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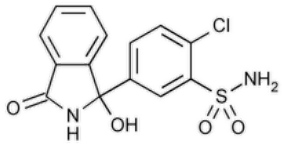
Chlorthalidone

Change to read:



$C_{14}H_{11}ClN_2O_4S$ ▲338.76▲ (USP 1-May-2023)

Benzenesulfonamide, 2-chloro-5-(2,3-dihydro-1-hydroxy-3-oxo-1*H*-isoindol-1-yl)-;

2-Chloro-5-(1-hydroxy-3-oxo-1-isoindolinyl)benzenesulfonamide CAS RN®: 77-36-1; UNII: Q0MQD1073Q.

DEFINITION

Chlorthalidone contains NLT 98.0% and NMT 102.0% of chlorthalidone ($C_{14}H_{11}ClN_2O_4S$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** ▲197A or▲ (USP 1-May-2023) 197M

Delete the following:

▲• **B. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*.**▲ (USP 1-May-2023)

Add the following:

▲• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2023)

Delete the following:

▲• **C.**▲ (USP 1-May-2023)

ASSAY

Change to read:

• **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

Time (min)	Solution C (%)	Methanol (%)
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 solution: 0.1 mg/mL of Chlorthalidone in *Diluent*. Sonicate to dissolve as needed.

Chromatographic system

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

Mode: LC

Detector: UV 220 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 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of chlorthalidone ($C_{14}H_{11}ClN_2O_4S$) in the portion of Chlorthalidone 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 = concentration of Chlorthalidone in the *Sample solution* (mg/mL)▲ (USP 1-May-2023)

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

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Chloride and Sulfate ⟨221⟩, *Chloride***

Standard solution: 0.50 mL of 0.020 N hydrochloric acid

Sample solution: Shake 1.0 g with 40 mL of water for 5 min, and pass through chloride-free filter paper previously rinsed with water. Use the filtrate.

Acceptance criteria: NMT 0.035%

Change to read:

• **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: 0.5 µg/mL of USP Chlorthalidone RS from the *Standard solution* in *Diluent*

Sample solution: 1 mg/mL of Chlorthalidone in *Diluent*. Sonicate to dissolve as needed.

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 Chlorthalidone 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 = 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 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Chlorthalidone related compound A	0.68	1.1	0.7
Chlorthalidone	1.00	—	—
Chlorthalidone dichloro analog[a]	5.64	1.1	0.20
Any unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0▲ (USP 1-May-2023)

[a] 3-(3,4-Dichlorophenyl)-2,3-dihydro-3-hydroxy-1*H*-isoindolin-1-one.

SPECIFIC TESTS

• **LOSS ON DRYING** ⟨731⟩

Sample: 2 g

Analysis: Dry at 105° for 4 h.

Acceptance criteria: NMT 0.4%

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers.

Change to read:

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Chlorthalidone RS

USP Chlorthalidone Related Compound A RS

▲2-(4-Chloro-3-sulfamoylbenzoyl)benzoic acid;
Also known as▲ (USP 1-May-2023) 4'-Chloro-3'-sulfamoyl-2-benzophenone carboxylic acid.

▲$C_{14}H_{10}ClNO_5S$ 339.75▲ (USP 1-May-2023)

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

Topic/Question	Contact	Expert Committee
CHLORTHALIDONE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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