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

ASSAY

• **PROCEDURE**

Solution A: Acetonitrile

Solution B: 1.36 g/L of monobasic potassium phosphate in water. Adjust with a 2% solution of phosphoric acid in water to a pH of 3.5 ± 0.05.

Diluent: Acetonitrile and water (3:7)

Mobile phase: See the gradient table below.

Time (min)	*Solution A* (%)	*Solution B* (%)
0	5	95
15	5	95
22	25	75
35	25	75
40	5	95
50	5	95

Standard stock solution: 5 mg/mL of USP Cetirizine Hydrochloride RS in water

Standard solution: 0.1 mg/mL of USP Cetirizine Hydrochloride RS in *Diluent*, from the *Standard stock solution*

Sample solution: Transfer an amount of Oral Solution to a suitable volumetric flask to obtain a nominal concentration of 0.1 mg/mL of cetirizine hydrochloride. Dissolve in 60% of the flask volume of *Diluent* by swirling. Sonicate 3 min, and dilute with *Diluent* to volume. Pass through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 233 nm

Column: 4.6-mm × 25-cm; 5-µm packing L10

Column temperature: 50°

Flow rate: 2 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{21}H_{25}ClN_2O_3 \cdot 2HCl$ in the portion of Oral Solution 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 = nominal concentration of cetirizine hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **DELIVERABLE VOLUME** ⟨**698**⟩**:** Meets the requirements

IMPURITIES

Organic Impurities

• **PROCEDURE**

Solution A: Transfer 50 mL of water to a 100-mL volumetric flask, add 5.5 mL of sulfuric acid, and dilute with water to volume.

Mobile phase: Acetonitrile, water, and *Solution A* (965:33:1)

Diluent: Acetonitrile and water (7:13)

Standard solution: 6 µg/mL of USP Cetirizine Hydrochloride RS in *Diluent*

Sample solution: 0.6 mg/mL of cetirizine hydrochloride in *Diluent*. Transfer an amount of Oral Solution to a suitable volumetric flask, dissolve in *Diluent*, sonicate for 10 min, and dilute with *Diluent* to volume. Pass through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

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

Column temperature: 30°

Flow rate: 2 mL/min

Injection size: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 10,000 theoretical plates

Tailing factor: NMT 1.5

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Oral Solution taken:

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

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 = nominal concentration of cetirizine hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: See *Impurity Table 1*.

Total impurities: NMT 0.8%

Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Cetirizine acetic acid[a]	0.69	P[b]
2-Chlorocetirizine[c]	0.83	P
Cetirizine	1.00	—
Cetirizineethanol[d]	1.30	P
Ethoxycetirizine[e]	1.38	P
CBHP[f]	1.52	P
Propylene glycol ester of cetirizine (diastereomer 1)[g]	1.53	0.2
Propylene glycol ester of cetirizine (diastereomer 2)[g]	1.61	0.2
Deschlorocetirizine[h]	1.65	P
Glyceryl ester of cetirizine[i]	2.20	0.5
Any individual unspecified impurity	—	0.2

[a] 2-[4-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl]acetic acid.

[b] P = Process impurity. Provided for information only; the content is not calculated and not reported. The content is controlled in the drug substance monograph.

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

[d] 2-[4-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl]ethanol.

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

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

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

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

[i] 2,3-Dihydroxypropyl 2-(2-{4-[(4-chlorophenyl)phenylmethyl]piperazin-1-yl}ethoxy)acetate.

SPECIFIC TESTS

• **pH** ⟨**791**⟩**:** 4.0–5.1

• **MICROBIAL ENUMERATION TESTS** ⟨**61**⟩ and **TESTS FOR SPECIFIED MICROORGANISMS** ⟨**62**⟩**:** The total aerobic microbial count does not exceed 100 cfu/mL, and the total combined molds and yeasts count does not exceed 10 cfu/mL. It meets the requirements of the tests for absence of *Escherichia coli*.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers, and protect from light. Store at controlled room temperature or in a cold place.
- **USP REFERENCE STANDARDS** ⟨11⟩
  USP Cetirizine Hydrochloride RS

Cetirizine Hydrochloride and Pseudoephedrine Hydrochloride Extended-Release Tablets

DEFINITION

Cetirizine Hydrochloride and Pseudoephedrine Hydrochloride Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of cetirizine hydrochloride ($C_{21}H_{25}ClN_2O_3 \cdot 2HCl$) and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$).

IDENTIFICATION

- The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **CETIRIZINE HYDROCHLORIDE**

  Buffer: 3.5 g/L of monobasic ammonium phosphate and 1.0 g/L of tetrabutylammonium bisulfate in water. Adjust with phosphoric acid to a pH of 2.5.
  Diluent: Methanol and *Buffer* (2:3)
  Solution A: Acetonitrile, methanol, and *Buffer* (9:2:29)
  Solution B: Acetonitrile
  Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	100	0
27.0	100	0
30.0	0	100
30.1	100	0
35.0	100	0

  Standard stock solution: 0.5 mg/mL of USP Cetirizine Hydrochloride RS in *Diluent*. [NOTE—Sonicate to dissolve.]
  Standard solution: 0.025 mg/mL of USP Cetirizine Hydrochloride RS in *Diluent* from the *Standard stock solution*
  Sample solution: 0.025 mg/mL of cetirizine hydrochloride (from NMT 10 finely powdered Tablets) prepared as follows. Dissolve the Tablets first in methanol, using 22.5% of the final flask volume. Sonicate for NLT 20 min with vigorous swirling every 5 min. To the solution add a volume of *Buffer* equal to 26% of the final flask volume. Allow the solution to equilibrate to room temperature. Dilute with *Diluent* to volume. Pass a portion through a membrane filter of 0.45- µm pore size.
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 230 nm
  Column: 4.6-mm × 15-cm; 3.5-µm packing L1
  Column temperature: 30°
  Autosampler temperature: 5°
  Flow rate: 1 mL/min
  Injection size: 25 µL
  System suitability
  Sample: *Standard solution*
  Suitability requirements
  Column efficiency: NLT 3000 theoretical plates
  Tailing factor: NMT 1.5
  Relative standard deviation: NMT 2.0%
  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 Tablets 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 = nominal concentration of cetirizine hydrochloride in the *Sample solution* (mg/mL)
  Acceptance criteria: 90.0%–110.0%

- **PSEUDOEPHEDRINE HYDROCHLORIDE**

  Buffer: 0.8 g/L of ammonium acetate in water. To 1 L of the solution add 1.0 mL of triethylamine. Adjust with glacial acetic acid to a pH of 4.5.
  Mobile phase: Acetonitrile and *Buffer* (3:7)
  Standard solution: 0.5 mg/mL of USP Pseudoephedrine Hydrochloride RS in *Mobile phase*. [NOTE—Sonicate to dissolve.]
  Sample stock solution: 2.4 mg/mL of pseudoephedrine hydrochloride (from 5 finely powdered Tablets) prepared as follows. Dissolve the crushed Tablets first in acetonitrile, using 24% of the final flask volume. Sonicate for NLT 15 min. To the solution add a volume of *Buffer* equal to 56% of the final flask volume. Sonicate for NLT 15 min. Shake the flask for NLT 10 min. Allow the solution to equilibrate to room temperature. Dilute with *Mobile phase* to volume. Centrifuge a portion for 15 min to obtain a clear supernatant.
  Sample solution: 0.5 mg/mL of pseudoephedrine hydrochloride in *Mobile phase*, from the *Sample stock solution.* Pass the solution through a membrane filter of 0.45-µm pore size.
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 254 nm
  Column: 4.6-mm × 15-cm; 5-µm packing L9
  Flow rate: 1.5 mL/min
  Injection size: 25 µL
  Run time: 2 times the retention time of pseudoephedrine
  System suitability
  Sample: *Standard solution*
  Suitability requirements
  Column efficiency: NLT 1000 theoretical plates
  Tailing factor: NMT 2.0
  Relative standard deviation: NMT 2.0%
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) in the portion of Tablets taken:

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

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