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Famciclovir Tablets

Change to read:

DEFINITION

Famciclovir Tablets contain Famciclovir ▲▲ (USP 1-Aug-2022) equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of famciclovir ($C_{14}H_{19}N_5O_4$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

Sample: Transfer a portion of finely powdered Tablets, equivalent to 1000 mg of famciclovir, to a 250-mL volumetric flask, and add 100 mL of acetonitrile. Sonicate for 5 min and centrifuge for 10 min. Pass a portion through a filter of 0.45-µm or finer pore size into a 250-mL evaporating flask. Evaporate the solution to dryness at low heat (about 70°).

Acceptance criteria: Meet 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**

Buffer A: 13.8 g/L of monobasic sodium phosphate in water. Adjust with 1 M sodium hydroxide or phosphoric acid to a pH of 4.5 ± 0.05.

Buffer B: 13.8 g/L of monobasic sodium phosphate in water. Adjust with 1 M sodium hydroxide to a pH of 7.0 ± 0.05.

Mobile phase: Methanol and *Buffer B* (30:70)

Standard solution: 0.1 mg/mL of USP Famciclovir RS in *Buffer A*

Sample stock solution: Nominally 1 mg/mL of famciclovir prepared as follows. Transfer an amount equivalent to 500 mg of famciclovir, from finely powdered Tablets (NLT 20), to an appropriate volumetric flask. Add about 50% of the flask volume of *Buffer A* and sonicate for about 15 min with intermittent shaking. Dilute with *Buffer A* to volume.

Sample solution: Nominally 0.1 mg/mL of famciclovir from *Sample stock solution* in *Buffer A*. Pass through a suitable filter of 0.45-µm or finer pore size.

Chromatographic system

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

Mode: LC

Detector: UV 222 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of famciclovir

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 famciclovir ($C_{14}H_{19}N_5O_4$) in the portion of Tablets taken:

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

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

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

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

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

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: 30 min

Buffer: 6.8 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 3.0. Pass through a suitable filter of 0.45-µm pore size.

Mobile phase: Methanol and *Buffer* (30:70)

Standard stock solution: 0.55 mg/mL of USP Famciclovir RS prepared as follows. Transfer 55 mg of USP Famciclovir RS to a 100-mL volumetric flask, dissolve in about 50 mL of *Medium*, and dilute with *Buffer* to volume.

Standard solution: 0.055 mg/mL of USP Famciclovir RS in *Buffer* from *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, and dilute with *Buffer* to obtain a concentration similar to that of the *Standard solution*.

Chromatographic system

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

Mode: LC

Detector: UV 310 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 35°

Flow rate: 1 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 famciclovir ($C_{14}H_{19}N_5O_4$) dissolved:

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

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

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

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

V = volume of *Medium*, 900 mL

D = dilution factor of the *Sample solution*, if applicable

L = label claim (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of famciclovir ($C_{14}H_{19}N_5O_4$) 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: 30 min

Standard solution: 0.55 mg/mL of USP Famciclovir RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter and dilute with *Medium*, if necessary.

Instrumental conditions

Mode: UV

Analytical wavelength: 262 nm

Cell: 5 mm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of famciclovir ($C_{14}H_{19}N_5O_4$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

D = dilution factor of the *Sample solution*, if applicable

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of famciclovir ($C_{14}H_{19}N_5O_4$) is dissolved.

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Standard solution: 0.55 mg/mL of USP Famciclovir RS prepared as follows. Transfer a suitable amount of USP Famciclovir RS to a suitable volumetric flask, add methanol to about 5% of the flask volume, and dilute with *Medium* to volume.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, and dilute with *Medium*, if necessary, to obtain a concentration similar to that of the *Standard solution*.

Instrumental conditions

Mode: UV

Analytical wavelength: 314 nm

Cell: 0.1 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of famciclovir ($C_{14}H_{19}N_5O_4$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

D = dilution factor of the *Sample solution*, if applicable

L = label claim (mg/Tablet)

Tolerances: NLT 85% (Q) of the labeled amount of famciclovir ($C_{14}H_{19}N_5O_4$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

Change to read:

• **Organic Impurities**

Solution A: 2.72 g/L of monobasic potassium phosphate in water. Adjust with 1 M phosphoric acid to a pH of 4.0 ± 0.05.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
50	75	25
60	75	25
65	95	5

Time (min)	Solution A (%)	Solution B (%)
75	95	5

Peak identification solution: 0.004 mg/mL of USP Famciclovir Related Compound A RS and 10 µg/mL of USP Famciclovir Related Compound B RS in *Solution A*

System suitability solution: 0.5 mg/mL of USP Famciclovir System Suitability Mixture RS in *Solution A*

Standard solution: 0.001 mg/mL of USP Famciclovir RS in *Solution A*

Sample solution: Nominally 1 mg/mL of famciclovir in *Solution A* prepared as follows. Transfer an amount equivalent to 250 mg of famciclovir, from finely powdered Tablets (NLT 10), to a 250-mL volumetric flask. Add about 125 mL of *Solution A*, and sonicate for 30 min with intermittent shaking. Dilute with *Solution A* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Temperatures

Autosampler: 6°

Column: 50°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.2 between propionyl famciclovir and 6-chloro famciclovir, *System suitability solution*

Relative standard deviation: NMT 5.0% for famciclovir, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual impurity in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Penciclovir[a]	0.16	—[b]
Famciclovir related compound A	0.2	0.2
4-Dimethylaminopyridine	0.23	—[b]
Famciclovir related compound B	0.5	1.0
N-7 isomer of famciclovir[c]	0.85	—[b]
Famciclovir	1.0	—

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
N-Acetyl famciclovir[d]	1.1	—[b]
▲Deoxychlorofamciclovir[e]▲ (USP 1-Aug-2022)	1.2	—[b]
6-Chloro famciclovir[f]	1.32	—[b]
Propionyl famciclovir[g]	1.35	—[b]
▲6-Alkylamino famciclovir[h]▲ (USP 1-Aug-2022)	2.0	—[b]
Any unspecified individual impurity	—	0.2
Total impurities	—	1.5

[a] 2-Amino-9-[4-hydroxy-3-(hydroxymethyl)butyl]-1*H*-purin-6(9*H*)-one; 9-[4-Hydroxy-3-(hydroxymethyl)butyl]guanine.

[b] This is a process impurity controlled in the drug substance and is included in the table for peak identification only. This impurity is excluded from the total impurities calculation.

[c] 2-[2-(2-Amino-7*H*-purin-7-yl)ethyl]propane-1,3-diyl diacetate.

[d] 2-[2-(2-Acetamido-9*H*-purin-9-yl)ethyl]propane-1,3-diyl diacetate.

[e] 4-(2-Amino-9*H*-purin-9-yl)-2-(chloromethyl)butyl acetate.

[f] 2-[2-(2-Amino-6-chloro-9*H*-purin-9-yl)ethyl]propane-1,3-diyl diacetate.

[g] 2-(Acetoxymethyl)-4-(2-amino-9*H*-purin-9-yl)butyl propionate.

[h] 2-(2-{[9-(4-Acetoxy-3-(acetoxymethyl)butyl]-2-amino-9*H*-purin-6-yl)amino}ethyl)propane-1,3-diyl diacetate.

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 *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** (11)

USP Famciclovir RS

USP Famciclovir Related Compound A RS

[2-[2-(2-Amino-9*H*-purin-9-yl)ethyl]propane-1,3-diol] hydrochloride.
$C_{10}H_{15}N_5O_2 \cdot HCl$ 273.72

USP Famciclovir Related Compound B RS

4-(2-Amino-9*H*-purin-9-yl)-2-(hydroxymethyl)butyl acetate.
$C_{12}H_{17}N_5O_3$ 279.30

USP Famciclovir System Suitability Mixture RS

Mixture of famciclovir, propionyl famciclovir, and 6-chloro famciclovir. (Other impurities may also be present.)

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

Topic/Question	Contact	Expert Committee
FAMCICLOVIR TABLETS	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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