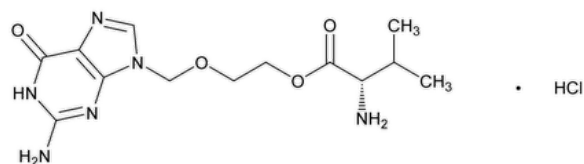


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Valacyclovir Hydrochloride



$C_{13}H_{20}N_6O_4 \cdot HCl$ 360.80

L-Valine, 2-[(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)methoxy] ethyl ester, monohydrochloride;

L-Valine, ester with 9-[(2-hydroxyethoxy)methyl]guanine, monohydrochloride CAS RN®: 124832-27-5; UNII: G447S0T1VC.

DEFINITION

Valacyclovir Hydrochloride contains NLT 95.0% and NMT 102.0% of valacyclovir hydrochloride ($C_{13}H_{20}N_6O_4 \cdot HCl$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

Change to read:

- **C. IDENTIFICATION TESTS—GENERAL (191), Chemical Identification Tests, Chloride**

Sample solution: 50 mg/mL ▲ of Valacyclovir Hydrochloride ▲ (USP 1-May-2023) in [water](#)

Acceptance criteria: Meets the requirements

ASSAY

Change to read:

PROCEDURE

Mobile phase: [Methanol](#), [water](#), and [perchloric acid](#) ▲ (5: 95: 0.5) ▲ (USP 1-May-2023)

Standard solution: 0.5 mg/mL of [USP Valacyclovir Hydrochloride RS](#) in 0.05 M [hydrochloric acid](#). [NOTE—[USP Valacyclovir Hydrochloride RS](#) contains a detectable quantity of D-valacyclovir.]

Sample solution: 0.5 mg/mL of Valacyclovir Hydrochloride in 0.05 M [hydrochloric acid](#)

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4-mm × 15-cm; 5-μm packing [L66](#)

Column temperature: 10°

Flow rate: 0.75 mL/min

Injection volume: 10 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between valacyclovir hydrochloride and D-valacyclovir

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of valacyclovir hydrochloride ($C_{13}H_{20}N_6O_4 \cdot HCl$) in the portion of Valacyclovir Hydrochloride taken:

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

r_U = peak response of valacyclovir from the *Sample solution*

r_S = peak response of valacyclovir from the *Standard solution*

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

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

Acceptance criteria: 95.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#)

Sample: 2 g

Acceptance criteria: NMT 0.1%

Delete the following:

▲ • **LIMIT OF PALLADIUM** (if present) ▲ (USP 1-May-2023)

Change to read:

• **ORGANIC IMPURITIES, PROCEDURE 1** (for related compounds E, F, and G)

Developing solvent: [Methylene chloride](#), [methanol](#), [tetrahydrofuran](#), and ammonia solution (54:34:12:3)

Standard stock solution: Transfer 5 mg each of [USP Valacyclovir Related Compound D RS](#) and [USP Valacyclovir Related Compound G RS](#), 10 mg of [USP Valacyclovir Related Compound E RS](#), and 8.4 mg of [USP Valacyclovir Related Compound F RS](#) into a 10-mL volumetric flask.

Add 2 mL of [water](#) with swirling, followed by 6 mL of [alcohol](#), and sonicate for 20 min. Allow to cool, and dilute with [alcohol](#) to volume.

Standard solutions: Transfer 1.0 and 0.5 mL of the *Standard stock solution* into two separate 10-mL volumetric flasks. Dilute the solution in both flasks with [alcohol](#) to volume.

Sample solution: Transfer 250 mg of Valacyclovir Hydrochloride into a 5-mL volumetric flask. Add 2 mL of [water](#), and sonicate for 20 min to dissolve. Add [alcohol](#) to about 95% of the flask volume. Cool, and dilute with [alcohol](#) to volume. Pass through a suitable filter of 0.45-μm pore size.

Chromatographic system

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

Mode: TLC

Detector: UV, long and short wavelength

Plate: TLC plate coated with a 0.25-mm layer of chromatographic silica gel mixture. Prewash the plate with [methanol](#).

Developing distance: NLT 7 cm from the origin

Application volume: 4 μL

Analysis

Samples: *Standard solutions* and *Sample solution*

Develop the plate to the specified distance. Remove the plate from the solvent chamber, and allow to dry. Examine the plate under short-wavelength UV light, and visually estimate the valacyclovir related compounds E and G in the sample using the appropriate standard spots. The chromatograms obtained with the *Standard solutions* each show three clearly separated spots due to valacyclovir related compounds D, E, and G. Spray the plate with 0.01% [fluorescamine](#) in [ethylene dichloride](#), and examine the sprayed plate under long-wavelength UV light to estimate the level of valacyclovir related compound F in the sample using the appropriate standard spot. The relative R_F values and limits for each impurity are provided in [Table 1](#).

Acceptance criteria: See [Table 1](#).

Table 1

Name	Relative R_F Value	Acceptance Criteria, NMT (%)
Valacyclovir hydrochloride	1	—
Valacyclovir related compound D ^a	1.1	—
Valacyclovir related compound E ^b	1.3	—