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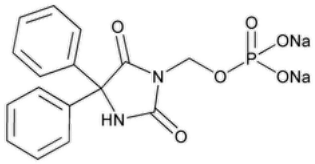
Fosphenytoin Sodium



$C_{16}H_{13}N_2Na_2O_6P$ 406.24

2,4-Imidazolidinedione, 5,5-diphenyl-3- [(phosphonooxy)methyl]-, disodium salt;

3-(Hydroxymethyl)-5,5-diphenylhydantoin, disodium phosphate (ester) CAS RN®: 92134-98-0; UNII: 7VLR55452Z.

DEFINITION

Fosphenytoin Sodium contains NLT 98.0% and NMT 102.0% of fosphenytoin sodium ($C_{16}H_{13}N_2Na_2O_6P$), calculated on the anhydrous 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*.

• **C.** **Identification Tests—General, *Sodium*⟨191⟩:** Meets the requirements

ASSAY

• **Procedure**

Buffer: Dissolve 6.80 g of monobasic potassium phosphate and 30 mL of 0.5 M dodecyltriethylammonium phosphate in 900 mL of water. Adjust with 1.5 M phosphoric acid to a pH of 5.0, and dilute with water to 1000 mL.

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

Standard solution: 0.15 mg/mL of USP Fosphenytoin Sodium RS in *Mobile phase*

Sample solution: 0.15 mg/mL of Fosphenytoin Sodium in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 214 nm

Column: 3.9-mm × 15-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 5000 theoretical plates

Tailing factor: NMT 1.6

Relative standard deviation: NMT 0.5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of fosphenytoin sodium ($C_{16}H_{13}N_2Na_2O_6P$) in the portion of Fosphenytoin Sodium 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 Fosphenytoin Sodium RS in the *Standard solution* (mg/mL)

C_U = concentration of Fosphenytoin Sodium in the *Sample solution* (mg/mL)

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

IMPURITIES

• **Organic Impurities**

Buffer and **Mobile phase:** Proceed as directed in the *Assay*.

Standard solution: 0.003 mg/mL of USP Phenytoin Related Compound A RS, 0.003 mg/mL of USP Phenytoin Related Compound B RS, and 0.0015 mg/mL of USP Phenytoin RS in *Mobile phase*

Sample solution: 3 mg/mL of Fosphenytoin Sodium in *Mobile phase*

Chromatographic system: Proceed as directed in the *Assay*, except use a run time of NLT 6 times the retention time of the major peak.

System suitability

Sample: *Standard solution*

[Note—The order of elution is phenytoin related compound A, phenytoin, phenytoin related compound B, followed by the major peak due to fosphenytoin.]

Suitability requirements

Resolution: NLT 2.0 between phenytoin and phenytoin related compound B

Relative standard deviation: NMT 5.0% for each compound

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of phenytoin, phenytoin related compound A, and phenytoin related compound B, if present, in the portion of Fosphenytoin Sodium 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* (mg/mL)

C_U = concentration of Fosphenytoin Sodium in the *Sample solution* (mg/mL)

Calculate the percentage of any unspecified individual impurity in the portion of Fosphenytoin Sodium taken:

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

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

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

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

C_U = concentration of Fosphenytoin Sodium in the *Sample solution* (mg/mL)

Acceptance criteria

Phenytoin: NMT 0.1%

Any other impurity: NMT 0.1%

Total impurities: NMT 0.5%

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample solution: 75 mg/mL of Fosphenytoin Sodium in water

Acceptance criteria: 8.5–9.5

• **Water Determination,** *Method I* ⟨921⟩**:** 21.7%–25.7%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

• **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	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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