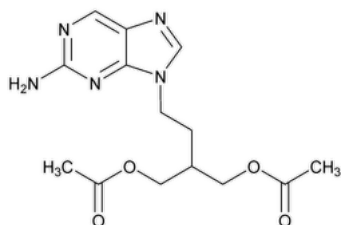


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Famciclovir



$C_{14}H_{19}N_5O_4$ 321.33

1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester);

2-[2-(2-Amino-9H-purin-9-yl)ethyl]-1,3-propanediol diacetate (ester) CAS RN®: 104227-87-4; UNII: QIC03ANI02.

DEFINITION

Famciclovir contains NLT 98.0% and NMT 102.0% of famciclovir ($C_{14}H_{19}N_5O_4$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A.** **SPECTROSCOPIC IDENTIFICATION TESTS** (197), **Infrared Spectroscopy: 197K** (CN 1-MAY-2020)
- **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

Dilute acid: Dilute 5 mL of phosphoric acid with water to 50 mL.

Buffer: 2.72 g/L of monobasic potassium phosphate in water. Adjust with *Dilute acid* to a pH of 4.0 ± 0.05 .

Mobile phase: Acetonitrile and *Buffer* (35:65)

Diluent: Water

Standard solution: 25 µg/mL of [USP Famciclovir RS](#) in *Diluent*

Sample solution: 25 µg/mL of Famciclovir in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

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

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: 5 times the retention time of famciclovir

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 2500 theoretical plates

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_s = concentration of [USP Famciclovir RS](#) in the *Standard solution* (mg/mL)

C_u = concentration of Famciclovir in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• ORGANIC IMPURITIES, PROCEDURE 1

[NOTE—On the basis of the synthetic route resulting in different impurity profiles, perform *Procedure 1* or *Procedure 2*. *Procedure 1* is recommended when dimethylaminopyridine, penciclovir, deoxychloro famciclovir, propionyl famciclovir, and 6-alkylamino famciclovir may be present (see [Table 2](#)). *Procedure 2* is recommended when famciclovir malonate, acetoxybutyl aminopurine, famciclovir methoxycarbonyl analog, famciclovir related compound C, famciclovir 8, N^2 -dimer, and famciclovir 6,6-dimer may be present (see [Table 4](#)).]

Dilute acid, Buffer, and Diluent: Proceed as directed in the Assay.

Solution A: *Buffer*

Solution B: Acetonitrile

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
35	70	30
40	70	30
42	95	5
50	95	5

System suitability solution: 0.5 mg/mL of [USP Famciclovir System Suitability Mixture RS](#) in *Diluent*

Standard solution: 0.5 µg/mL of [USP Famciclovir RS](#), 1 µg/mL of [USP Famciclovir Related Compound A RS](#), and 3 µg/mL of [USP Famciclovir Related Compound B RS](#) in *Diluent*

Sample solution: 500 µg/mL of Famciclovir in *Diluent*. [NOTE—The solution is stable for 15 h at 6°.]

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between the propionyl famciclovir and 6-chloro famciclovir peaks, *System suitability solution*

Column efficiency: NLT 20,000 theoretical plates for the famciclovir peak, *System suitability solution*

Tailing factor: NMT 1.5 for the famciclovir peak, *System suitability solution*

Relative standard deviation: NMT 5.0% for the famciclovir peak; NMT 10.0% for the famciclovir related compound A and famciclovir related compound B peaks, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Famciclovir taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times (1/F) \times 100$$

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* (µg/mL)

C_u = concentration of Famciclovir in the *Sample solution* (µg/mL)

F = relative response factor for each individual impurity (see [Table 2](#))

Acceptance criteria: See [Table 2](#).

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Dimethylaminopyridine ^a	0.12	0.59	0.05
Penciclovir ^b	0.16	0.29	0.50
Famciclovir related compound A ^c	0.19	1.3	0.20
Famciclovir related compound B ^d	0.51	1.1	0.60
N-7 Isomer of famciclovir ^e	0.89	0.92	0.10
Famciclovir	1.0	—	—
N-Acetyl famciclovir ^f	1.05	0.56	0.10
Deoxychloro famciclovir ^g	1.26	0.87	0.20
Propionyl famciclovir ^h	1.32	0.88	0.15
6-Chloro famciclovir ⁱ	1.36	0.85	0.15
6-Alkylamino famciclovir ^j	1.83	0.46	0.10
Any other unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

^a *N,N*-Dimethylpyridin-4-amine.

^b 9-[4-Hydroxy-3-(hydroxymethyl)butyl]guanine.

^c 2-[2-(2-Amino-9*H*-purin-9-yl)ethyl]propane-1,3-diol.

^d 4-(2-Amino-9*H*-purin-9-yl)-2-(hydroxymethyl)butyl acetate.

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

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

^g 4-(2-Amino-9*H*-purin-9-yl)-2-(chloromethyl)butyl acetate.

^h 2-(Acetoxymethyl)-4-(2-amino-9*H*-purin-9-yl)butyl propionate.

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

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

• **ORGANIC IMPURITIES, PROCEDURE 2**

Buffer: 3.85 g/L of ammonium acetate in water. Adjust with acetic acid to a pH of 5.0.

Solution A: 4.14 g/L of monobasic sodium phosphate in water. Adjust with phosphoric acid to a pH of 2.2.

Solution B: Acetonitrile and *Solution A* (25:75)

Mobile phase: See [Table 3](#).

Table 3

Time (min)	Solution A (%)	Solution B (%)
0	99.5	0.5



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