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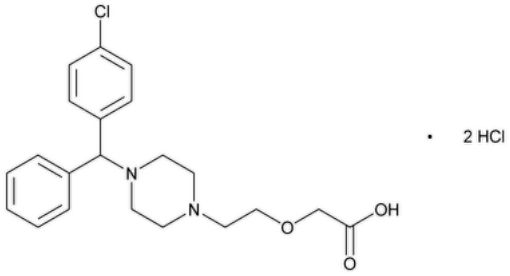
Cetirizine Hydrochloride



$C_{21}H_{25}ClN_2O_3 \cdot 2HCl$ 461.81

(±)-[2-[4-[(4-Chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]acetic acid, dihydrochloride;

(±)-[2-[4-(*p*-Chloro-α-phenylbenzyl)-1-piperazinyl]ethoxy]acetic acid, dihydrochloride;

(2-{4-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl}ethoxy)acetic acid dihydrochloride CAS RN®: 83881-52-1; UNII: 64O047KTOA.

DEFINITION

Cetirizine Hydrochloride contains NLT 98.0% and NMT 102.0% of cetirizine hydrochloride ($C_{21}H_{25}ClN_2O_3 \cdot 2HCl$), calculated on the dried basis.

IDENTIFICATION

- **A. Spectroscopic Identification tests ⟨197⟩, *Infrared Spectroscopy*:** 197K or 197A
- **B. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride*:** Meets the requirements
- **C.** 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**

Mobile phase: Acetonitrile, water, and 1 M sulfuric acid (93: 6.6: 0.4)

Standard solution: 0.5 mg/mL of USP Cetirizine Hydrochloride RS in *Mobile phase*

Sample solution: 0.5 mg/mL of Cetirizine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 25-cm; 5-µm packing L3

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 3 times the retention time of the cetirizine peak

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 cetirizine hydrochloride ($C_{21}H_{25}ClN_2O_3 \cdot 2HCl$) in the portion of Cetirizine Hydrochloride taken:

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

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

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

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

C_U = concentration of Cetirizine Hydrochloride in the *Sample solution* (mg/mL)

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

IMPURITIES

• **Residue on Ignition ⟨281⟩**

Acceptance criteria: NMT 0.2%

• **Organic Impurities, Procedure 1**

[Note—It is recommended that *Organic Impurities, Procedure 2* be performed if either cetirizine ethanol (2-{4-[(4-chloro phenyl)phenylmethyl]piperazin-1-yl}ethanol) or cetirizine acetic acid (2-{4-[(4-chloro phenyl)phenylmethyl]piperazin-1-yl}acetic acid) may be present in the test substance.]

Mobile phase and **Sample solution:** Prepare as directed in the *Assay*.

System suitability solution: 4 µg/mL each of USP Cetirizine Hydrochloride RS and USP Cetirizine Related Compound A RS in *Mobile phase*

Sensitivity solution: 0.1 µg/mL of USP Cetirizine Hydrochloride RS in *Mobile phase*

Standard solution: 0.5 µg/mL of USP Cetirizine Hydrochloride RS in *Mobile phase*

Chromatographic system: Proceed as directed in the *Assay*.

System suitability

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

[Note—See *Table 1* for relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between cetirizine and cetirizine related compound A, *System suitability solution*

Tailing factor: NMT 2.0 for cetirizine, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual specified or unspecified impurity in the portion of Cetirizine Hydrochloride taken:

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

r_U = peak response of each individual specified or unspecified impurity from the *Sample solution*

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

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

C_U = concentration of Cetirizine Hydrochloride in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. The reporting threshold is 0.02%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
4-CBH[a]	0.3	1.4	0.1
Cetirizine dimer[b]	0.5	1.8	0.1
2-Chlorocetirizine[c]	0.85	0.49	0.1
Cetirizine related compound A	0.9	0.95	0.1
Cetirizine	1.0	—	—
Deschlorocetirizine[d]	1.4	0.45	0.1
CBHP[e]	1.45	1.6	0.1
Any individual unspecified impurity	—	1.0	0.10

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Total impurities	—	—	0.3

[a] 4-Chlorobenzhydrol.

[b] 1,4-Bis[(4-chlorophenyl)phenylmethyl]piperazine.

[c] 2-(2-{4-[(2-Chlorophenyl)phenylmethyl]piperazin-1-yl}ethoxy)acetic acid.

[d] 2-{2-[4-(Diphenylmethyl)piperazin-1-yl]ethoxy}acetic acid.

[e] 1-[(4-Chlorophenyl)phenylmethyl]piperazine.

Change to read:

• **Organic Impurities, Procedure 2**

Solution A: 2 g/L of ▲tetrabutylammonium▲ (ERR-1-Oct-2024) hydrogen sulfate and 3 g/L of monobasic sodium phosphate monohydrate in water. Adjust with 1 N sodium hydroxide to a pH of 2.8 ± 0.05.

Solution B: Methanol

Buffer: 1.4 g/L of monobasic sodium phosphate monohydrate and 2.7 g/L of dibasic sodium phosphate heptahydrate. Adjust with either 1 N sodium hydroxide or 10% phosphoric acid to a pH of 6.9 ± 0.1.

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)	Flow Rate (mL/min)
0	58	42	1.2
40	58	42	1.2
68	20	80	1.5
108	20	80	1.5
110	58	42	1.2
120	58	42	1.2

Diluent: Acetonitrile and *Buffer* (50:50)

Sensitivity solution: 1 µg/mL of USP Cetirizine Hydrochloride RS in *Diluent*

Standard solution: 2 µg/mL of USP Cetirizine Hydrochloride RS in *Diluent*

Sample solution: 2 mg/mL of Cetirizine Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 232 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: See *Table 2*.

Injection volume: 10 µL

System suitability

Samples: *Standard solution* and *Sensitivity solution*

[Note—See *Table 3* for relative retention times.]

Suitability requirements

Column efficiency: NLT 6000 theoretical plates, *Standard solution*

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual specified or unspecified impurity in the portion of Cetirizine Hydrochloride taken:

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

r_U = peak response of each individual specified or unspecified impurity from the *Sample solution*

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

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

C_U = concentration of Cetirizine Hydrochloride in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*. The reporting threshold is 0.05%.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Deschlorocetirizine[a]	0.35	0.56	0.1
Cetirizine ethanol[b]	0.53	1.2	0.1
CBHP[c]	0.66	1.3	0.1
2-Chlorocetirizine[d]	0.70	0.52	0.1
Cetirizine methyl ester[e]	0.81	0.96	0.1
3-Chlorocetirizine[f]	0.87	0.52	0.1
Cetirizine	1.0	—	—
Cetirizine acetic acid[g]	1.15	0.97	0.1
Cetirizine *N*-oxide[h]	1.25	0.81	0.1
4-CBH[i]	1.55	1.2	0.1
4-Chlorobenzophenone[j]	1.66	0.50	0.1
Cetirizine dimer[k]	2.48	1.4	0.1
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.3

[a] 2-{2-[4-(Diphenylmethyl)piperazin-1-yl]ethoxy}acetic acid.

[b] 2-{4-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl}ethanol.

[c] 1-[(4-Chlorophenyl)phenylmethyl]piperazine.

[d] 2-(2-{4-[(2-Chlorophenyl)phenylmethyl]piperazin-1-yl}ethoxy)acetic acid.

[e] Methyl 2-(2-{4-[(4-chlorophenyl)phenylmethyl]piperazin-1-yl}ethoxy)acetate.

[f] 2-[2-[4-[(3-Chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]acetic acid.

[g] 2-{4-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl}acetic acid.

[h] 2-(2-{4-[(4-Chlorophenyl)(phenyl)methyl]piperazin-1-yl}ethoxy)acetic acid N^1-oxide.

[i] 4-Chlorobenzhydrol.

[j] (4-Chlorophenyl)phenylmethanone.

[k] 1,4-Bis[(4-chlorophenyl)phenylmethyl]piperazine.

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample solution: 50 mg/mL in water

Acceptance criteria: 1.2–1.8

- **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° to a constant weight.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, protected from light and moisture. Store at room temperature.
- **Labeling:** Label it to indicate with which impurity procedures the article complies.
- **USP Reference Standards ⟨11⟩**

USP Cetirizine Hydrochloride RS

USP Cetirizine Related Compound A RS

(*RS*)-2-[2-[4-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]acetic acid ethyl ester oxalate; also known as Ethyl 2-[2-{4-[(4-chlorophenyl)(phenyl)methyl]piperazin-1-yl}ethoxy]acetate oxalate salt.

$C_{23}H_{29}ClN_2O_3 \cdot C_2H_2O_4$ 506.97

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

Topic/Question	Contact	Expert Committee
CETIRIZINE HYDROCHLORIDE	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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