

BRIEFING

Cetirizine Hydrochloride, page 317 of *PF* 32(2) [Mar.–Apr. 2006]. This new monograph was published in *PF* for public review and comment before the establishment of the USP Pending Standards Web page. The MD-PS Expert Committee reviewed the comments received and approved the monograph as an Authorized USP Pending Standard. The following is the summary of the comments and Expert committee decisions:

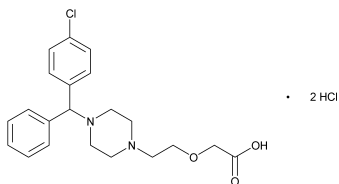
1. Comment Summary 1: Commenter suggested that the *Color of solution* and the *Clarity of solution* tests be deleted. Response: Comment incorporated.
2. Comment Summary 2: Commenter suggested that the limits for the *Assay*, procedures for *Chloride* identification, and the test for *Related compounds* should be brought in line with the tests in the current EP monograph for this item: Comment not incorporated.
3. Comment Summary 3: Commenter suggested that a test for *Residual Solvents* (467) be included in the monograph. Response: Comment not incorporated, since this is covered under *General Notices*.

(MD-PS: D. Bempong) RTS—C43753

Add the following:

■ **Cetirizine Hydrochloride**

v.1 Authorized March 16, 2007



$C_{21}H_{25}ClN_2O_3 \cdot 2HCl$ 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].

» Cetirizine Hydrochloride contains not less than 98.0 percent and not more than 102.0 percent of $C_{21}H_{25}ClN_2O_3 \cdot 2HCl$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers, protected from light and moisture. Store at room temperature.

USP Reference standards (11)—*USP Cetirizine Hydrochloride RS*. *USP Cetirizine Related Compound A RS*.

Identification—

A: *Infrared Absorption* (197K).

B: It meets the requirements of the test for *Chloride* (191).

pH (791): between 1.2 and 1.8, in an aqueous solution 1 in 20.

Loss on drying (731)—Dry it at 105° to constant weight: it loses not more than 0.5% of its weight.

Residue on ignition (281): not more than 0.2%.

Heavy metals, Method I (231): not more than 0.001%.

Related compounds—

Mobile phase—Proceed as directed in the *Assay*.

System suitability solution—Dissolve an accurately weighed quantity of USP Cetirizine Hydrochloride RS and USP Cetirizine Related Compound A RS in *Mobile phase*, and dilute quantitatively, and stepwise if necessary, to obtain a solution having concentrations of about 4 µg per mL of USP Cetirizine Hydrochloride RS and about 4 µg per mL of USP Cetirizine Related Compound A RS.

Standard solution—Dissolve an accurately weighed quantity of USP Cetirizine Hydrochloride RS in *Mobile phase*, and dilute quantitatively, and stepwise if necessary, to obtain a solution having a known concentration of about 0.5 µg per mL.

Test solution—Prepare as directed for the *Assay preparation* in the *Assay*.

Chromatographic system (see *Chromatography* (621))—Proceed as directed in the *Assay*. Chromatograph the *System suitability solution* and record the peak responses as directed for *Procedure*: the resolution, *R*, between cetirizine related compound A and cetirizine is not less than 2.0; and the tailing factor for the cetirizine peak is not more than 2.0. Chromatograph the *Standard solution*, and record the peak responses as directed for *Procedure*: the relative standard deviation for replicate injections is not more than 2.0%.

2 / **Cetirizine Hydrochloride**

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 responses for all the peaks. [NOTE—Record the chromatogram of the *Test solution* for a period of time equivalent to 3 times the retention time of cetirizine.] Calculate the percentage of each related compound in the portion of Cetirizine Hydrochloride taken by the formula:

$$0.1C_s / C_v(1/F)(r_i / r_s)$$

in which C_s is the concentration, in mg per mL, of USP Cetirizine Hydrochloride RS in the *Standard solution*; C_v is the concentration, in mg per mL, of Cetirizine Hydrochloride in the *Test solution*; F is the relative response factor as indicated in *Table 1*; r_i is the 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*.

Assay—

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile, water, and 1 M sulfuric acid (93 : 6.6 : 0.4). Make adjustments if necessary (see *System Suitability* under *Chromatography* (621)).

Standard preparation—Dissolve an accurately weighed quantity of USP Cetirizine Hydrochloride RS in *Mobile phase*, and dilute quantitatively, and stepwise if necessary, to obtain a solution having a known concentration of about 0.5 mg per mL.

Assay preparation—Transfer about 50 mg of Cetirizine Hydrochloride, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix.

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 1 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure*: the tailing factor for the cetirizine peak is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

Table 1

Compound Name	Approximate Relative		
	Retention Time	Relative Response Factor (<i>F</i>)	Limit (%)
4-CBH ¹	0.3	1.4	0.1
Dimer ²	0.5	1.8	0.1
2-Chlorocetirizine ³	0.85	0.49	0.1
Cetirizine related compound A ⁴	0.9	0.95	0.1
Cetirizine	1.0	—	—
Deschlorocetirizine ⁵	1.4	0.45	0.1
CBHP ⁶	1.45	1.6	0.1
Individual unknown	—	1.0	0.1
Total	—	—	0.3

¹ 4-Chlorobenzhydrol

² 1,4-Bis[(4-chlorophenyl)phenylmethyl]piperazine

³ (RS)-2-[2-[4-(2-Chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]acetic acid

⁴ (RS)-2-[2-[4-(4-Chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]acetic acid, ethyl ester (Cetirizine Ethyl Ester)

⁵ (RS)-2-[2-[4-(Diphenylmethyl)piperazin-1-yl]ethoxy]acetic acid

⁶ (RS)-1-[(4-Chlorophenyl)phenylmethyl]piperazine

Procedure—Separately inject equal volumes (about 10 μL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the cetirizine peaks. Calculate the quantity, in mg, of $\text{C}_{21}\text{H}_{25}\text{ClN}_2\text{O}_3 \cdot 2\text{HCl}$ in the portion of Cetirizine Hydrochloride taken by the formula:

$$100C(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Cetirizine Hydrochloride RS in the *Standard preparation*; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively. ■