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 (C₁₆H₁₃N₂Na₂O₆P).

IDENTIFICATION

• A. INFRARED ABSORPTION (197K)
  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 (C₁₆H₁₃N₂Na₂O₆P) in the portion of Injection taken:

\[
\text{Result} = \left( \frac{r_U}{r_S} \times \frac{C_U}{C_S} \right) \times 100
\]

\(r_U = \) peak response of fosphenytoin sodium from the Sample solution
\(r_S = \) peak response of fosphenytoin sodium from the Standard solution
\(C_U = \) concentration of USP Fosphenytoin Sodium RS in the Standard solution (µg/mL)
\(C_S = \) 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:

\[
\text{Result} = \left( \frac{r_U}{r_S} \times \frac{C_U}{C_S} \right) \times 100
\]

\(r_U = \) 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
\(C_U = \) concentration of the corresponding analyte in the Sample solution (µg/mL)
\(C_S = \) nominal concentration of fosphenytoin sodium in the Sample solution (µg/mL)

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

\[
\text{Result} = \left( \frac{r_U}{r_S} \times \frac{C_U}{C_S} \right) \times 100
\]

\(r_U = \) peak response of each unspecified degradation product from the Sample solution
\(r_S = \) peak response of phenytoin from the Standard solution
\(C_U = \) concentration of USP Phenytoin RS in the Standard solution (µg/mL)
\(C_S = \) nominal concentration of fosphenytoin sodium in the Sample solution (µg/mL)

Acceptance criteria: See Table 1.

Table 1

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenytoin related compound B</td>
<td>0.3</td>
<td>1.5</td>
</tr>
<tr>
<td>Phenytoin related compound A</td>
<td>0.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Fosphenytoin</td>
<td>1.0</td>
<td>—</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>3.8</td>
<td>0.2</td>
</tr>
</tbody>
</table>

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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* (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.

Change to read:

- **Labeling:** Both the actual content of fosphenytoin sodium and the content of phenytoin sodium, expressed in terms of phenytoin sodium equivalents, are stated (RB 1-Feb-2015) on the label.