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Fosinopril Sodium Tablets

DEFINITION
Fosinopril Sodium Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of fosinopril sodium ($C_{30}H_{45}NNaO_7P$).

IDENTIFICATION

Change to read:

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

Sample: Transfer a portion of finely powdered Tablets, equivalent to 25 mg of fosinopril sodium, to a 100-mL beaker containing 40 mL of water. Heat at 25° for 5 min with stirring, and pass through a fritted-disc funnel of medium pore size. Centrifuge the filtrate at 2500 rpm for 30 min. Adjust the filtrate with phosphoric acid to a pH of 3 to precipitate the fosinopril, and pass through a fritted-disc funnel. Dissolve the precipitate by passing chloroform through the filter, and evaporate the chloroform solution to dryness under a current of air. Proceed as directed, using the oily residue so obtained.

Standard: Transfer 25 mg of USP Fosinopril Sodium RS to a 100-mL beaker containing 40 mL of water. Proceed as directed for the *Sample*, beginning with "Heat at 25° for 5 min with stirring". Use the residue.

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**

Mobile phase: Methanol and 0.2% phosphoric acid (780:220)

Diluent: Acetonitrile and 0.2 M urea solution (20:80)

System suitability solution: 30 µg/mL of USP Fosinopril Related Compound A RS and 70 µg/mL of USP Fosinopril Sodium RS in *Diluent*

Standard solution: 0.1 mg/mL of USP Fosinopril Sodium RS in *Diluent*

Sample stock solution: Transfer NLT 10 Tablets to a 500-mL volumetric flask, add 400 mL of *Diluent*, and stir for 40 min. Dilute with *Diluent* to volume, mix, and centrifuge. Use the clear supernatant.

Sample solution: Nominally 0.1 mg/mL of fosinopril sodium in *Diluent* from *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.0-mm × 30-cm; packing L1

Flow rate: 2 mL/min

Injection volume: 50 µL

Run time: NLT 1.5 times the retention time of the fosinopril peak

System suitability

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

[Note—The relative retention times for fosinopril related compound A and fosinopril are about 0.4 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between the fosinopril and fosinopril related compound A peaks, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fosinopril sodium ($C_{30}H_{45}NNaO_7P$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Mobile phase: Acetonitrile and 0.2% phosphoric acid (640:360)

System suitability solution: 0.02 mg/mL each of USP Fosinopril Sodium RS and USP Fosinopril Related Compound G RS in *Mobile phase*

Standard stock solution: 0.1 mg/ml of USP Fosinopril Sodium RS prepared as follows. Add methanol, about 3% of the total volume, to a suitable quantity of USP Fosinopril Sodium RS in a suitable volumetric flask, sonicate briefly, and dilute with *Medium* to volume.

Standard solution: Dilute the *Standard stock solution* with *Medium* as directed in *Table 1*.

Table 1

Label Claim (mg)	Standard Stock Solution (mL)	Final Volume (flask size)
5	5.0	100
10	10	100
20	20	100
40	40	100

Sample solution: Pass portions of the solution under test through a 1.2-µm acrylic filter. [Note—Do not use glass filters.]

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

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

Column temperature: 40°

Flow rate: 3 mL/min

Injection volume: 50 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.7 between fosinopril and fosinopril related compound G, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fosinopril sodium ($C_{30}H_{45}NNaO_7P$) dissolved.

Tolerances: NLT 80% (*Q*) of the labeled amount of fosinopril sodium ($C_{30}H_{45}NNaO_7P$) is dissolved.

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

IMPURITIES

• **Limit of Fosinopril Related Compound A**

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

Standard stock solution: 0.1 mg/mL of USP Fosinopril Related Compound A RS in methanol

Standard solution: 0.0025 mg/mL of USP Fosinopril Related Compound A RS in *Diluent* from *Standard stock solution*

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of fosinopril related compound A in the portion of Tablets taken:

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

r_U = peak response of fosinopril related compound A from the *Sample solution*

r_S = peak response of fosinopril related compound A from the *Standard solution*

C_S = concentration of fosinopril related compound A in the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 4%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩

USP Fosinopril Related Compound A RS

(4*S*)-4-Cyclohexyl-[(4-phenylbutyl)phosphinyl]acetyl-L-proline.

$C_{23}H_{34}NO_5P$ 435.49

USP Fosinopril Related Compound G RS

(4-Phenylbutyl)phosphinylacetic acid, disodium salt.

$C_{12}H_{15}Na_2O_4P$ 300.20

USP Fosinopril Sodium RS

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

Topic/Question	Contact	Expert Committee
FOSINOPRIL SODIUM TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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