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Chlorthalidone Tablets

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DEFINITION
Chlorthalidone Tablets contain NLT 92.0% and NMT 108.0% of the labeled amount of chlorthalidone (C₁₄H₁₁ClN₂O₄S).

IDENTIFICATION

- A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- 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**
Solution A: 69 mL/L of [phosphoric acid](#) in [water](#)
Solution B: 2 g/L of [sodium hydroxide](#) in [water](#)
Solution C: Dissolve 1.32 g of [ammonium phosphate, dibasic](#) in about 900 mL of [water](#). Adjust with *Solution A* to a pH of 5.5. Dilute with [water](#) to 1000 mL.
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution C (%)	Methanol (%)
0	65	35
16	65	35
21	50	50
40	50	50
50	65	35
55	65	35

Diluent: [Methanol](#), *Solution C*, and *Solution B* (48:50:2)
Standard solution: 0.1 mg/mL of [USP Chlorthalidone RS](#) in *Diluent*. Sonicate to dissolve as needed.
Sample stock solution: Nominally 1 mg/mL of chlorthalidone in *Diluent* prepared as follows. Weigh and finely powder Tablets (NLT 20). Transfer an amount of powder, equivalent to about 50 mg of chlorthalidone, into a 50-mL volumetric flask. Add *Diluent* to about 60% of the flask volume and sonicate. [NOTE—Sonicating for NLT 10 min is recommended.] Dilute with *Diluent* to volume. Centrifuge a portion and use the supernatant.
Sample solution: Nominally 0.1 mg/mL of chlorthalidone from the *Sample stock solution* in *Diluent*
Chromatographic system
(See [Chromatography \(621\)](#), *System Suitability*.)
Mode: LC
Detector: UV 220 nm. For *Identification A*, use a diode array detector in the range of 190–400 nm.
Column: 4.6-mm × 25-cm; 5-µm packing [L7](#)
Column temperature: 40°
Flow rate: 1.4 mL/min
Injection volume: 10 µL
System suitability
Sample: *Standard solution*
Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of chlorthalidone ($C_{14}H_{11}ClN_2O_4S$) in the portion of Tablets taken:

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

r_U = peak response of chlorthalidone from the *Sample solution*

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

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

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

Acceptance criteria: 92.0%–108.0%

PERFORMANCE TESTS

Change to read:

- [DISSOLUTION \(711\)](#).

▲Test 1▲ (RB 1-Oct-2024)

Medium: [Water](#); 900 mL

Apparatus 2: 75 rpm

Time: 60 min

Standard stock solution: 5 mg/mL of [USP Chlorthalidone RS](#) in [methanol](#)

Standard solution: A known concentration of [USP Chlorthalidone RS](#) in [water](#)

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with [water](#) to a concentration that is similar to that of the *Standard solution*.

Instrumental conditions

Mode: UV

Analytical wavelength: 275 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of chlorthalidone ($C_{14}H_{11}ClN_2O_4S$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

D = dilution factor, if needed

L = label claim (mg/Tablet)

Tolerances: NLT 70% (Q) of the labeled amount of chlorthalidone ($C_{14}H_{11}ClN_2O_4S$) is dissolved.

▲Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: 0.25% [sodium dodecyl sulfate](#) in [water](#). Heat to dissolve, if necessary; 900 mL.

Apparatus 2: 75 rpm

Time: 45 min

Standard stock solution: 5 mg/mL of [USP Chlorthalidone RS](#) in [methanol](#). Sonicate to dissolve, if necessary.

Standard solution:

For Tablets labeled to contain 25 mg/Tablet: 0.025 mg/mL of [USP Chlorthalidone RS](#) in *Medium* from the *Standard stock solution*

For Tablets labeled to contain 50 mg/Tablet: 0.05 mg/mL of [USP Chlorthalidone RS](#) in *Medium* from the *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-μm pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained.

Instrumental conditions

Mode: UV

Analytical wavelength: 275 nm

Cell: 2 cm