

BRIEFING

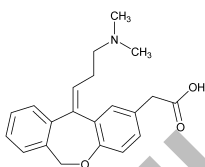
**Olopatadine Hydrochloride; Olopatadine Hydrochloride Ophthalmic Solution.** These monographs were posted on the USP Website as a draft USP Pending Standards for public comment. No comments were received. The MD-ODD Expert Committee reviewed the draft and approved the monograph as an Authorized USP Pending Standard. The liquid chromatographic procedures in the test for *Related compounds* and in the *Assay* are based on analyses performed with the Waters 5- $\mu$ m Symmetry C18 brand of L1 column. The typical retention times for olopatadine hydrochloride related compound A and olopatadine hydrochloride are about 5 minutes and 8 minutes, respectively.

(MD-ODD: F. Mao)    RTS—C50841

**Add the following:**

**■ Olopatadine Hydrochloride**

v. 1 Authorized September 20, 2007



$C_{21}H_{23}NO_3 \cdot HCl$     373.87

Dibenz[*b,e*]oxepin-2-acetic acid, 11-[3-(dimethylamino)propylidene]-6,11-dihydro-, hydrochloride, (*Z*)-.

11-[(*Z*)-3-(Dimethylamino)propylidene]-6,11-dihydrodibenz[*b,e*]oxepin-2-acetic acid, hydrochloride  
[140462-76-6].

» Olopatadine Hydrochloride contains not less than 98.0 percent and not more than 102.0 percent of  $C_{21}H_{23}NO_3 \cdot HCl$ , calculated on the dried basis.

**Packaging and storage**—Preserve in tight containers. Store at room temperature.

**USP Reference standards** <11>—*USP Olopatadine Hydrochloride RS. USP Olopatadine Hydrochloride Related Compound A RS.*

**Identification**—

**A:** *Infrared Absorption* <197K>.

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

**Loss on drying** <731>—Dry it at 105° for 3 hours: it loses not more than 1.0% of its weight.

**Residue on ignition** <281>: not more than 0.1%.

**Heavy metals, Method I** <231>: not more than 0.002%.

**Related compounds**—

*Mobile phase and Chromatographic system*—Proceed as directed in the *Assay*.

*Standard solution*—Dissolve accurately weighed quantities of USP Olopatadine Hydrochloride RS and USP Olopatadine Hydrochloride Related Compound A RS in methanol, with sonication if necessary, to obtain a solution having known concentrations of about 0.001 mg per mL and 0.005 mg per mL, respectively.

*Test solution*—Dissolve an accurately weighed quantity of Olopatadine Hydrochloride in methanol, with sonication if necessary, to obtain a solution having a known concentration of about 1.0 mg per mL.

## 2 / Olopatadine Hydrochloride

*Procedure*—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into a chromatograph, and allow the chromatogram to run for at least three times the retention time of the major peak. Record the chromatograms and measure the peak areas. Calculate the percentage of olopatadine hydrochloride related compound A in the portion of Olopatadine Hydrochloride taken by the formula:

$$100(C_s/C_v)(r_v/r_s)$$

in which  $C_s$  is the concentration, in mg per mL, of olopatadine hydrochloride related compound A in the *Standard solution*;  $C_v$  is the concentration, in mg per mL, of olopatadine hydrochloride in the *Test solution*; and  $r_v$  and  $r_s$  are the peak areas of olopatadine hydrochloride related compound A obtained from the *Test solution* and the *Standard solution*, respectively: not more than 0.5% of olopatadine hydrochloride related compound A is found. Calculate the percentage of any individual impurity in the portion of Olopatadine Hydrochloride taken by the formula:

$$100(C_s/C_v)(r_v/r_s)$$

in which  $C_s$  is the concentration, in mg per mL, of olopatadine hydrochloride in the *Standard solution*;  $C_v$  is the concentration, in mg per mL, of Olopatadine Hydrochloride in the *Test solution*;  $r_v$  is the peak area of any individual impurity obtained from the *Test solution*; and  $r_s$  is the peak area of olopatadine hydrochloride obtained from the *Standard solution*: not more than 0.10% of any individual impurity is found; and not more than 1.0% of total impurities is found.

[NOTE—USP Olopatadine Hydrochloride Related Compound A RS is the *E*-isomer of Olopatadine Hydrochloride. Its chemical name is 11-[(*E*)-3-(dimethylamino)propylidene]-6,11-dihydrodibenz[*b,e*]oxepin-2-acetic acid, hydrochloride.]

**Assay**—

*Phosphate buffer*—Prepare a 0.05 M solution of potassium phosphate monobasic in water.

*Mobile phase*—Prepare a mixture of *Phosphate buffer*, acetonitrile, and triethylamine (760: 240: 2). Adjust with 85% phosphoric acid to a pH of 4.5. Make adjustments if necessary (see *System Suitability* under *Chromatography* (621)).

*System suitability solution*—Dissolve accurately weighed quantities of USP Olopatadine Hydrochloride RS and USP Olopatadine Hydrochloride Related Compound A RS in methanol, with sonication if necessary, to obtain a solution having known concentrations of about 0.1 mg per mL and 0.01 mg per mL, respectively.

*Standard preparation*—Dissolve an accurately weighed quantity of USP Olopatadine Hydrochloride RS in methanol, with sonication if necessary, to obtain a solution having a known concentration of about 0.1 mg per mL.

*Assay preparation*—Dissolve an accurately weighed quantity of Olopatadine Hydrochloride in methanol, with sonication if necessary, to obtain a solution having a known concentration of about 0.1 mg per mL.

*Chromatographic system* (see *Chromatography* (621))—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm × 15-cm column that contains 5-µm packing L1. The flow rate is about 1 mL per minute. Chromatograph the *System suitability solution*, and record the peak areas as

directed for *Procedure*: the relative standard deviation for replicate injections is not more than 2.0%; the tailing factor of the olopatadine hydrochloride peak is not more than 2.0; the column efficiency, determined from the olopatadine hydrochloride peak, is not less than 1500 theoretical plates; and the resolution,  $R$ , between olopatadine hydrochloride and olopatadine hydrochloride related compound A is not less than 5.0. [NOTE—The relative retention time of olopatadine hydrochloride related compound A, measured with respect to olopatadine hydrochloride, is about 0.6.]

*Procedure*—Inject equal volumes (about 10  $\mu\text{L}$ ) of the *Standard preparation* and the *Assay preparation* into a chromatograph, record the chromatograms, and measure

the peak areas. Calculate the percentage of  $\text{C}_{21}\text{H}_{23}\text{NO}_3 \cdot \text{HCl}$  in the portion of Olopatadine Hydrochloride taken by the formula:

$$100(C_s/C_u)(r_u/r_s)$$

in which  $C_s$  is the concentration, in mg per mL, of olopatadine hydrochloride in the *Standard preparation*;  $C_u$  is the concentration, in mg per mL, of olopatadine hydrochloride in the *Assay preparation*; and  $r_u$  and  $r_s$  are the peak areas obtained from the *Assay preparation* and the *Standard preparation*, respectively. ■