Add the following:

•Cetirizine Hydrochloride Oral Solution

» Cetirizine Hydrochloride Oral Solution contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of cetirizine hydrochloride ($C_{21}H_{25}ClN_2O_3 \cdot 2HCl$).

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*.

Identification—

A: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

B: It meets the requirements of the test for *Chloride* ⟨191⟩.

Microbial enumeration tests ⟨61⟩ and **Tests for specified microorganisms** ⟨62⟩**—**It meets the requirements of the tests for absence of *Escherichia coli*. The total aerobic microbial count does not exceed 100 cfu per mL, and the total combined molds and yeasts count does not exceed 10 cfu per mL.

Deliverable volume ⟨698⟩**:** meets the requirements.

pH ⟨791⟩**:** between 4.3 and 5.1.

Related compounds—

Dilute sulfuric acid—Transfer about 50 mL of water into a 100-mL volumetric flask, add 5.5 mL of sulfuric acid, dilute with water to volume, and mix.

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile, water, and *Dilute sulfuric acid* (965 : 33 : 1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Diluent—Prepare a mixture of water and acetonitrile (65 : 35).

Standard solution—Dissolve an accurately weighed quantity of USP Cetirizine Hydrochloride RS in *Diluent*, and dilute quantitatively to obtain a solution having a known concentration of about 6 µg per mL.

Test solution—Transfer an accurately measured volume of Oral Solution, equivalent to about 15 mg of cetirizine hydrochloride, into a 25-mL volumetric flask, dilute with *Diluent*, and sonicate for about 10 minutes. Dilute with *Diluent* to volume, and mix. Pass the solution through a 0.45-µm polyvinylidene fluoride (PVDF) filter, and use the filtrate.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 230-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L3. The flow rate is about 2.0 mL per minute. The column is maintained at 30°. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the column efficiency is not less than 10,000 theoretical plates; the tailing factor is not more than 1.5; and the relative standard deviation for replicate injections is not more than 5.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the amount of each impurity, as a percentage of the label claim of cetirizine hydrochloride, in the Oral Solution taken by the formula:

$$100(C_S / C_U)(r_i / r_S)$$

in which C_S is the concentration, in mg per mL, of cetirizine hydrochloride in the *Standard solution*; C_U is the concentration, in mg per mL, of cetirizine hydrochloride in the *Test solution*, based on the label claim; r_i is the individual peak response of each impurity obtained from the *Test solution*; and r_S is the peak response of cetirizine obtained from the *Standard solution*. The limits of impurities are as specified in *Table 1*.

Table 1

Compound	Approximate Relative Retention Time	Limit (%)
Cetirizine acetic acid[1]	0.69	P[2]
2-Chlorocetirizine[3]	0.83	P
Cetirizine	1.00	—
Cetirizineethanol[4]	1.30	P
Ethoxycetirizine[5]	1.38	P
CBHP[6]	1.52	P
Propylene glycol ester of cetirizine (diastereomer 1)[7]	1.53	0.2
Propylene glycol ester of cetirizine (diastereomer 2)[7]	1.61	0.2
Deschlorocetirizine[8]	1.65	P
Glyceryl ester of cetirizine[9]	2.20	0.5
Individual unknown	—	0.2
Total	—	0.8

[1]2-[4-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl]acetic acid.
[2]P = Process impurity, provided for information only, the content is not calculated and not reported. The content is controlled in the drug substance monograph.
[3]2-[2-[4-[(2-Chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]acetic acid.
[4]2-[4-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl]ethanol.
[5]2-[2-[2-[4-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy] ethoxy]acetic acid (ethoxycetirizine).
[6]1-[(4-Chlorophenyl)phenylmethyl]piperazine.
[7]2-Hydroxypropyl 2-(2-{4-[(4-chlorophenyl)phenylmethyl]piperazin-1-yl}ethoxy)acetate.
[8]2-{2-[4-(Diphenylmethyl)piperazin-1-yl]ethoxy]acetic acid.
[9]2,3-Dihydroxypropyl 2-(2-{4-[(4-chlorophenyl)phenylmethyl]piperazin-1-yl}ethoxy)acetate.

Assay—

Buffer solution—Dissolve 1.36 g of monobasic potassium phosphate in 1000 mL of water. Adjust with a 2% solution of phosphoric acid in water to a pH of 3.5 ± 0.05.

Mobile phase—Use variable mixtures of *Buffer solution* and acetonitrile as directed for *Chromatographic system*. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Diluent—Prepare a degassed mixture of water and acetonitrile (70 : 30).

Standard preparation—Dissolve an accurately weighed quantity of USP Cetirizine Hydrochloride RS in water to obtain a solution having a known concentration of about 5 mg per mL. Dilute an aliquot of this solution with *Diluent* to obtain a solution having a known concentration of about 0.1 mg per mL.

Assay preparation—Accurately transfer an amount of Oral Solution, equivalent to about 5 mg of cetirizine hydrochloride, to a 50-mL volumetric flask, add 30 mL of *Diluent,* and mix by swirling. Sonicate for about 3 minutes, and dilute with *Diluent* to volume.

Pass through a suitable 0.45-µm membrane filter, and use the filtrate.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 233-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L10. The flow rate is about 2.0 mL per minute. The column temperature is maintained at 50°. The chromatograph is programmed as follows.

Time (minutes)	Acetonitrile (%)	*Buffer solution* (%)	Elution
0–15	5	95	isocratic
15–22	5→25	95→75	linear gradient
22–35	25	75	isocratic
35–40	25→5	75→95	linear gradient
40–50	5	95	isocratic

Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor is not more than 1.5; and the relative standard deviation for replicate injections is not more than 1.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the amount of cetirizine hydrochloride ($C_{21}H_{25}ClN_2O_3 \cdot 2HCl$), as a percentage of the label claim, by the formula:

$$100(C_S / C_U)(r_U / r_S)$$

in which C_S is the concentration, in mg per mL, of cetirizine hydrochloride in the *Standard preparation;* C_U is the concentration, in mg per mL, of cetirizine hydrochloride in the *Assay preparation*, based on the label claim; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.● (RB 1-May-2010)