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Chlorothiazide Oral Suspension

DEFINITION
Chlorothiazide Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of chlorothiazide ($C_7H_6ClN_3O_4S_2$).

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*.
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
- **Procedure**

Solution A: 0.1% formic acid in water

Solution B: Methanol

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	94	6
4	94	6
14	80	20
18	40	60
25	40	60
26	94	6
30	94	6

Diluent: Acetonitrile and *Solution A* (30:70)

Standard solution: 0.1 mg/mL of USP Chlorothiazide RS in *Diluent*

Sample stock solution: 0.5 mg/mL of chlorothiazide in *Diluent* prepared as follows. Transfer a suitable amount of Oral Suspension, equivalent to 25 mg of chlorothiazide, to a 50-mL volumetric flask. Add 40 mL of *Diluent* and sonicate to dissolve. Dilute with *Diluent* to volume. Centrifuge and use the supernatant.

Sample solution: Nominally 0.1 mg/mL of chlorothiazide in *Diluent*, from *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 275 nm. For *Identification* test *B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 5-µm packing L1

Temperatures

Autosampler: 5°

Column: 30°

Flow rate: 1 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 chlorothiazide ($C_7H_6ClN_3O_4S_2$) in the portion of Oral Suspension taken:

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

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

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

C_S = concentration of USP Chlorothiazide RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩**

For single-unit containers

Acceptance criteria: Meets the requirements

• **Deliverable Volume ⟨698⟩**

For multiple-unit containers

Acceptance criteria: Meets the requirements

IMPURITIES

• **Organic Impurities**

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

Standard solution: 10 µg/mL of USP Benzothiadiazine Related Compound A RS and 2 µg/mL of USP Chlorothiazide RS in *Diluent*

Sample solution: Nominally 1 mg/mL of chlorothiazide in *Diluent* prepared as follows. Transfer a suitable amount of Oral Suspension, equivalent to 25 mg of chlorothiazide, to a 25-mL volumetric flask. Add 20 mL of *Diluent* and sonicate to dissolve. Dilute with *Diluent* to volume. Centrifuge and use the supernatant.

System suitability

Sample: *Standard solution*

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

Suitability requirements

Resolution: NLT 4.0 between the benzothiadiazine related compound A and chlorothiazide peaks

Relative standard deviation: NMT 5.0% for chlorothiazide

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual unspecified degradation product in the portion of Oral Suspension 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 chlorothiazide from the *Standard solution*

C_S = concentration of USP Chlorothiazide RS in the *Standard solution* (µg/mL)

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

Acceptance criteria: See *Table 2*. Disregard any peak below 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Benzothiadiazine related compound A[a]	0.7	—
Chlorothiazide	1.0	—
Any individual unspecified degradation product	—	0.2
Total degradation products	—	2.0

[a] Not included in the total degradation products.

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 3.2–4.0

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Protect from freezing and store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Benzothiadiazine Related Compound A RS

4-Amino-6-chloro-1,3-benzenedisulfonamide.

$C_6H_8ClN_3O_4S_2$ 285.73

USP Chlorothiazide RS

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

Topic/Question	Contact	Expert Committee
CHLOROTHIAZIDE ORAL SUSPENSION	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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