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Fosphenytoin Sodium Injection

DEFINITION

Fosphenytoin Sodium Injection is a sterile solution of Fosphenytoin Sodium in Water for Injection. Fosphenytoin Sodium is a prodrug. Injection containing 1 mg/mL of Fosphenytoin Sodium is equivalent to 0.667 mg/mL of Phenytoin Sodium after injection. It contains NLT 90.0% and NMT 110.0% of the labeled amount of fosphenytoin sodium ($C_{16}H_{13}N_2Na_2O_6P$).

IDENTIFICATION

Change to read:

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

Sample: Transfer a 5-mL aliquot of Injection to a 100-mL beaker. Add 30 mL of acetone to form a white precipitate, and stir for 20 min using a magnetic stirrer. Filter under vacuum, and collect the precipitate using suitable filter paper. Allow to dry under vacuum for 15 min.

Acceptance criteria: Meets 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: 8.2 g/L of monobasic potassium phosphate in water. Adjust with 6 N potassium hydroxide solution to a pH of 6.5 ± 0.05.

Mobile phase: Methanol, acetonitrile, and *Buffer* (25:2:73)

Standard stock solution A: 0.75 mg/mL of USP Fosphenytoin Sodium RS prepared as follows. Transfer a suitable amount of the standard in a suitable volumetric flask. Dissolve in a minimum amount of methanol. Dilute with *Buffer* to volume.

Standard stock solution B: 7.5 µg/mL of USP Phenytoin RS, 7.5 µg/mL of USP Phenytoin Related Compound A RS, and 15 µg/mL of USP Phenytoin Related Compound B RS in methanol

Standard solution: 150 µg/mL of USP Fosphenytoin Sodium RS from *Standard stock solution A*, 0.75 µg/mL each of USP Phenytoin RS and USP Phenytoin Related Compound A RS, and 1.5 µg/mL of USP Phenytoin Related Compound B RS from *Standard stock solution B* in *Buffer*

Sample stock solution: Nominally 1.5 mg/mL of fosphenytoin sodium from a volume of Injection prepared in methanol

Sample solution: Nominally 150 µg/mL of fosphenytoin sodium from *Sample stock solution* in *Buffer*

Chromatographic system

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

Mode: LC

Detector: UV 214 nm

Column: 4.6-mm × 15-cm; packing L11

Flow rate: 1.25 mL/min

Injection volume: 40 µL

System suitability

Sample: *Standard solution*

[Note—See *Table 1* for the approximate relative retention times.]

Suitability requirements

Resolution: NLT 4.0 between phenytoin related compound B and phenytoin related compound A

Column efficiency: NLT 2250 theoretical plates for fosphenytoin

Tailing factor: NMT 1.8 for fosphenytoin

Relative standard deviation: NMT 1.0% for fosphenytoin and NMT 5.0% for phenytoin, phenytoin related compound A, and phenytoin related compound B

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fosphenytoin sodium ($C_{16}H_{13}N_2Na_2O_6P$) in the portion of Injection taken:

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

r_U = peak response of fosphenytoin sodium from the *Sample solution*

r_S = peak response of fosphenytoin sodium from the *Standard solution*

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

C_U = nominal concentration of fosphenytoin sodium in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **Organic Impurities**

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentages of phenytoin, phenytoin related compound A, and phenytoin related compound B in the portion of Injection taken:

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

r_U = peak response of phenytoin, phenytoin related compound A, or phenytoin related compound B from the *Sample solution*

r_S = peak response of phenytoin, phenytoin related compound A, or phenytoin related compound B from the *Standard solution*

C_S = concentration of the corresponding analyte in the *Standard solution* (µg/mL)

C_U = nominal concentration of fosphenytoin sodium in the *Sample solution* (µg/mL)

Calculate the percentages of unspecified degradation products in the portion of Injection taken:

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

r_U = peak response of each unspecified degradation product from the *Sample solution*

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

C_S = concentration of USP Phenytoin RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of fosphenytoin sodium in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Phenytoin related compound B	0.3	1.5
Phenytoin related compound A	0.5	0.2
Fosphenytoin	1.0	—
Phenytoin	3.8	0.2
Any other individual unspecified degradation product	—	0.1
Total impurities	—	2.0

SPECIFIC TESTS

• **Bacterial Endotoxins Test** ⟨85⟩**:** NMT 14 USP Endotoxin Units/mL

• **pH** ⟨791⟩**:** 8.3–9.3

• **Other Requirements:** It meets the requirements in *Injections and Implanted Drug Products* ⟨1⟩.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose or multiple-dose containers, preferably of Type I glass. Store between 2° and 8°. Do not store at room temperature for more than 48 h.

• **Labeling:** Both the actual content of fosphenytoin sodium and the content of phenytoin sodium, expressed in terms of phenytoin sodium equivalents, are stated on the label.

• **USP Reference Standards** ⟨11⟩

USP Fosphenytoin Sodium RS

USP Phenytoin RS

USP Phenytoin Related Compound A RS

Diphenylglycine.

$C_{14}H_{13}NO_2$ 227.26

USP Phenytoin Related Compound B RS

Diphenylhydantoic acid.

$C_{15}H_{14}N_2O_3$ 270.29

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

Topic/Question	Contact	Expert Committee
FOSPHENYTOIN SODIUM INJECTION	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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