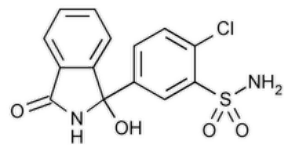


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Chlorthalidone

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-1H-isoindol-1-yl)-;
2-Chloro-5-(1-hydroxy-3-oxo-1-isoindoliny)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