrochloride in [0.001 N hydrochloric acid](#)

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 3.5-μm packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 20 μL

Run time: NLT 2.5 times the retention time of valganciclovir diastereomer peak 2

System suitability

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

[NOTE—The relative retention times for methoxymethylguanine and valganciclovir diastereomer peak 1 are 0.93 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.0 between methoxymethylguanine and valganciclovir diastereomer peak 1; NLT 3.0 between valganciclovir diastereomer peak 1 and valganciclovir diastereomer peak 2, *System suitability solution*

Tailing factor: NMT 2.0 for valganciclovir diastereomer peak 2, *System suitability solution*

Relative standard deviation: NMT 1.0% for the sum of valganciclovir diastereomer peak 1 and valganciclovir diastereomer peak 2, *Standard solution*

Analysis**Samples:** *Standard solution* and *Sample solution*Calculate the percentage of valganciclovir hydrochloride ($C_{14}H_{22}N_6O_5 \cdot HCl$) in the portion of Valganciclovir Hydrochloride taken:

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

 r_U = sum of the peak responses of valganciclovir diastereomer peaks 1 and 2 from the *Sample solution* r_S = sum of the peak responses of valganciclovir diastereomer peaks 1 and 2 from the *Standard solution* C_S = concentration of [USP Valganciclovir Hydrochloride RS](#) in the *Standard solution* (mg/mL) C_U = concentration of Valganciclovir Hydrochloride in the *Sample solution* (mg/mL)**Acceptance criteria:** 97.0%–102.0% on the anhydrous and solvent-free basis**IMPURITIES**• **RESIDUE ON IGNITION (281):** NMT 0.10%• **LIMIT OF ISOPROPYL ALCOHOL****Internal standard solution:** Transfer 0.1 mL of [1,4-dioxane](#) to a 100-mL volumetric flask and dilute with [dimethylformamide](#) to volume.**Standard stock solution:** Transfer 1.0 mL of [isopropyl alcohol](#) and 0.1 mL of [toluene](#) to a 100-mL volumetric flask, and dilute with [dimethylformamide](#) to volume. [NOTE—Toluene is used to verify the system suitability.]**Standard solution:** Combine 2.0 mL of the *Internal standard solution* and 0.1 mL of the *Standard stock solution*.**Sample solution:** Transfer 90–100 mg of Valganciclovir Hydrochloride to a vial, add 2.0 mL of the *Internal standard solution*, and mix.**Chromatographic system**(See [Chromatography \(621\)](#), [System Suitability](#).)**Mode:** GC**Detector:** Flame ionization**Column:** 0.53-mm × 30-m capillary; coated with 3.0-μm film of phase [G43](#)**Carrier gas:** Helium**Temperatures****Injection port:** 250°**Detector:** 300°**Column:** See [Table 1](#).**Table 1**

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
40	—	40	10
40	25	240	—
240	—	240	15

Flow rate: 10.5 mL/min**Injection volume:** 0.5 μL**Injection type:** Split, split ratio 1:1**System suitability****Sample:** *Standard solution***Suitability requirements****Resolution:** NLT 8 between 1,4-dioxane and toluene**Relative standard deviation:** NMT 15% of the peak area ratio of isopropyl alcohol to 1,4-dioxane**Analysis****Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of isopropyl alcohol in the portion of Valganciclovir Hydrochloride taken:

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

R_U = peak area ratio of isopropyl alcohol to the internal standard from the *Sample solution*

R_S = peak area ratio of isopropyl alcohol to the internal standard from the *Standard solution*

C_S = concentration of isopropyl alcohol in the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 1.0%

Change to read:

• **ORGANIC IMPURITIES**

Solution A: 11.5 g/L of [monobasic ammonium phosphate](#) in [water](#). Adjust with [phosphoric acid](#) (85%) to a pH of 2.8 ± 0.2 prior to final dilution.

Solution B: [Methanol](#)

Mobile phase: See [Table 2](#).

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	92	8
5	92	8
15	80	20
30	30	70
30.1	92	8
45	92	8

System suitability solution: 0.2 mg/mL of [USP Valganciclovir Hydrochloride RS](#) and 0.01 mg/mL of [USP Methoxymethylguanine RS](#) in [0.001 N hydrochloric acid](#)

Sample solution: 0.2 mg/mL of Valganciclovir Hydrochloride in [0.001 N hydrochloric acid](#)

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 3.5-μm packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 20 μL

System suitability

Sample: *System suitability solution*

[NOTE— See [Table 3](#) for the relative retention times.]

Suitability requirements

Resolution: NLT 1.0 between methoxymethylguanine and valganciclovir diastereomer peak 1; NLT 3.0 between valganciclovir diastereomer peak 1 and valganciclovir diastereomer peak 2

Tailing factor: NMT 2.0 for valganciclovir diastereomer peak 2

Analysis

Sample: *Sample solution*

Calculate the percentage of any individual impurity in the portion of Valganciclovir Hydrochloride taken:

$$\text{Result} = \{(r_i/F_i)/[r_s + \Sigma(r_i/F_i)]\} \times 100$$

r_i = peak response for each individual impurity in the *Sample solution*