***Add the following:***

## ▪Cetirizine Hydrochloride Tablets

**DEFINITION**
Cetirizine Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of $C_{21}H_{25}ClN_2O_3 \cdot 2HCl$.

**IDENTIFICATION**
• 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**
**Solution A:** 2 N sulfuric acid and water (2:33)
**Buffer:** 2.9 mL/L of phosphoric acid in water
**Mobile phase:** Acetonitrile and *Buffer* (3:7)
**Diluent:** Acetonitrile, *Solution A*, and water (100:1:100)
**Standard solution:** 0.2 mg/mL of USP Cetirizine Hydrochloride RS in *Diluent*
**Sample solution:** 0.2 mg/mL of cetirizine hydrochloride in *Diluent*, from NLT 20 powdered Tablets. [NOTE—Sonicate, if necessary.]
**Chromatographic system**
(See *Chromatography* ⟨621⟩, *System Suitability*.)
**Mode:** LC
**Detector:** UV 230 nm
**Column:** 4.6-mm × 25-cm; 5-µm packing L1
**Flow rate:** 1.5 mL/min
**Injection size:** 10 µL
**Run time:** 1.3 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 $C_{21}H_{25}ClN_2O_3 \cdot 2HCl$ 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**
• **DISSOLUTION** ⟨**711**⟩
**Medium:** Water; 900 mL, degassed
**Apparatus 2:** 50 rpm
**Time:** 30 min
**Buffer:** 2.9 mL/L of phosphoric acid in water
**Mobile phase:** Acetonitrile and *Buffer* (2:3)
**Standard solution:** 11 µg/mL of USP Cetirizine Hydrochloride RS in water. This solution can be stored for 48 h at room temperature.
**Sample solution:** Pass a portion of the solution under test through a suitable 0.45-µm filter.
**Chromatographic system**
(See *Chromatography* ⟨621⟩, *System Suitability*.)
**Mode:** LC
**Detector:** UV 230 nm
**Column:** 4.6-mm × 25-cm; 5-µm packing L1
**Flow rate:** 1 mL/min
**Injection size:** 50 µL
**Run time:** 1.3 times the retention time of cetirizine
**System suitability**
**Sample:** *Standard solution*
**Suitability requirements**
**Tailing factor:** NMT 2.0
**Relative standard deviation:** NMT 2.0%
Calculate the percentage of cetirizine dissolved:

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

$r_U$ = peak response from the *Standard solution*
$r_S$ = peak response from the *Sample solution*
$C_S$ = concentration of the *Standard solution* (mg/mL)
L = Tablet label claim, mg
V = volume of *Medium*, 900 mL

**Tolerances:** NLT 80% (Q) of the labeled amount of cetirizine hydrochloride is dissolved.
• **UNIFORMITY OF DOSAGE UNITS** ⟨**905**⟩**:** Meet the requirements

**IMPURITIES**
**Organic Impurities**
• **PROCEDURE**
**Solution A:** 2 N sulfuric acid and water (2:33)
**Buffer:** 3.4 g/L of tetrabutyl ammonium hydrogen sulfate in water
**Diluent:** Acetonitrile, *Solution A*, and water (910:27:63)
**Mobile phase:** Acetonitrile, *Solution A*, and *Buffer* (93:5:2)
**Standard solution:** 1.5 µg/mL of USP Cetirizine Hydrochloride RS in *Diluent*
**Sample solution:** 0.5 mg/mL of cetirizine hydrochloride in *Diluent*, from NLT 20 powdered Tablets. [NOTE—Sonicate, if necessary.]
**Chromatographic system**
(See *Chromatography* ⟨621⟩, *System Suitability*.)
**Mode:** LC
**Detector:** UV 230 nm
**Column:** 4.0-mm × 25-cm; 5-µm packing L3
**Flow rate:** 0.8 mL/min
**Injection size:** 20 µL
**Run time:** 2.5 times the retention time of cetirizine
**System suitability**
**Sample:** *Standard solution*
**Suitability requirements**
**Tailing factor:** NMT 2.0
**Relative standard deviation:** NMT 10.0%
**Analysis**
**Samples:** *Standard solution* and *Sample solution*
Calculate the percentage of each impurity in the portion of Tablets taken:

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

$r_U$ = peak response of 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)
F = relative response factor (see *Impurity Table 1*)

**Acceptance criteria**
**Individual impurities:** See *Impurity Table 1*.
**Total impurities:** NMT 0.8%

**Impurity Table 1**

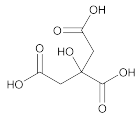
| Name | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|---|---|---|---|
| Cetirizine lactose ester[a] | 0.56 | 1.0 | 0.40 |
| Cetirizine | 1.0 | — | — |
| Cetirizine ethanol[b] | 1.67 | 1.2 | 0.15 |
| Any unspecified degradation product | — | — | 0.2 |

[a] 6-*O*-[2-(2-{4-[(4-Chlorophenyl)(phenyl)methyl]piperazin-1-yl}ethoxy)acetyl]-*β*-D-galactopyranosyl-(1→4)*β*-D-glucopyranose.
[b] 2-[4-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl]ethanol.

**ADDITIONAL REQUIREMENTS**
- **PACKAGING AND STORAGE:** Preserve in well-closed containers, and store below 30°.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Cetirizine Hydrochloride RS■1S *(USP35)*

## Anhydrous Citric Acid

Portions of the monograph text that are national *USP* text, and are not part of the harmonized text, are marked with symbols (✦✦) to specify this fact.



$C_6H_8O_7$ 192.1
1,2,3-Propanetricarboxylic acid, 2-hydroxy-;
Citric acid [77-92-9].

**DEFINITION**
Anhydrous Citric Acid contains NLT 99.5% and NMT 100.5% of $C_6H_8O_7$, calculated on the anhydrous basis.

**IDENTIFICATION**
- **A. INFRARED ABSORPTION** ⟨**197K**⟩**:** Dry the substance to be examined at 105° for 2 h.

**ASSAY**
- **PROCEDURE**
**Sample:** 0.550 g of Anhydrous Citric Acid; record weight accurately.
**Analysis:** Dissolve the *Sample* in 50 mL of water. Add 0.5 mL of phenolphthalein TS. Titrate with 1 N sodium hydroxide VS. Each mL of 1 N sodium hydroxide is equivalent to 64.03 mg of $C_6H_8O_7$.
**Acceptance criteria:** 99.5%–100.5% on the anhydrous basis

**IMPURITIES**
- **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.1%, determined on 1.0 g
- ✦**HEAVY METALS** ⟨**231**⟩**:** NMT 10 µg/g✦
- **SULFATE**
**Standard sulfate solution A:** 1.81 mg/mL of potassium sulfate in 30% alcohol. Immediately before use, transfer 10.0 mL of this solution to a 1000-mL volumetric flask, dilute with 30% alcohol to volume, and mix. This solution contains 10 µg/mL of sulfate.
**Standard sulfate solution B:** 1.81 mg/mL of potassium sulfate in water. Immediately before use, transfer 10.0 mL of this solution to a 1000-mL volumetric flask, dilute with water to volume, and mix. This solution contains 10 µg/mL of sulfate.
**Sample stock solution:** 66.7 mg/mL of Anhydrous Citric Acid
**Sample solution:** To 4.5 mL of *Standard sulfate solution A*, add 3 mL of a barium chloride solution (1 in 4), shake, and allow to stand for 1 min. To 2.5 mL of the resulting suspension, add 15 mL of the *Sample stock solution* and 0.5 mL of 5 N acetic acid, and mix.
**Standard solution:** Prepare as directed for the *Sample solution*, except use 15 mL of *Standard sulfate solution B* instead of the *Sample stock solution*.
**Analysis**
**Samples:** *Sample solution* and *Standard solution*
**Acceptance criteria:** Any turbidity produced in the *Sample solution* after 5 min standing is not greater than that produced in the *Standard solution* (0.015%).
- **LIMIT OF ALUMINUM** (where it is labeled as intended for use in dialysis)
**Standard aluminum solution:** To 352 mg of aluminum potassium sulfate in a 100-mL volumetric flask, add a few mL of water, swirl to dissolve, add 10 mL of diluted sulfuric acid, dilute with water to volume, and mix. Immediately before use, dilute 1.0 mL of this solution with water to 100.0 mL.
**pH 6.0 acetate buffer:** Dissolve 50 g of ammonium acetate in 150 mL of water, adjust with glacial acetic acid to a pH of 6.0, dilute with water to 250 mL, and mix.
**Sample solution:** Dissolve 20.0 g of Anhydrous Citric Acid in 100 mL of water, and add 10 mL of *pH 6.0 acetate buffer*. Extract this solution with successive portions of 20, 20, and 10 mL of a 0.5% solution of 8-hydroxyquinoline in chloroform, combining the chloroform extracts in a 50-mL volumetric flask. Dilute the combined extracts with chloroform to volume, and mix.
**Standard solution:** Prepare a mixture of 2.0 mL of *Standard aluminum solution*, 10 mL of *pH 6.0 acetate buffer*, and 98 mL of water. Extract this mixture as described for the *Sample solution*, dilute the combined extracts with chloroform to volume, and mix.
**Blank solution:** Prepare a mixture of 10 mL of *pH 6.0 acetate buffer* and 100 mL of water. Extract this mixture as described for *Sample solution,* dilute the combined extracts with chloroform to volume, and mix.
**Fluorometric conditions**
**Excitation wavelength:** 392 nm
**Emission wavelength:** 518 nm
**Analysis**
**Samples:** *Sample solution* and *Standard solution*
Determine the fluorescence intensities of the *Samples* in a fluorometer set as directed under *Fluorometric conditions*, using the *Blank solution* to set the instrument to zero.
**Acceptance criteria:** The fluorescence of the *Sample solution* does not exceed that of the *Standard solution* (0.2 ppm).

***Change to read:***

- **LIMIT OF OXALIC ACID**
**Sample stock solution:** ■0.80 g of Anhydrous Citric Acid in 4 mL of water■1S *(USP35)*
**Sample solution:** To■■1S *(USP35)* the *Sample stock solution* add 3 mL of hydrochloric acid and 1 g of granular zinc, boil for 1 min, and allow to stand for 2 min. Transfer the supernatant to a test tube containing 0.25 mL of a phenylhydrazine hydrochloride solution (1 in 100), and heat to boiling. Cool rapidly, transfer to a graduated cylinder, and add an equal volume of hydrochloric acid and 0.25 mL of a potassium ferricyanide solution (1 in 20). Shake, and allow to stand for 30 min.
**Standard solution:** Prepare as directed for the *Sample solution,* except use 4 mL of 0.10 mg/mL oxalic acid