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Valganciclovir Tablets

DEFINITION
Valganciclovir Tablets contain NLT 93.0% and NMT 105.0% of the labeled amount of valganciclovir ($C_{14}H_{22}N_6O_5$).

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**▲ (CN 1-May-2020)

Sample solution: 10 µg/mL in 0.001 M hydrochloric acid
Wavelength range: 200–350 nm
Medium: 0.001 M hydrochloric acid
Acceptance criteria: Meet the requirements

• **B.** The retention time of the diastereomeric peaks of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: Dilute 2.5 mL of triethylamine with water to 1000 mL, and adjust with trifluoroacetic acid to a pH of 3.0 ± 0.05.
Mobile phase: Methanol and *Buffer* (7:93)
Diluent: 1 mM hydrochloric acid
System suitability solution: 0.1 µg/mL of USP Ganciclovir Mono-N-methyl Valinate RS and 78 µg/mL of USP Valganciclovir Hydrochloride RS in *Diluent*
Standard solution: 0.09 mg/mL of USP Valganciclovir Hydrochloride RS in *Diluent*. Pass a portion of the solution through a filter of 0.45-µm or finer pore size, and use the filtrate, discarding the initial 2 mL.
Sample stock solution: Nominally 5 mg/mL of valganciclovir hydrochloride prepared as follows. Transfer 5 Tablets into a 500-mL volumetric flask, add about 300 mL of *Diluent*, and shake well until the Tablets are fully disintegrated. Dilute with *Diluent* to volume, mix, and allow the solution to settle.
Sample solution: Nominally 0.075 mg/mL of valganciclovir hydrochloride prepared as follows. Transfer 3.0 mL of the supernatant from the *Sample stock solution* into a 200-mL volumetric flask, and dilute with *Diluent* to volume. Pass a portion of this solution through a filter of 0.45-µm or finer pore size, and use the filtrate, discarding the initial 2 mL.
Chromatographic system
(See *Chromatography ⟨621⟩, System Suitability*.)
Mode: LC
Detector: UV 254 nm
Column: 4.6-mm × 15-cm; packing L11
Column temperature: 30°
Flow rate: 1 mL/min
Injection volume: 50 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
Suitability requirements
Resolution: NLT 2.0 between the second diastereomeric valganciclovir peak and the first ganciclovir mono-*N*-methyl valinate peak, *System suitability solution*
Column efficiency: NLT 3000 theoretical plates for the second diastereomeric valganciclovir peak, *Standard solution*
Tailing factor: NMT 3 for the second diastereomeric valganciclovir peak, *Standard solution*
Relative standard deviation: NMT 2.0% for the total areas of the two valganciclovir peaks, *Standard solution*
Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of valganciclovir ($C_{14}H_{22}N_6O_5$) 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 = sum of the peak responses of the valganciclovir diastereomers from the *Sample solution*

r_S = sum of the peak responses of the valganciclovir diastereomers from the *Standard solution*

C_S = concentration of USP Valganciclovir Hydrochloride RS in the *Standard solution*, corrected for water content (mg/mL)

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

M_{r1} = molecular weight of valganciclovir, 354.36

M_{r2} = molecular weight of valganciclovir hydrochloride, 390.82

Acceptance criteria: 93.0%–105.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 900 mL, deaerated

Apparatus 2: 50 rpm

Time: 30 min

Standard stock solution: 5 mg/mL of valganciclovir in *Medium*. Expose the USP Valganciclovir Hydrochloride RS to ambient conditions overnight, and determine the water content before use.

Standard solution: 0.5 mg/mL of valganciclovir in *Medium* from the *Standard stock solution*. Pass a portion of this solution through a polyethylene filter of 10-µm pore size, discarding the first 2 mL of the filtrate.

Sample solution: Pass 10 mL of the solution under test through a polyethylene filter of 10-µm pore size, discarding the first 2 mL of the filtrate. Suitably dilute with *Medium*, if necessary, in comparison with the *Standard solution*.

Instrumental conditions

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

Mode: UV

Analytical wavelength: Absorption maximum at about 254 nm

Cell length: 0.02 cm quartz cell

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of valganciclovir ($C_{14}H_{22}N_6O_5$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times (M_{r1}/M_{r2}) \times D \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of USP Valganciclovir Hydrochloride RS in the *Standard solution*, corrected for water content (mg/mL)

L = label claim of valganciclovir (mg/Tablet)

V = volume of *Medium*, 900 mL

M_{r1} = molecular weight of valganciclovir, 354.36

M_{r2} = molecular weight of valganciclovir hydrochloride, 390.82

D = dilution factor

Tolerances: NLT 80% (Q) of the labeled amount of valganciclovir ($C_{14}H_{22}N_6O_5$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩**

Procedure for content uniformity

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

Sample solution: Transfer 1 Tablet to a 100-mL volumetric flask, add about 80 mL of *Diluent*, and sonicate until the Tablet is fully disintegrated. Dilute with *Diluent* to volume, mix, and allow the solution to settle. Pipet 3.0 mL of the top portion of the resulting solution into a 200-mL volumetric flask, and dilute with *Diluent* to volume. Pass a portion of the solution through a filter of 0.45-µm or finer pore size, and use the filtrate, discarding the initial 2 mL.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of valganciclovir ($C_{14}H_{22}N_6O_5$) in the Tablet taken:

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

r_U = sum of the peak responses of the valganciclovir diastereomers from the *Sample solution*

r_S = sum of the peak responses of the valganciclovir diastereomers from the *Standard solution*

C_S = concentration of USP Valganciclovir Hydrochloride RS in the *Standard solution*, corrected for water content (mg/mL)

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

M_{r1} = molecular weight of valganciclovir, 354.36

M_{r2} = molecular weight of valganciclovir hydrochloride, 390.82

Acceptance criteria: Meet the requirements

IMPURITIES

• **Organic Impurities**

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

Sample solution: Nominally 0.45 mg/mL of valganciclovir prepared as follows. Transfer an equivalent to 450 mg of valganciclovir from finely powdered Tablets (NLT 20) to a 1000-mL volumetric flask. Add about 800 mL of *Diluent*, and sonicate until the solid sample is fully disintegrated. Dilute with *Diluent* to volume. Pass a portion of this solution through a filter of 0.45-µm or finer pore size, and use the filtrate, discarding the initial 2 mL.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ganciclovir and guanine 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 ganciclovir or guanine from the *Sample solution*

r_S = sum of the peak responses of the valganciclovir diastereomers from the *Standard solution*

C_S = concentration of USP Valganciclovir Hydrochloride RS in the *Standard solution*, corrected for water content (mg/mL)

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

M_{r1} = molecular weight of valganciclovir, 354.36

M_{r2} = molecular weight of valganciclovir hydrochloride, 390.82

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

Calculate the percentage of each individual unidentified and identified impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_T) \times 100$$

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

r_T = sum of all the peak responses from the *Sample solution*

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Guanine	0.51	1.9	1.0[a]
Ganciclovir	0.66	1.4	2.0[a]
Valganciclovir 1	1.00	—	—
Valganciclovir 2	1.07	—	—
Ganciclovir mono-*N*-methyl valinate 1	1.21	—	—[b]
Ganciclovir mono-*N*-methyl valinate 2	1.30	—	—[b]
Methoxymethylguanine	1.45	—	—[b]
Isovalganciclovir 1	1.55	—	—[b]
Isovalganciclovir 2	1.61	—	—[b]
Ganciclovir divalinate	2.13	—	—[b]
Monoacetoxyganciclovir	2.31	—	—[b]
Isomonochloroganciclovir	2.52	—	—[b]
Homologue 1	2.69	—	—[b]
Homologue 2	2.77	—	—[b]
Each individual unidentified degradation product	—	—	0.2
Total individual unidentified degradation products	—	—	0.5
Total degradation products	—	—	3.5

[a] Degradant.

[b] Impurity.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers. Store at 25°, excursions permitted between 15° and 30°.
- **USP Reference Standards** ⟨11⟩

USP Ganciclovir Mono-N-methyl Valinate RS

2-(*RS*)-[(Guanin-9-yl)methoxy]-3-hydroxypropyl *N*-methyl-L-valinate.

$C_{15}H_{24}N_6O_5$ 368.39

USP Valganciclovir Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
VALGANCICLOVIR 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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