Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-Oct-2024
Document Type: USP Monographs
DocId: GUID-442F55DE-D03F-45E0-896A-9AC505A208E4_4_en-US
DOI: https://doi.org/10.31003/USPNF_M17040_04_01
DOI Ref: ly7od

Chlorthalidone Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-chlorthalidone-tabs-20240927 .

DEFINITION
Chlorthalidone Tablets contain NLT 92.0% and NMT 108.0% of the labeled amount of chlorthalidone ($C_{14}H_{11}ClN_2O_4S$).

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

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of chlorthalidone ($C_{14}H_{11}ClN_2O_4S$) is dissolved.▲ (RB 1-Oct-2024)

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

IMPURITIES

• **Organic Impurities**

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

System suitability solution: 1 mg/mL of USP Chlorthalidone RS and 5 µg/mL of USP Chlorthalidone Related Compound A RS in *Diluent*. Sonicate to dissolve as needed.

Standard solution: 10 µg/mL of USP Chlorthalidone RS in *Diluent*. Sonicate to dissolve as needed.

Sensitivity solution: 1 µg/mL of USP Chlorthalidone RS from the *Standard solution* in *Diluent*

Sample 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.

System suitability

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

[Note—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 5.0 between chlorthalidone related compound A and chlorthalidone, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any specified or unspecified impurity in the portion of Tablets taken:

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

r_U = peak response of any specified or unspecified impurity 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)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.1%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Chlorthalidone related compound A	0.68	1.1	1.0
Chlorthalidone	1.00	—	—

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Any unspecified impurity	—	1.0	0.2
Total impurities[a]	—	—	1.0

[a] Excluding chlorthalidone related compound A.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature. Protect from light.

Add the following:

▲• **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.▲ (RB 1-Oct-2024)

• **USP Reference Standards** ⟨11⟩

USP Chlorthalidone RS

USP Chlorthalidone Related Compound A RS

2-(4-Chloro-3-sulfamoylbenzoyl)benzoic acid;
Also known as 4'-Chloro-3'-sulfamoyl-2-benzophenone carboxylic acid.
$C_{14}H_{10}ClNO_5S$ 339.75

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

Topic/Question	Contact	Expert Committee
CHLORTHALIDONE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 47(5)

Current DocID: GUID-442F55DE-D03F-45E0-896A-9AC505A208E4_4_en-US

DOI: https://doi.org/10.31003/USPNF_M17040_04_01

DOI ref: ly7od