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Cetirizine Hydrochloride Orally Disintegrating Tablets

DEFINITION

Cetirizine Hydrochloride Orally Disintegrating Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of cetirizine hydrochloride ($C_{21}H_{25}ClN_2O_3 \cdot 2HCl$).

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**

Buffer A: Dissolve 13.2 g of sodium 1-decanesulfonate in 2760 mL of water. Add 5.5 g of monobasic sodium phosphate and 1.2 mL of phosphoric acid. Pass through a suitable filter.

Buffer B: Dissolve 13.2 g of sodium 1-decanesulfonate in 2000 mL of water. Add 5.5 g of monobasic sodium phosphate and 1.2 mL of phosphoric acid. Pass through a suitable filter.

Solution A: Acetonitrile and *Buffer A* (31:69)

Solution B: Acetonitrile and *Buffer B* (50:50)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
35.0	0	100
35.1	100	0
45.0	100	0

Diluent: Acetonitrile and 0.01 N hydrochloric acid (20:80)

System suitability stock solution: 0.04 mg/mL of USP Meclizine Related Compound A RS, prepared as follows. Transfer a quantity of the compound into a suitable volumetric flask. Add 5% of the flask volume of acetonitrile to dissolve the components. Sonicate if needed. Dilute with *Diluent* to volume.

System suitability solution: 0.4 mg/mL of USP Cetirizine Hydrochloride RS and 1.2 µg/mL of USP Meclizine Related Compound A RS, prepared as follows. In a 100-mL volumetric flask, dissolve 40 mg of USP Cetirizine Hydrochloride RS in *Diluent*, and then pipet 3.0 mL of the *System suitability stock solution*. Dilute with *Diluent* to volume.

Standard solution: 0.4 mg/mL of USP Cetirizine Hydrochloride RS in *Diluent*

Sample solution: Nominally 0.4 mg/mL of cetirizine hydrochloride, prepared as follows. Transfer 20 Tablets into a 500-mL volumetric flask, add 375 mL of *Diluent*, and stir for at least 30 min. Dilute with *Diluent* to volume and pass a portion of this solution through a suitable filter (GHP or PVDF), discarding the first 1 mL of filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm. For *Identification* test *B*, use a diode array detector in the range of 210–300 nm.

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Column temperature: 30°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

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

[NOTE—Identify the components on the basis of their relative retention times, as shown in *Table 2*.]

Suitability requirements

Resolution: NLT 1.5 between cetirizine and meclizine related compound A, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount 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 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

- **DISINTEGRATION ⟨701⟩:** NMT 30 s
- **DISSOLUTION ⟨711⟩**

Medium: pH 6.5 phosphate buffer (4.77 g/L monobasic potassium phosphate and 2.62 g/L of dibasic potassium phosphate); 900 mL, degassed by USP procedure

Apparatus 2: 50 rpm

Time: 15 min

Buffer: 2.7 g/L of monobasic potassium phosphate in water. Add 0.6 mL/L of phosphoric acid.

Mobile phase: Acetonitrile and *Buffer* (33:67)

Diluent: Acetonitrile and 0.01 N hydrochloric acid (20:80)

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

Standard solution: 0.01 mg/mL of USP Cetirizine Hydrochloride RS from *Standard stock solution*, in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first 1–2 mL.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 7.5-cm; 3.5-µm packing L1

Column temperature: 40°

Flow rate: 2.5 mL/min

Injection volume: 100 µL

Run time: 2.7 times the retention time of cetirizine

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 the labeled amount of cetirizine hydrochloride ($C_{21}H_{25}ClN_2O_3 \cdot 2HCl$) dissolved:

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

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)

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of cetirizine hydrochloride ($C_{21}H_{25}ClN_2O_3 \cdot 2HCl$) is dissolved.

- **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

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

System suitability stock solution: 0.04 mg/mL each of USP Cetirizine Related Compound G RS, USP Cetirizine Related Compound B RS, USP 4-Chlorobenzophenone RS, USP Meclizine Related Compound A RS, and USP Cetirizine Related Compound A RS, and 0.06 mg/mL each of USP Hydroxyzine Related Compound A RS and USP Cetirizine Related Compound C RS, prepared as follows. Transfer a quantity of each compound into a suitable volumetric flask. Add 5% of the flask volume of acetonitrile to dissolve the compounds. Sonicate as needed. Dilute with *Diluent* to volume.

System suitability solution: 0.4 mg/mL of USP Cetirizine Hydrochloride RS; 1.2 µg/mL each of USP Cetirizine Related Compound G RS, USP Cetirizine Related Compound B RS, USP 4-Chlorobenzophenone RS, USP Meclizine Related Compound A RS, and USP Cetirizine Related Compound A RS; and 1.8 µg/mL each of USP Hydroxyzine Related Compound A RS and USP Cetirizine Related Compound C RS, prepared as follows. In a 100-mL volumetric flask, dissolve 40 mg of USP Cetirizine Hydrochloride RS in *Diluent*, and then pipet 3.0 mL of the *System suitability stock solution*. Dilute with *Diluent* to volume.

Standard stock solution: 0.04 mg/mL each of USP Cetirizine Hydrochloride RS, USP Cetirizine Related Compound G RS, USP Hydroxyzine Related Compound A RS, and USP 4-Chlorobenzophenone RS, prepared as follows. Transfer a quantity of each compound into a suitable volumetric flask. Add 5% of the flask volume of acetonitrile to dissolve the compounds. Sonicate if needed. Dilute with *Diluent* to volume.

Standard solution: 0.8 µg/mL each of USP Cetirizine Hydrochloride RS, USP Cetirizine Related Compound G RS, USP Hydroxyzine Related Compound A RS, and USP 4-Chlorobenzophenone RS from *Standard stock solution*, in *Diluent*

Sample solution: Nominally 400 µg/mL of cetirizine hydrochloride, prepared as follows. Transfer 20 Tablets into a 500-mL volumetric flask, add 375 mL of *Diluent,* and stir for at least 30 min. Dilute with *Diluent* to volume and pass a portion of this solution through a suitable filter (GHP or PVDF), discarding the first 1 mL of filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm and 260 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Column temperature: 30°

Flow rate: 1.5 mL/min

Injection volume: 50 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between cetirizine and meclizine related compound A, *System suitability solution*

Relative standard deviation: NMT 10.0% for each component, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Chromatograph the *System suitability solution*, and identify the components on the basis of their relative retention times, as shown in *Table 2*. Use the peak response at 260 nm for 4-chlorobenzophenone. Use 230 nm for all other degradation products.

Calculate the percentage of cetirizine related compound G, hydroxyzine related compound A, and 4-chlorobenzophenone 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 related compound G, hydroxyzine related compound A, or 4-chlorobenzophenone from the *Sample solution*

r_S = peak response of the appropriate USP Reference Standard from the *Standard solution*

C_S = concentration of the appropriate USP Reference Standard in the *Standard solution* (µg/mL)

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

Calculate the percentage of all other degradation products in the portion of Tablets taken:

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

r_U = peak response of any other degradation product 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* (µg/mL)

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

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

Table 2

Compound	Relative Retention Time	Wavelength (nm)	Acceptance Criteria, NMT (%)
Cetirizine related compound B	0.88	230	0.2
Meclizine related compound A	0.95	230	0.2
Cetirizine	1.00	230	—
Bromocetirizine	1.07	—	P[a]
Cetirizine related compound C	1.09	—	P[a]
Cetirizine related compound G	1.15	230	0.2
Hydroxyzine related compound A	1.23	230	0.2
4-Chlorobenzophenone	1.45	260	0.2
Cetirizine related compound A	1.53	230	0.2
Any individual unspecified degradation product	—	230	0.2
Total degradation products	—	—	0.8

[a] Process impurity included in the table for identification only. Process impurities are controlled in the drug substance, and are not to be reported or included in the total impurities for the drug product.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.

Change to read:

• **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.

$C_{23}H_{29}ClN_2O_3 \cdot C_2H_2O_4$ ▲506.97▲ (ERR 1-May-2020)

USP Cetirizine Related Compound B RS

2-(4-Benzhydrylpiperazin-1-yl)ethan-1-ol.

$C_{19}H_{24}N_2O$ 296.41

USP Cetirizine Related Compound C RS

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

$C_{21}H_{26}ClN_3O_2$ 387.90

USP Cetirizine Related Compound G RS

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

$C_{19}H_{23}ClN_2O$ 330.85

USP 4-Chlorobenzophenone RS

(4-Chlorophenyl)phenylmethanone.

$C_{13}H_9ClO$ 216.66

USP Hydroxyzine Related Compound A RS

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

$C_{17}H_{19}ClN_2$ 286.80

USP Meclizine Related Compound A RS
4-Chlorobenzhydrol.
$C_{13}H_{11}ClO$ 218.68

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

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

Chromatographic Database Information: Chromatographic Database

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