Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Sep-2023
Document Type: USP Monographs
DocId: GUID-D445FC16-19FB-4CDE-85DB-CB8B89C22450_4_en-US
DOI: https://doi.org/10.31003/USPNF_M1045_04_01
DOI Ref: 4b2y5

Fosamprenavir Calcium Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-fosamprenavir-calcium-tabs-20230825.

DEFINITION

Fosamprenavir Calcium Tablets contain an amount of fosamprenavir calcium ($C_{25}H_{34}CaN_3O_9PS$) equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of fosamprenavir ($C_{25}H_{34}N_3O_9PS$).

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197M or 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*.

ASSAY

- **Procedure**

Buffer: 4.68 g/L of monobasic sodium phosphate dihydrate in water. Add 1.5 mL of phosphoric acid per 1 L of this solution.

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

Diluent: Acetonitrile and *Buffer* (20:80)

Standard solution: 0.26 mg/mL of USP Fosamprenavir Calcium RS in *Diluent*. Sonicate to dissolve prior to final dilution, if necessary.

Sample solution: Nominally 0.28 mg/mL of fosamprenavir from Tablets in *Diluent* prepared as follows. Transfer an amount equivalent to 14 mg of fosamprenavir from finely powdered Tablets (NLT 20) to a 50-mL volumetric flask. Add about 40 mL of *Diluent* and sonicate to dissolve, if necessary. Dilute with *Diluent* to volume. Pass a portion of the solution through a suitable filter, and discard the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 266 nm

Column: 4.6-mm x 15-cm; 3.5-µm packing L1

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fosamprenavir ($C_{25}H_{34}N_3O_9PS$) 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 of fosamprenavir from the *Sample solution*

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

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

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

M_{r1} = molecular weight of fosamprenavir, 585.61

M_{r2} = molecular weight of fosamprenavir calcium, 623.67

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

▲Test 1▲ (RB 1-Sep-2023)

Medium: ▲0.02 M sodium acetate buffer, pH 3.5, prepared as follows. Dissolve 2.67 g of sodium acetate in 100 mL of water. Add 13.3 mL of glacial acetic acid and then dilute with water to 1000 mL; 900 mL.▲ (ERR 1-Sep-2023)

Apparatus 2: 75 rpm

Time: 30 min

Standard solution: 0.83 mg/mL of USP Fosamprenavir Calcium RS in *Medium*. Sonicate to dissolve prior to final dilution, if necessary.

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

Mode: UV

Analytical wavelength: 263 nm

Cell path length: 0.02 cm

Blank: *Medium*

System suitability

Sample: *Standard solution*

Suitability requirement

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fosamprenavir ($C_{25}H_{34}N_3O_9PS$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times (M_{r1}/M_{r2}) \times 100$$

A_U = absorbance from the *Sample solution*

A_S = absorbance from the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

M_{r1} = molecular weight of fosamprenavir, 585.61

M_{r2} = molecular weight of fosamprenavir calcium, 623.67

Tolerances: NLT 80% (*Q*) of the labeled amount of fosamprenavir ($C_{25}H_{34}N_3O_9PS$) is dissolved.

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

Solution A: 10 N acetic acid solution prepared as follows. Dilute 145 mL of glacial acetic acid to 250 mL with water.

Medium: 0.25 M sodium acetate buffer, pH 3.5, prepared as follows. Dissolve 34 g of sodium acetate in 500 mL of water. Add 300 mL of *Solution A*. Adjust with *Solution A* if necessary to a pH of 3.5 and then dilute with water to 1000 mL; 900 mL, deaerated

Apparatus 2: 75 rpm

Time: 30 min

Solution B: Methanol and acetonitrile (60:40)

Buffer: Dissolve 3.14 g of ammonium formate in 1000 mL of water. Adjust with formic acid to a pH of 3.2.

Mobile phase: *Solution B* and *Buffer* (60:40)

Solution C: 1.5 mL/L of phosphoric acid in water

Diluent: Acetonitrile and *Solution C* (55:45)

Standard stock solution: 0.5 mg/mL of USP Fosamprenavir Calcium RS in *Diluent*. Sonicate to dissolve.

Standard solution: 0.1 mg/mL of USP Fosamprenavir Calcium RS from *Standard stock solution* in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.

Chromatographic system

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

Mode: LC

Detector: UV 266 nm

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

Temperatures

Autosampler: 10°

Column: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 2.2 times the retention time of fosamprenavir

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 fosamprenavir ($C_{25}H_{34}N_3O_9PS$) dissolved:

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

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

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

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

V = volume of *Medium*, 900 mL

D = dilution factor for the *Sample solution*

M_{r1} = molecular weight of fosamprenavir, 585.61

M_{r2} = molecular weight of fosamprenavir calcium, 623.67

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of fosamprenavir ($C_{25}H_{34}N_3O_9PS$) is dissolved.▲ (RB 1-Sep-2023)

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

IMPURITIES

• **Organic Impurities: Early-Eluting Impurities**

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

System suitability solution: 0.26 mg/mL of USP Fosamprenavir System Suitability Mixture RS in *Diluent*. Sonicate to dissolve prior to final dilution, if necessary.

Standard solution: 0.28 µg/mL of USP Fosamprenavir Calcium RS in *Diluent*. Sonicate to dissolve prior to final dilution, if necessary.

System suitability

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

[Note—The relative retention times for fosamprenavir pyrophosphate and fosamprenavir *n*-propyl homolog are 0.7 and 0.8, respectively.]

Suitability requirements

Resolution: NLT 1.5 between fosamprenavir pyrophosphate and fosamprenavir *n*-propyl homolog, *System suitability solution*

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

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of any early-eluting 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 any impurity from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Fosamprenavir amine[a]	0.4	0.4
Fosamprenavir	1.0	—
Any unspecified impurity[b]	—	0.1
Total impurities[c]	—	1.5

[a] (2*R*,3*S*)-3-Amino-1-[(4-amino-*N*-isobutylphenyl)sulfonamide]-4-phenylbutan-2-yl dihydrogen phosphate.

[b] Exclude any individual unspecified impurity that elutes after fosamprenavir.

[c] Total impurities include the sum of all impurities determined in *Organic Impurities: Early-Eluting Impurities* and *Organic Impurities: Late-Eluting Impurities*.

- **Organic Impurities: Late-Eluting Impurities**

Buffer: 1.58 g/L of ammonium formate in water. Adjust with ammonia solution to a pH of 9.0.

Solution A: Acetonitrile and *Buffer* (19:81)

Solution B: Acetonitrile, tetrahydrofuran, and *Buffer* (45:5:50)

Solution C: 4.68 g/L of monobasic sodium phosphate dihydrate in water. Add 1.5 mL of phosphoric acid per 1 L of this solution.

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	100	0
15	100	0
40	0	100
43	0	100
45	100	0
55	100	0

Diluent: Acetonitrile and *Solution C* (20:80)

System suitability solution: 0.26 mg/mL of USP Fosamprenavir System Suitability Mixture RS in *Diluent*. Sonicate to dissolve prior to final dilution, if necessary.

Standard solution: 0.28 µg/mL of USP Fosamprenavir Calcium RS in *Diluent*. Sonicate to dissolve prior to final dilution, if necessary.

Sample solution: Nominally 0.28 mg/mL of fosamprenavir from Tablets in *Diluent* prepared as follows. Transfer an amount equivalent to 14 mg of fosamprenavir from finely powdered Tablets (NLT 20) to a 50-mL volumetric flask. Add about 40 mL of *Diluent* and sonicate to dissolve, if necessary. Dilute with *Diluent* to volume. Pass a portion of the solution through a suitable filter, and discard the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 266 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times for fosamprenavir and fosamprenavir *n*-butyl isomer are 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 2 between fosamprenavir and fosamprenavir *n*-butyl isomer, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any late-eluting impurity in the portion of fosamprenavir calcium taken:

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

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

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

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

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

Acceptance criteria: See *Table 3*. The reporting threshold is 0.05%.

Table 3

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Fosamprenavir	1.0	—
Amprenavir[a]	3.1	0.5
Any unspecified impurity[b]	—	0.1
Total impurities[c]	—	1.5

[a] (*S*)-Tetrahydrofuran-3-yl {(2*S*,3*R*)-4-[(4-amino-*N*-isobutylphenyl)sulfonamide]-3-hydroxy-1-phenylbutan-2-yl}carbamate.

[b] Exclude any individual unspecified impurity that elutes before fosamprenavir.

[c] Total impurities include the sum of all impurities determined in *Organic Impurities: Early-Eluting Impurities* and *Organic Impurities: Late-Eluting Impurities*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.

Add the following:

▲• **Labeling:** The labeling states the *Dissolution* test used only if *Test 1* is not used.▲ (RB 1-Sep-2023)

• **USP Reference Standards** ⟨11⟩

USP Fosamprenavir Calcium RS

USP Fosamprenavir System Suitability Mixture RS

A mixture of fosamprenavir calcium, fosamprenavir pyrophosphate, fosamprenavir *n*-propyl homolog, and fosamprenavir *n*-butyl isomer. Other impurities may also be present.

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 46(4)

Current DocID: GUID-D445FC16-19FB-4CDE-85DB-CB8B89C22450_4_en-US

DOI: https://doi.org/10.31003/USPNF_M1045_04_01

DOI ref: 4b2y5