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Phenytoin Chewable Tablets

DEFINITION

Phenytoin Chewable Tablets contain NLT 95.0% and NMT 105.0% of the labeled amount of phenytoin ($C_{15}H_{12}N_2O_2$).

IDENTIFICATION

• **A.** 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**

Solution A: Triethylamine and water (1:99)

Mobile phase: Methanol, acetonitrile, water, *Solution A*, and acetic acid (270:230:500:5:1)

Standard solution: 0.5 mg/mL of USP Phenytoin RS in *Mobile phase*

Sample solution: Nominally 0.5 mg/mL of phenytoin from NLT 20 finely powdered Chewable Tablets in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

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

Flow rate: 1.5 mL/min

Injection volume: 25 µL

Run time: NLT 2 times the retention time of the phenytoin peak

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of phenytoin ($C_{15}H_{12}N_2O_2$) in the portion of Chewable Tablets 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 Phenytoin RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: Dissolve 6 g of tromethamine in 600 mL of water. Dilute with water to 1 L, and adjust with phosphoric acid to a pH of 9.0. Dissolve 10 g of sodium lauryl sulfate in 1 L of the prepared buffer; 900 mL.

Apparatus 2: 100 rpm

Time: 120 min

Solution A, Mobile phase, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard stock solution: 3.0 mg/mL of USP Phenytoin RS in methanol

Standard solution: 0.012 mg/mL of USP Phenytoin RS prepared as follows. Transfer a suitable volume of the *Standard stock solution* to a suitable volumetric flask, and dilute with *Medium* to volume to obtain an intermediate concentration of 0.06 mg/mL of USP Phenytoin RS. Transfer a suitable volume of the resulting solution to a suitable volumetric flask, and dilute with *Mobile phase* to volume.

Sample solution: Withdraw a portion of the solution under test and filter, discarding the first 3 mL of the filtrate. Pipet 10.0 mL of this solution into a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of phenytoin ($C_{15}H_{12}N_2O_2$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times 100$$

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)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 70% (Q) of the labeled amount of phenytoin ($C_{15}H_{12}N_2O_2$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

Solution A: 6.8 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 2.5.

Solution B: Acetonitrile and methanol (40:60)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	60	40
23	60	40
38	42	58
45	30	70
50	30	70
51	60	40
55	60	40

Diluent: *Solution B* and water (50:50)

Standard solution: 1 µg/mL of USP Phenytoin RS, 5 µg/mL of USP Phenytoin Related Compound A RS, and 9 µg/mL of USP Phenytoin Related Compound B RS in *Diluent*

Sample solution: Nominally 1000 µg/mL of phenytoin prepared as follows. Finely powder NLT 20 Chewable Tablets and transfer a portion of the powder to an appropriate volumetric flask. Add *Diluent* to about 50% of the final flask volume, and shake the mixture mechanically for 15 min or until dissolved. Dilute with *Diluent* to volume, centrifuge, and use the supernatant. Pass a portion of the solution through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 5.0% for the phenytoin peak

Signal-to-noise ratio: NLT 10 for the phenytoin peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of phenytoin related compound A and phenytoin related compound B in the portion of Chewable Tablets taken:

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

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

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

C_S = concentration of USP Phenytoin Related Compound A RS or USP Phenytoin Related Compound B RS in the *Standard solution* (µg/mL)

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

Calculate the percentage of any individual unspecified degradation product in the portion of Chewable Tablets 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 phenytoin in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 2*. Disregard any degradation product less than 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Phenytoin related compound A	0.14	0.5
Phenytoin related compound B	0.51	0.9
Phenytoin	1.0	—
Any individual unspecified degradation product	—	0.2
Total degradation products	—	1.5

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature. Protect from moisture.
- **Labeling:** Label the Chewable Tablets to indicate that they are to be chewed before swallowing.

- **USP Reference Standards** ⟨11⟩

USP Phenytoin RS

USP Phenytoin Related Compound A RS

2,2-Diphenylglycine.

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

USP Phenytoin Related Compound B RS

2,2-Diphenyl-2-ureidoacetic acid.

$C_{15}H_{14}N_2O_3$ 270.28

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

Topic/Question	Contact	Expert Committee
PHENYTOIN CHEWABLE TABLETS	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

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