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Valacyclovir Tablets

DEFINITION

Valacyclovir Tablets contain an amount of Valacyclovir Hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of valacyclovir ($C_{13}H_{20}N_6O_4$).

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*.
- **B. Identification Tests—General, *Chloride*⟨191⟩:** Meet the requirements

ASSAY

- **Procedure**

Diluent: 0.1% (v/v) phosphoric acid in water

Mobile phase: Methanol and *Diluent* (5:95)

Standard solution: 0.1 mg/mL of USP Valacyclovir Hydrochloride RS in *Diluent*. [Note—USP Valacyclovir Hydrochloride RS contains a detectable quantity of D-valacyclovir.]

Sample solution: Transfer NLT 5 Tablets into a suitable volumetric flask, and add 0.1 M hydrochloric acid (approximately 80% of the volume of the flask). Mechanically shake the sample until the Tablets disintegrate into a fine suspension (60 min), and sonicate for 10 min. Cool to ambient temperature, dilute with 0.1 M hydrochloric acid to volume, and mix to obtain a solution having a concentration of 2.5 mg/mL. Dilute a portion of the sample with *Diluent* to obtain a nominal concentration of 0.1 mg/mL of valacyclovir, and mix. Pass a portion of this solution through a membrane filter of 0.45-µm or finer pore size, and use the filtrate.

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 1.3 between the D-valacyclovir and valacyclovir peaks

Tailing factor: NMT 2.0 for the valacyclovir peak

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of valacyclovir ($C_{13}H_{20}N_6O_4$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

M_{r1} = molecular weight of valacyclovir, 324.34

M_{r2} = molecular weight of valacyclovir hydrochloride, 360.80

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Test 1

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Diluent: Prepare as directed in the *Assay*.

Mobile phase: Acetonitrile and *Diluent* (5:95)

Standard solution: Prepare a solution in *Diluent* containing USP Valacyclovir Hydrochloride RS equivalent to 0.044 mg/mL of valacyclovir free base.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Dilute with *Diluent* to obtain a final concentration of about 0.044 mg/mL of valacyclovir free base considering complete dissolution of the Tablet label claim.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 5-cm, 5-µm packing L1

Flow rate: 2.0 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of valacyclovir ($C_{13}H_{20}N_6O_4$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (M_{r1}/M_{r2}) \times (1/L) \times D \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

V = volume of *Medium*, 900 mL

M_{r1} = molecular weight of valacyclovir, 324.34

M_{r2} = molecular weight of valacyclovir hydrochloride, 360.80

L = label claim (mg/Tablet)

D = dilution factor of the *Sample solution*

Tolerances: NLT 75% (Q) of the labeled amount of valacyclovir ($C_{13}H_{20}N_6O_4$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Analytical wavelength: 252 nm

Cell: 0.02 cm

Blank: *Medium*

Standard solution

For Tablets labeled to contain 500 mg: 0.6 mg/mL of USP Valacyclovir Hydrochloride RS in *Medium*. A small volume of methanol, not exceeding 5% of the final volume, may be used to help solubilize valacyclovir.

For Tablets labeled to contain 1000 mg: 1.2 mg/mL of USP Valacyclovir Hydrochloride RS in *Medium*. A small volume of methanol, not exceeding 5% of the final volume, may be used to help solubilize valacyclovir.

Sample solution: Pass a portion of the solution under test through a filter of 0.45-µm pore size. Discard the first 3 mL of sample filtrate.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of valacyclovir ($C_{13}H_{20}N_6O_4$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (M_{r1}/M_{r2}) \times (1/L) \times D \times 100$$

r_U = absorbance of the *Sample solution*

r_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

M_{r1} = molecular weight of valacyclovir, 324.34

M_{r2} = molecular weight of valacyclovir hydrochloride, 360.80

L = label claim (mg/Tablet)

D = dilution factor of the *Sample solution*

Tolerances: NLT 80% (Q) of the labeled amount of valacyclovir ($C_{13}H_{20}N_6O_4$) is dissolved.

Change to read:

• **Uniformity of Dosage Units ⟨905⟩:** ▲Meet the requirements▲ (CN 1-Aug-2023)

Procedure for content uniformity

[Note—All of the concentrations are expressed as valacyclovir free base.]

Diluent: Prepare as directed in the *Assay*.

Mobile phase: Acetonitrile and *Diluent* (5:95)

Standard solution: Prepare a solution of USP Valacyclovir Hydrochloride RS, equivalent to 0.04 mg/mL of valacyclovir, in *Diluent*.

Sample solution: Transfer 1 Tablet into a suitable volumetric flask. Add *Diluent* (approximately 60% of the volume of the flask), and mechanically shake the samples until the Tablet disintegrates into a fine suspension, and sonicate for 10 min. Cool, dilute with *Diluent* to volume, and mix. Dilute a portion of each sample with *Diluent* to obtain a nominal concentration of 0.04 mg/mL of valacyclovir. Pass a portion of each sample through a membrane filter of 0.45-µm pore size, and use the filtrate.

Chromatographic system and **System suitability:** Proceed as directed in *Dissolution*, *Test 1*.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of valacyclovir ($C_{13}H_{20}N_6O_4$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

M_{r1} = molecular weight of valacyclovir, 324.34

M_{r2} = molecular weight of valacyclovir hydrochloride, 360.80

▲▲ (CN 1-Aug-2023)

IMPURITIES

• **Organic Impurities**

Diluent, Mobile phase, Standard solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of D-valacyclovir and acyclovir in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times (1/F) \times 100$$

r_U = peak response of D-valacyclovir or acyclovir from the *Sample solution*

r_S = peak response of USP Valacyclovir Hydrochloride RS from the *Standard solution*

C_S = concentration of valacyclovir hydrochloride in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of valacyclovir, 324.34

M_{r2} = molecular weight of valacyclovir hydrochloride, 360.80

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

Acceptance criteria

Individual impurities: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
D-Valacyclovir[a]	0.82	1.0	—
Acyclovir[b]	0.56	1.4	2.5

[a] D-Valine, 2-[(2-amino-1,6-dihydro-6-oxo-9*H*-purin-9-yl)methoxy] ethyl ester, monohydrochloride. [Note—This is a process impurity.]

[b] 2-Amino-9-[(2-hydroxyethoxy)methyl]-1,9-dihydro-6*H*-purin-6-one (acyclovir).

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.

• **Labeling:** When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used.

• **USP Reference Standards** ⟨11⟩

USP Valacyclovir Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
VALACYCLOVIR TABLETS	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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