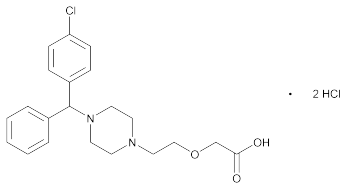
the cephradine and cephalexin peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

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 [83881-52-1].

DEFINITION

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

IDENTIFICATION

- **A. Infrared Absorption** ⟨197K⟩
- **B. Identification Test—General,** *Chloride* ⟨191⟩**:** Meets the requirements

ASSAY

- **Procedure**

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

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

Sample solution: 0.5 mg/mL 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 size: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{21}H_{25}ClN_2O_3 \cdot 2HCl$ in the portion of Cetirizine Hydrochloride taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response 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

Inorganic Impurities

- **Residue on Ignition** ⟨281⟩**:** NMT 0.2%
- **Heavy Metals,** *Method I* ⟨231⟩**:** 10 ppm

Organic Impurities

[NOTE—It is recommended that *Test 2* be performed if either cetirizine ethanol (2-{4-[(4-chlorophenyl)phenylmethyl] piperazin-1-yl}ethanol) or cetirizine acetic acid (2-{4-[(4-chlorophenyl)phenylmethyl]piperazin-1-yl}acetic acid) may be present in the test substance.]

- **Procedure 1**

Mobile phase and **Sample solution:** Proceed 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*

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

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

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

Run time: Three times the retention time of cetirizine

System suitability

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

Suitability requirements

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

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each 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 for each impurity from the *Sample solution*

r_S = peak response for 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 *Impurity Table 1* for values)

Acceptance criteria: See *Impurity Table 1*.

Total impurities: NMT 0.3%. [NOTE—Disregard peaks below 0.02%.]

Impurity Table 1

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

[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-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]acetic acid, ethyl ester (cetirizine ethyl ester).

[e] 2-[2-[4-(Diphenylmethyl]piperazin-1-yl]ethoxy]acetic acid.

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

- **Procedure 2**

Solution A: 2 g/L tetrabutyl ammonium 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 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.
Diluent: Acetonitrile and *Buffer* (1:1)
Mobile phase: See the gradient table below.

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

Standard solution: 2 µg/mL of USP Cetirizine Hydrochloride RS in *Diluent*
Sample solution: 2 mg/mL 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°
Injection size: 10 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 2
Column efficiency: NLT 6000 theoretical plates
Relative standard deviation: NMT 5.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of each 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 for each impurity from the *Sample solution*
r_S = peak response for 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 *Impurity Table 2* for values)

Acceptance criteria: See *Impurity Table 2*.
Total impurities: NMT 0.3%. [NOTE—Disregard peaks below 0.05%.]

Impurity Table 2

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

[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**⟩**:** 1.2-1.8, in an aqueous solution 1 in 20
- **Loss on Drying** ⟨**731**⟩**:** Dry a sample at 105 ° to a constant weight: it loses NMT 0.5% of its weight.

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 dihyrochloride.
$C_{23}H_{29}ClN_2O_3 \cdot 2HCl$ 489.86

Cetirizine Hydrochloride Oral Solution

DEFINITION
Cetirizine Hydrochloride Oral Solution contains NL T 90.0% and NMT 110.0% of the labeled amount of $C_{21}H_{25}ClN_2O_3 \cdot 2HCl$.

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. Identification Tests—General,** *Chloride* ⟨**191**⟩**:** Meets the requirements