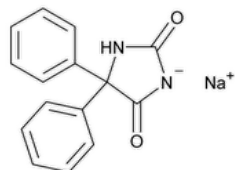


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## Phenytoin Sodium



$C_{15}H_{11}N_2NaO_2$  274.25  
 2,4-Imidazolidinedione, 5,5-diphenyl-, monosodium salt;  
 5,5-Diphenylhydantoin sodium salt CAS RN<sup>®</sup>: 630-93-3; UNII: 4182431BJH.

### DEFINITION

Phenytoin Sodium contains NLT 98.0% and NMT 102.0% of phenytoin sodium ( $C_{15}H_{11}N_2NaO_2$ ), calculated on the dried basis.

### IDENTIFICATION

**Change to read:**

- **A.** [▲SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Infrared Spectroscopy: 197K▲](#) (CN 1-MAY-2020)
- **B.** [IDENTIFICATION TESTS—GENERAL, Sodium \(191\)](#)
  - Solution A:** Dissolve 2.7 g of methoxyphenylacetic acid in 6 mL of tetramethylammonium hydroxide TS, and add 20 mL of dehydrated alcohol.
  - Solution B:** 158 mg/mL of ammonium carbonate in water
  - Sample solution:** Ignite 1 g, and cool. Add 2 mL of water to the residue, and neutralize the solution with hydrochloric acid. Filter, and dilute the filtrate with water to 4 mL.
  - Analysis:** To 0.1 mL of the *Sample solution* add 1.5 mL of *Solution A*, and cool in ice water for 30 min. A voluminous, white, crystalline precipitate is formed. Place in water at 20°, and stir for 5 min.
  - Acceptance criteria:** The precipitate does not disappear. Add 1 mL of ammonia TS. The precipitate dissolves completely. Add 1 mL of *Solution B*. No precipitate is formed.
- **C.** 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:** 0.05 M monobasic ammonium phosphate buffer, adjusted with phosphoric acid to a pH of 2.5

**Mobile phase:** Acetonitrile, methanol, and *Buffer* (35:20:45)

**System suitability solution:** 0.1 mg/mL of [USP Phenytoin RS](#) and 0.15 mg/mL of benzoin in *Mobile phase*

**Standard solution:** 0.05 mg/mL of [USP Phenytoin RS](#) in *Mobile phase*

**Sample solution:** 0.05 mg/mL of Phenytoin Sodium in *Mobile phase*

#### Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

**Mode:** LC

**Detector:** UV 220 nm

**Column:** 4.6-mm × 25-cm; 5-μm packing L1

**Flow rate:** 1.5 mL/min

**Injection volume:** 20 μL

#### System suitability

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

[NOTE—The relative retention times for phenytoin and benzoin are 1.0 and 1.3, respectively.]

#### Suitability requirements

**Resolution:** NLT 1.5 between phenytoin and benzoin, *System suitability solution*

**Tailing factor:** NMT 1.5, *Standard solution*

**Relative standard deviation:** NMT 1.0%, *Standard solution*

#### Analysis

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of phenytoin sodium ( $C_{15}H_{11}N_2NaO_2$ ) in the portion of Phenytoin Sodium taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

$r_U$  = peak response from the *Sample solution*

$r_S$  = peak response from the *Standard solution*

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

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

$M_{r1}$  = molecular weight of phenytoin sodium, 274.25

$M_{r2}$  = molecular weight of phenytoin, 252.27

**Acceptance criteria:** 98.0%–102.0% on the dried basis

#### IMPURITIES

##### • ORGANIC IMPURITIES

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

**Standard solution:** 0.5 µg/mL of benzophenone, 1 µg/mL of [USP Phenytoin RS](#), 9 µg/mL of [USP Phenytoin Related Compound A RS](#), and 9 µg/mL of [USP Phenytoin Related Compound B RS](#) in *Mobile phase*

**Sample solution:** 1 mg/mL of Phenytoin Sodium in *Mobile phase*

##### System suitability

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

[NOTE—The relative retention times for phenytoin and benzoin are 1.0 and 1.3, respectively.]

##### Suitability requirements

**Resolution:** NLT 1.5 between phenytoin and benzoin, *System suitability solution*

**Relative standard deviation:** NMT 5.0% for each compound, *Standard solution*

#### Analysis

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of phenytoin related compound A, phenytoin related compound B, and benzophenone in the portion of Phenytoin Sodium taken:

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

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

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

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

$C_U$  = concentration of Phenytoin Sodium in the *Sample solution* (µg/mL)

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

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

$r_U$  = peak response of each impurity 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)

$C_U$  = concentration of Phenytoin Sodium in the *Sample solution* (µg/mL)